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Laboratory surveillance of uncommon pathogens causing bacteraemia in England, Wales and Northern Ireland: 2018

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The analysis presented in this report is based on data extracted from the Public Heath England (PHE) voluntary surveillance database (Second Generation Surveillance System) on 6 September 2019 for the period between 1 January 2014 and 31 December 2018. Data from Wales and Northern Ireland were extracted separately from DataStore (on 23 July 2019) and CoSurv (on 18 June 2019), respectively. This report describes uncommon pathogens (bacterial genera with fewer than 50 reports in 2018) causing infections identified from blood cultures. Reports for England and Northern Ireland represent clinically significant isolates, whereas reports for Wales include isolates that may not be of clinical significance. Data in this report may differ slightly from data in earlier publications due to inclusion of late reports and reclassification of organisms.

There were 5,918 cases of bacteraemia caused by uncommon genera reported between 2014 and 2018. A total of 172 uncommon genera were identified, 54.1% of which were Gram-negative, representing 69% of the 249 genera associated with bacteraemia during this period [1].

Of the 1,299 episodes of bacteraemia caused by uncommon genera in 2018 specifically, 56.7% (n=737) were due to Gram-negative pathogens (see web appendix). By definition of inclusion in this analysis, small numbers of reports preclude robust or meaningful analysis of trends, but of note are continuing decreases between 2014 and 2018 in reports of the Gram-positive genera *Atopobium* and *Erysipelothrix* and the addition of *Abiotrophia, Lactococcus* and *Leuconostoc* whose numbers fell below 50 reports in 2018. Decreases in reported cases were also seen in the Gram-negative genera *Eikenella*, *Ochrobactrum,* and *Sphingobacterium* together with the addition of *Agrobacterium, Burkholderia* and *Hafnia*, in 2018 compared to 2017. In contrast, an increase was noted for the following Gram-positive genera: *Actinotignum, Arcanobacterium, Dolosigranulum, Facklamia, Globicatella,* and the following Gram-negatives: *Aggregatibacter, Anaerobiospirillum* and *Legionella* species, in 2018 compared to 2017.

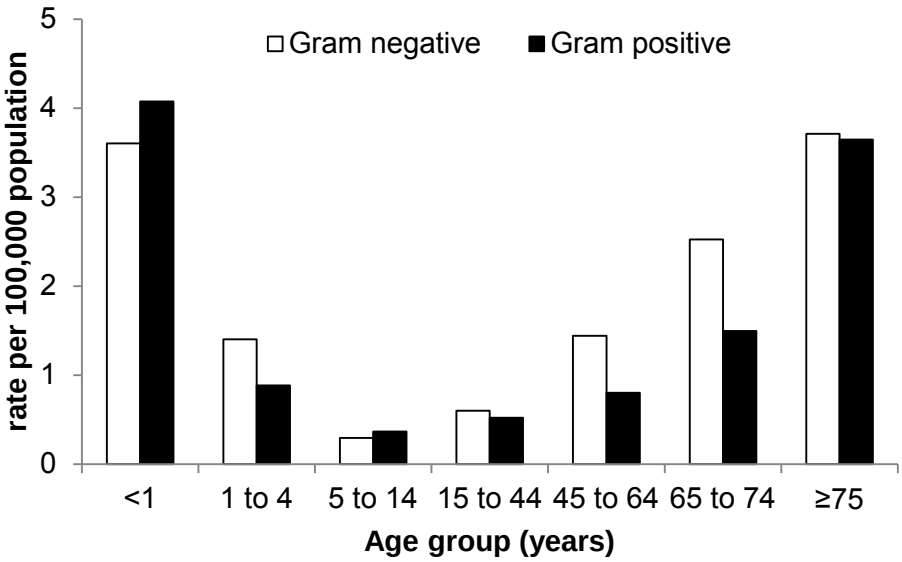
A number of genera were reported in 2018 that were not seen in the previous four years including the Gram-positive genera *Bhargavaea, Carnobacterium, Catabacter, Coprobacillus, Kurthia,*

Lachnoanaerobaculum, Olsenella, Pseudarthrobacter, Robinsoniella, Thermoanaerobacterium, and the Gram-negative genera*, Francisella, Gabonibacter, Mannheimia, Pluralibacter* and *Variovorax*.

Age distribution

The highest rates of bacteraemia due to these uncommon pathogens in England were observed in infants aged under one year, 4.1 and 3.6 Gram-positive and Gram-negative per 100,000 population respectively, and those aged 75 years and older (3.7 for Gram-positive and Gram-negatives).

