Initial report on the findings of the NHS Greater Glasgow and Clyde: Queen Elizabeth University Hospital/Royal Hospital for Children water contamination incident and recommendations for NHS Scotland

Report prepared on behalf of HPS/HFS by:

Title: NHS GGC potential water contamination
Version: 1.0
Date: 31/05/2018
Status: Final (highlighted)
Contents

Executive summary.............................................................................................................. 3
Introduction........................................................................................................................ 3
Background........................................................................................................................ 4
  Organisms linked to cases of infection in this incident.................................................. 5
  The role of biofilm......................................................................................................... 5
Initial findings................................................................................................................... 5
Current management of situation .................................................................................... 7
  Point of use filters.......................................................................................................... 7
  Water treatment............................................................................................................ 7
Hypothesis......................................................................................................................... 8
Summary ............................................................................................................................ 9
Recommendations ............................................................................................................ 9
Appendix 1 - NHSScotland Incident and Outbreak Summary Ward 2a RHC (January 2016- April 2018).............................................................................................. 10
Appendix 2 - Timeline of cases ..................................................................................... 12
Appendix 3 - Cupriavidus, Stenotrophomonas, Pseudomonas ........................................ 14
References ....................................................................................................................... 18
Executive summary

NHS Greater Glasgow and Clyde (NHSGGC) are currently investigating a potentially contaminated water system across the Queen Elizabeth University Hospital (QEUH) and Royal Hospital for Children (RHC) with possible linked cases of bloodstream infections associated with ward 2A RHC.

Ward 2A RHC is a haemato-oncology unit, also known as Schiehallion, and houses the National Bone Marrow Transplant Unit. In 2016 a patient within ward 2A RHC was identified as having a blood stream infection (BSI) as a result of Cupriavidus pauculus. NHSGGC investigations included water samples from outlets within the aseptic suite of the pharmacy department where the parenteral nutrition was made that the child had received. Cupriavidus pauculus was isolated from water samples taken from a tap on a wash hand basin within this area. The wash hand basin was subsequently removed as a result. A further single case of Cupriavidus pauculus was identified in September 2017 however no environmental or water sampling was undertaken at this time.

Between the period of 29th January and 3rd April 2018 7 cases of blood stream infections (3 different organisms) with potential links to water contamination were identified. As a result widespread testing of the water supply was undertaken across both hospital sites. This testing identified widespread contamination of the water system. Control measures implemented included sanitisation of the water supply to ward 2A, the use of point of use filters in wash hand basins and showers in ward 2A and other areas where patients were considered high risk. There have been no new linked cases identified since the implementation of the control measures and whilst the investigation remains ongoing the clinical incident has been declared over with a full debrief held on 15th May 2018.

NHSGGC requested support from HPS with this incident on 16th March 2018 and Scottish Government invoked the national support framework on 20th March 2018 which requires HPS to lead an investigation and provide board support. This report is an initial summary of the findings from this investigation. A detailed technical report will be produced for NHSGGC by 31st July 2018.

Introduction

NHS Greater Glasgow and Clyde (NHSGGC) are currently investigating a potentially contaminated water system across the Queen Elizabeth University Hospital (QEUH) and Royal Hospital for Children (RHC) with possible linked cases of bloodstream infections associated with ward 2A RHC. NHSGGC requested support from HPS with this incident on 16th March 2018 and Scottish Government invoked the national support framework on 20th March 2018 which requires HPS to lead an investigation and provide board support. This report is an initial summary of the findings from this investigation. A detailed technical report will be produced for NHSGGC by 31st July 2018.
Background

NHS Greater Glasgow and Clyde's (NHSGGC) Queen Elizabeth University hospital (QEUH) is a 1109 bedded hospital with 100% en suite single side rooms which was handed over to the Board on 26th January 2015 with patient migration commencing from 24th April 2015 until 7th June 2015. The adjoining Royal Hospital for Children (RHC) is a 256 bedded childrens hospital which was handed over to the Board on 26th January 2015 with migration of patients occurring between 10th and 14th June 2015. The QEUH and RHC were both fully occupied from 15th June 2015. There are a number of additional healthcare facilities in the surrounding grounds including the maternity unit, neurosurgical unit, elderly care unit and the national spinal injuries unit.

Ward 2A RHC is a haemato- oncology unit, also known as Shiehallion, and houses the National Bone Marrow Transplant Unit. A patient in ward 2A was identified as having a bloodstream infection (BSI) as a result of *Cupriavidus pauculus*. NHSGGC investigations included water samples from outlets within the aseptic suite of the pharmacy department where the parenteral nutrition was made that the child had received. *Cupriavidus pauculus* was isolated from water samples taken from a tap on a wash hand basin within this area. The wash hand basin was subsequently removed as a result. A further single case of *Cupriavidus pauculus* was identified in September 2017 however no environmental or water sampling was undertaken at this time. Appendix 1 details all incidents reported to Health Protection Scotland under the Healthcare associated incident investigation tool related to ward 2A since 1st January 2016.

*Cupriavidus pauculus* was identified from a bloodstream infection (BSI) in a patient in ward 2A. A series of investigations were undertaken including water sampling from outlets within the ward area. *Pseudomonas* was identified from a BSI and between *Stenotrophomonas maltophilia* and *Pseudomonas* in Paediatric ICU. *Cupriavidus*, *Pseudomonas* and *Stenotrophomonas* (amongst other gram negative bacillus and fungi) were identified. This led to enhanced control measures being applied within ward 2A and an extensive investigation into the potentially contaminated water system across the QEUH and RHC. Testing of the organisms in this incident has not provided an exact link to the patient cases and the water system. Testing in an incident like this can be difficult and should only be used to include cases rather than exclude. To attain appropriate representation of the bacteria within the water would require significant sampling of each organism identified to ensure a representation of strains was identified. A timeline of the patients with infections included in this incident is detailed in Appendix 2. *Stenotrophomonas* bacteraemia presented on admission. Due to previous ward contact before implementation of control measures was included.

This report is an overview report of this investigation due to the large volume of data and complexities associated with this incident. A second more detailed and technical report is currently being produced which will cover more technical details and will be issued to Scottish Government and NHS GGC by end of July 2018. The longer timescale for this report is as a result of this incident being an ongoing live situation and covers information from the design and commissioning of the hospitals to the current position. HPS worked with
the support of Health Facilities Scotland (HFS) as the technical engineering experts to support this investigation and report production.

Organisms linked to cases of infection in this incident

Details on the 3 organisms (Cupriavidus, Stenotrophomonas and Pseudomonas) are covered in appendix 3.

The role of biofilm

Biofilm is a group of microorganisms in which the cells adhere to each other and often to a surface. These cells then become embedded within a slimy substance and can be prevalent in natural, industrial and hospital settings. There is a multitude of information in the published literature which directly links biofilm production/biofilm producing organisms to water source related outbreaks. In addition, 3 recent review articles focussed on the role of water in healthcare associated infections, with specific mention of biofilm formation as a key mechanism for sustained contamination of water systems. Biofilm formation has been described for Cupriavidus species and Pseudomonas spp, particularly in association with water systems. Biofilm formation with Stenotrophomonas on a variety of surfaces has also been demonstrated. As a specific example; an S maltophilia biofilm was found to be formed within a flexible tube running from a carbon filter to a chiller, which was connected to a tap in a kitchen sink, used to supply patients with drinking water.

Initial findings

HPS, HFS and NHS GGC initiated a detailed investigation into the contaminated water system within QEUH/RHC. This includes reviewing commission, installation and maintenance records provided by the contractor. TVCs are indicators that there are hygiene issues within the water system and are quantified as a generic indicator for microbial contamination. Specific microorganisms which can be tested for include: Coliforms, Escherichia coli (including O157), Pseudomonas aeruginosa, Salmonella spp, Campylobacter spp and Environmental Mycobacteria. Testing for these is not conducted as standard within current guidance and typically occurs in response to a suspected or confirmed outbreak, or due to identification of a series of sequential cases.
Commissioning and design of the hospital system

The taps in place across all clinical wash hand basins in the hospital are not compatible with silver hydrogen peroxide, a product used during commission stage to sanitise the water system in view of the high TVC results. It is unclear whether this has caused any degradation of the taps, however NHS GGC have sent taps removed from the installation for metallurgical testing. In addition a tap was deconstructed and examined for the presence of biofilm, in addition to microbiological sampling. The presence of high levels of gram negative bacteria and fungus in the water system suggests that temperature control required has not always been achieved. This will be reviewed as part of the wider review being undertaken. In line with the national guidance there is a water safety group (WSG), and local Sector/Hospital Water Safety Groups. The Board Water Safety Group is a sub group of the Board Infection Control Group. Water Safety is a standing agenda item for the infection Control Team Senior Managers Team meeting.

There is a flushing regime in place across both hospitals however it is unclear whether the flushing process is adequate and all outlets are being flushed, including little used outlets, water coolers, baths etc. Due to the size of the system this is extremely difficult to assess. The wider report will review this.
Current management of situation

Point of use filters

Point of use (POU) filters were installed as one of the main control measures initially in high risk areas (wash hand basins and showers) to ensure a safe water supply at the point of use. These filters have been installed across all areas within QEUH and RHC where there are likely to be immunocompromised patients or in identified clinically higher risk areas. POU filters require to be changed every 30 days and are a costly approach. However, in the interim until the water contamination can be addressed, is the only feasible approach to ensure safe delivery of water. A number of studies found that installation of point of use filters reduced either infection rates in associated healthcare settings\textsuperscript{9,10} or pathogen counts within tested water samples.\textsuperscript{11}

Water treatment

It is well recognised that drinking water distribution systems contain a diverse range of microorganisms.\textsuperscript{12-14} The presence of microorganisms is affected by various factors including; the disinfection processes employed, the location and age of the system as well as pipe material.\textsuperscript{16}

There are a number of options to be explored for longer term water treatment and NHS GGC are preparing a feasibility report on the most appropriate solution: these options include

**Chlorine dioxide**

A number of studies were identified which utilised chlorine dioxide systems within hospital settings, and use of these was found to reduce bacterial numbers.\textsuperscript{14,16,17}

Various advantages and limitations associated with use of chlorine dioxide are known, with the most relevant summarised below.\textsuperscript{16,19}

**Advantages:** Known to be effective against a wide range of bacteria, viruses and some protozoa including Giardia.

**Limitations:** Production of disinfection by-products (DBP’s). Although potential production of DBP’s always needs to be considered, the efficacy of water disinfection should not be compromised in trying to eliminate these.\textsuperscript{19}

**UV light**

A number of drinking-water treatment technologies are available which employ UV light radiation to inactivate microorganisms.\textsuperscript{16}

As with chlorine dioxide, various advantages and limitations associated with use UV are known, with the most relevant summarised below.\textsuperscript{16,20}

**Advantages:** Bacteria, fungi and protozoa (considered to be more effective at killing Cryptosporidium than chlorine dioxide) are readily inactivated at low UV doses, with higher doses required for virus inactivation. In addition, UV disinfection does not result in the formation of DBP’s like chlorine dioxide.
Limitations: UV disinfection does not leave any residual compound in treated water and therefore does not offer protection against possible microbial re-growth in distribution pipe-work.

Thermal disinfection

Very limited information was identified in the published literature in relation to advantages and limitations of thermal disinfection.

One study found that heat shock treatment at 80°C reduced Gram negative bacteria in a hospital water system but did not lead to complete eradication.21

A risk benefit analysis of each option will be undertaken as part of the wider report. An additional approach for sanitisation which will also be reviewed is copper silver ionisation.

Hypothesis

There are a number of workable hypotheses being explored; it is currently considered the most likely cause of the widespread contamination is a combination of hypothesis B and C.

A: Ingress contamination

A small low level number of micro-organisms may have been present in the water supply at the point of entry. Lack of temperature or chemical control may have enabled biofilm formation. Due to the increasing biofilm throughout the system this may have allowed any subsequent micro-organisms present at point of entry an opportunity to flourish and cause widespread contamination of the system.

B: Regressional contamination

This may have occurred due to contamination occurring at the taps/outlets or flow straighteners and contamination has regressed backwards throughout the system causing widespread contamination. The widespread positive results and array of bacteria point to contaminated outlets at installation or contamination of high risk components in the tap from ingress as opposed to the patient contact route.

C: Contamination at installation/commissioning

Contamination may have occurred due to presence of contaminated pipework or outlets. Prior to handover the system required to be sanitised due to high TVC counts. It is unclear if a robust flushing regime was in place from installation to handover and from handover to occupancy to prevent contamination.
Summary

There have been no new reported cases and the clinical aspect of this incident has been closed. This will be reopened if any new cases are identified. Control measures are in place to mitigate the risk however further work to address the widespread contamination is required. HPS will continue to liaise with HFS and NHSGGC and co-ordinate and produce a detailed technical report for NHSGGC and Scottish government which will include the review of installation, commission and maintenance and the risk/benefits of remedial approaches such as water dosing and tap replacement. This report will be prepared by July 2018.

Recommendations:

- Point of use filters will continue to be in place in ward 2A and other areas identified by the IMT until the risk to patients from the current situation of water contamination has been minimised.

- HPS will continue to liaise with HFS and NHSGGC and co-ordinate a wider technical report by 31st July 2018

- HPS via the existing Infection Control Built environment programme will, in conjunction with HFS:
  
  A. Prioritise water safety and undertake a review of NHS Scotland current approach to water safety
  
  B. Review existing national and international guidance relating to water safety and consider robust requirements for building handover requirements in relation to the water systems.
  
  C. Establish a risk based approach to water testing and any remedial action required, including roles and responsibilities.
Appendix 1 - NHSScotland Incident and Outbreak Summary RHC (January 2016- April 2018).

NHS Greater Glasgow and Clyde have reported a total of 10 outbreaks and incidents for the clinical setting paediatric haemato-oncology. Of the 10 incidents and outbreaks HIIAT assessed; 4 were Red, 2 were Amber and 4 were Green. The data is displayed in the tables below providing a breakdown of the outbreaks reported by annual period with exception of the current period to date for 2018 and HIIAT Green in 2016 following introduction of mandatory report (non Norovirus) from April. Comparative data for this setting within NHSScotland identified no reported incidents or outbreaks out with NHS Greater Glasgow and Clyde.

2018:

<table>
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<tbody>
<tr>
<td>01/03/2018</td>
<td>BSI</td>
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Table 2 NHS Greater Glasgow & Clyde, RHC haemato-oncology (___) HIIAT AMBER 2018 ± Total (1)

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### 2017:

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<td>BSI</td>
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<tr>
<td>03/03/2017</td>
<td>BSI</td>
</tr>
<tr>
<td>31/5/2017</td>
<td>GI</td>
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### 2016:

#### Table 5 NHS Greater Glasgow & Clyde, RHC haemato-oncology (ward) HIIAT GREEN 2016- Total (1)

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<td>GI</td>
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</table>

#### Table 6 NHS Greater Glasgow & Clyde, RHC haemato-oncology HIIAT AMBER 2016- Total (1)

<table>
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<th>Date reported to HPS</th>
<th>Infection Category</th>
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</thead>
<tbody>
<tr>
<td>05/08/2016</td>
<td>Respiratory</td>
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</tbody>
</table>
Appendix 2 Timeline of cases
Appendix 3 - Cupriavidus, Stenotrophomonas, Pseudomonas

Cupriavidus pauculus

1. Background

Cupriavidus species are Gram-negative, aerobic, non-spore-forming, motile bacilli.22 Various naming conventions have previously been associated with this organism (formerly known as Ralstonia paucula, Wautersia paucula and CDC group IVc-2)22-24

a. Reservoir/s
C. pauculus and other Cupriavidus species are considered to be environmental organisms,24,26 (although negative environmental screening when investigating incidents/outbreaks has occasionally been reported26,27). More specifically, water is known to be a potential source of infection, including drinking water.24,28-30

b. Mode/s of transmission
Very limited information on the mode of transmission of the organism is available. Contact with the environment has been proposed as the primary mode of transmission.25-27 Person-to-person spread has been considered, but has not been proven.31 In addition, other modes of transmission, including following a cat bite32 have also been reported.

c. Biofilm formation
Biofilm formation has been described for Cupriavidus species, particularly in association with water systems.26,30,33-35

2. Summary of published incidents/outbreaks

There are numerous case reports of infections caused by C. pauculus within the published literature. Many of these occurred in Europe.31,32,39-42 but to date, there have been no case reports of infection in Scotland, or the UK.

The majority of case reports identified one affected patient23,26,27,32,36-38,40-50 therefore it may be most appropriate to consider these as ‘incidents’ rather than true outbreaks.

A number of the reports23,31,38,43,44,47,49 considered infections to be nosocomial, although many of the patients had prolonged/intermittent hospital stays and it was therefore difficult to accurately establish healthcare versus community acquisition.

The majority of reports were associated with immunocompromised patients,27,31,38,39,41-43,48,50 or those with various co-morbidities, with or without known immunosupression.23,37,40,44,46,47

A significant number of reports were associated with neonates, or paediatric patients.23,25,31,39,44-46,48

Various types of infections were described, the majority of reports described bacteremia/septicaemia.23,26,37,41-46,47,49,50 Other presentations included pneumonia,30,38,46 meningitis,26 peritonitis,40 and osteomyelitis/septic arthritis.43 In addition, catheter associated infections were also reported.27,42 A number of patient deaths
occurred, \textsuperscript{37,44,46,48} but in most cases it was difficult to determine whether these were directly due to infection with the organism, or other factors associated with patient immunosuppression / chronic disease.

Water as a source\textsuperscript{23,27,28,43,44,47} was suspected in a number of reports, but no source was determined in the majority of cases.

In addition, two pseudo-outbreaks were reported, due likely environmental contamination by this organism of specimen swabs\textsuperscript{29} and blood culture bottles.\textsuperscript{28}

\textbf{Stenotrophomonas maltophilia}

1. Background

\textit{Stenotrophomonas maltophilia} is a non-lactose fermenting Gram-negative aerobic bacillus, previously known as \textit{Xanthomonas maltophilia} and \textit{Pseudomonas maltophilia}. The organism has been implicated in causing outbreaks since the 1970's.\textsuperscript{51}

a. Reservoirs

The organism is found in a variety of environments, including water, sewage and soil. Specifically within healthcare settings, \textit{S. maltophilia} has been isolated from various reservoirs including taps, humidifiers, nebulizers, and ventilation equipment.\textsuperscript{61} In addition, the organism has been isolated from bottled water.\textsuperscript{52}

b. Mode/s of transmission

Although numerous outbreaks associated with this organism have been reported, the source and mode of transmission it often difficult to establish. Typically, direct or indirect contact with a contaminated healthcare environment/equipment has been reported. Human carriage has also been noted in a number of studies, and therefore gives rise to the potential for person-to-person transmission.\textsuperscript{51}

c. Biofilm formation

Biofilm formation on a variety of surfaces has been demonstrated.\textsuperscript{5} As a specific example; an \textit{S maltophilia} biofilm was found to be formed within a flexible tube running from a carbon filter to a chiller, which was connected to a tap in a kitchen sink, used to supply patients with drinking water.\textsuperscript{63}

Under laboratory conditions, optimum temperature for growth is considered to be 37 UC, although environmental isolates tend to have a propensity for growth at lower temperatures (20-30 UC). The organism is also known to survive in temperatures as low as 4°C for significant periods of time. In addition, it has been indicated that biofilm formation is temperature dependent, with one study citing optimum biofilm formation at 32°C (in comparison to 18 and 37°C).\textsuperscript{55}

2. Summary of published incidents/outbreaks

There are numerous published case reports and outbreak studies describing nosocomial infection and/or colonisation. One of these referred to an outbreak which occurred in the UK.\textsuperscript{53}

The majority of studies were associated with immunocompromised patients,\textsuperscript{56-60} or those with various co-morbidities, with or without known immunosuppression.\textsuperscript{53,61-86}
25% (4 out of 16) of identified studies were associated with neonates, or paediatric patients.\textsuperscript{62,64,66,67} 

Various types of infections were described; predominantly bacteremia/septicaemia.\textsuperscript{56-61,64,66,67} Other presentations included endophthalmitis,\textsuperscript{68} as well as respiratory,\textsuperscript{53,62,65,69} soft tissue\textsuperscript{59} and catheter associated infections.\textsuperscript{59} In addition, a number of studies described cases of both colonisation and infection\textsuperscript{53,60,63,64} and one described colonisation alone.\textsuperscript{70} 

Various sources of infection were reported including taps/tap water\textsuperscript{53,58,64,70,71} and related environments (wash-hand basins\textsuperscript{62,65} and a shower outlet\textsuperscript{60}), medical solutions,\textsuperscript{55,58} and various medical equipment\textsuperscript{61,63,66,69,71-75} predominantly bronchoscopes (N.B all bronchoscope related outbreaks were found to be pseudo-outbreaks). 

Limited information was provided on the mode of transmission but most studies considered this to be contact with the healthcare environment, relating to the sources described above. Two outbreaks stipulated that person-to-person transmission from colonised healthcare workers may have occurred.\textsuperscript{66,67} 

In addition, a number of reports described co-infections; primarily with other Gram negative organisms.\textsuperscript{71-74} 

\textbf{Pseudomonas spp} 

Biofilm formation 

\textit{Pseudomonas spp} are known to form biofilms both within the environment and in patient infections (i.e. on implanted biomaterials).\textsuperscript{75} 

\textit{P. aeruginosa} is known to survive a range of temperatures; typically 4-42°C, with optimum growth occurring at 37°C.\textsuperscript{78} Biofilm formation has been shown to be temperature dependent, with one experimental study citing optimum biofilm formation at 37°C (in comparison to 28, 33 and 42°C).\textsuperscript{3} 

Further specific information in relation to biofilm formation associated with water sources can be found in ‘Are biofilms associated with water source related transmission with healthcare settings?’ below. 

\textbf{Summary of published incidents/outbreaks} 

A multitude of nosocomial \textit{Pseudomonas spp} outbreaks have been reported in the published literature. The summary below includes outbreaks occurring in the last 10 years only. 

Outbreaks were reported internationally, with four of these occurring in the UK.\textsuperscript{5,9,10} 

The majority of studies were associated with immunocompromised patients,\textsuperscript{58,77-89} or those with various co-morbidities, with or without known immunosuppression.\textsuperscript{4,8,10,90-118} 

9\% (7 out of 63) of identified studies were associated with neonates, or paediatric patients.\textsuperscript{77,79,96,101,106,110,114} A recent systematic review outlines risk factors and environmental sources associated with \textit{P. aeruginosa} outbreaks in neonatal intensive care settings.\textsuperscript{119}
Various types of infections were described; predominantly bacteraemia/septicaemia, endocarditis, as well as respiratory, and urinary tract infections. Other presentations included endophthalmitis, surgical site and urinary tract infections. In addition, a number of studies described cases of both colonisation and infection.

Various sources of infection were reported including bottled water, taps/tap water, as well as wider wash-hand basin environments including a soap dispenser. In addition, a further study demonstrated isolation of P. aeruginosa from various water fittings in intensive care rooms, in the absence of a recognised outbreak. Outbreaks have also been associated with various medical solutions and medical equipment, including various types of endoscopes, arthroscopic shavers, a urodynamic transducer and a transesophageal echocardiogram probe.

Limited information was provided on the mode of transmission but most studies considered this to be contact with the healthcare environment, relating to the sources described above. A number of outbreak reports stipulated that person-to-person transmission from colonised healthcare workers/patients may have occurred.

The majority of outbreaks were associated with P. aeruginosa but other species were also reported including P. putida, P. fulva and P. fluorescens.
References


(28) Weyant RS. Identification of unusual pathogenic gram-negative aerobic and facultatively anaerobic bacteria. Williams & Wilkins; 1996.