Figure 1. Age-specific rates of uncommon pathogens associated with bacteraemia (England only): 2018



Antimicrobial resistance

Antimicrobial resistance was explored for genera with >30 episodes in 2018 (England data only), however relatively little data on antimicroibial suseptibility testing was available for several of these genera. Of the Gram-positive genera, penicillin susceptibility was reported for >50% of *Abiotrophia, Arcanobacterium* and *Lactococcus* episodes, with 24%, 5% and 8% resistant respectively. Equivalent analysis for Gram-negative genera identified third-generation cephalosporins resistance in 65% of *Brevundimonas*, aminoglycoside resistance in 11% and quinolones resistance in 62% of episodes. For *Burkholderia,* 36% were reported as resistant to

third-generation cephalosporins, 48% to carbapenems and 68% to aminoglycosides and for *Hafnia* 27% were resistant to third-generation cephalosporins, and 93% resistant to ampicillin/amoxicillin.

Discussion

This report describes the frequency of bacteraemia caused by bacterial genera many of which are not routinely included in PHE Health Protection Reports (with the exception of *Brucella* bacteraemia). Monitoring trends in these uncommon pathogens allows emerging or re-emerging infections to be identified [2], providing an alert to facilitate preventative measures or education of frontline clinical staff.

There has been a general improvement in the identification of cultured organisms through increased use of automated biochemical identification systems, molecular techniques such as 16S ribosomal RNA, and the introduction of MALDI-TOF mass spectrometry in some laboratories. This has increased the accuracy of species identification, and improved our understanding of the relative importance of these hitherto difficult to identify species in causing disease. It should be noted that isolates identified by MALDI-TOF reflect organisms that are present in its reference database and therefore identification is expected to improve with expansion of the database. Where new species have been added or reference entries amended in the database, these may appear as new organisms due to increased ascertainment rather than being novel or emerging bacteria causing disease e.g. *Bhargavaea, Kurthia Robinsoniella peoriensis, Weissella confuse, Alistipes putredinis* (new genus/species)*, Carnobacterium maltaromaticum, Thermoanaerobacterium thermosaccharolyticum, Flavobacterium lindanitolerans, Pluralibacter* (further reference entry). In addition, there are concerns that MALDI-TOF could not be used for accurate speciation of *Elizabethkingia* [3] until the recent addition of *Elizabethkingia anopheles* to the database in 2019.

Although uncommon bacteria only account for a very low proportion of total bloodstream infections, they can be associated with important clinical consequences, such as endocarditis [4]. Amongst other causes, endocarditis may arise through bacteraemia following occupational exposure to farm livestock (e.g. *Brucella* and *Erysipelothrix*) or from heart surgery (*Nocardia*). A *Facklamia hominis* bacteraemia has also been associated with infectious endocarditis [5], as have bacteraemia caused by organisms normally found in the oral cavity such as *Aggregatibacter actinomycetemcomitans* [6]. Please note that the *Brucella* spp. reported here are not all necessarily confirmed by the national reference laboratory. (For brucellosis, please refer to the common animal associated infections quarterly reports for England and Wales in 2018 based on

culture positive results confirmed at the OIE/FAO Reference Laboratory for brucellosis at the Animal and Plant Health Agency (APHA) [7].)

Although Burkholderia are an important cause of infections in patients with cyctic fibrosis, these infections are predominantly isolated from sputum rather than blood [8]. However, *Burkholderia* bacteraemia, including *Burkholderia cepacian,* can cause healthcare associated infections in non-cystic fibrosis patients and outbreaks due to *Burkholderia* species have been reported in Intensive Care Units [8,9]. These infections are complicated by intrinsic resistance to key antibiotics via a number of mechanisms [10,11], and in this dataset, where more than 50% of isolates have been tested, resistance to cephalosporins, carbapenems and aminoglycosides was noted. Antimicrobial resistance to penicillin was noted for *Abiotrophia* (24%), simillar to published findings [12].

Three of the *Burkholderia* bacteraemia reports in 2018 were *Burkholderia pseudomallei,* an imported pathogen which is the causative agent of meliodosis. *Burkholderia pseudomallei* is found mainly in Southeast Asia and Northern Australia and is acquired by exposure to contaminated soil or water droplets via wounded skin or inhalation [13]. Another imported pathogen is *Francisella tularensis*, the causative agent for the zoonotic disease tularemia, which is distributed throughout the northern hemisphere including Europe but is not found in the UK [14,15]. *Francisella tularensis* is mainly transmitted through contact with infected animals or via bites from infected insects and ticks [16].

Bacteraemia caused by *Gordonia* spp. and *Anaerobiospirillum succiniciproducens* have been noted in immunocompromised patients [17,18], whilst other uncommon genera causing bacteraemia have been associated with the use of catheters in patients with underlying morbidity eg *Delftia acidovorans* [19], *Dermacoccus* [20], and *Gordonia sputi* [21]. *Actinotignum* bacteraemia have been found to affect elderly patients with underlying conditions, a majority having the urinary tract as a focus of the bacteraemia [22]. *Globicatella sanguinis* bacteraemia have been identified predominantly in older females [23] whereas *Kingella kingae* bacteraemia has been reported more frequently in children than in adults [24].

Gardnerella vaginalis is found in the genitourinary tract of women and bacteraemia has been associated with gynaecology, obstetric, and neonatal patients, and very rarely adult male patients [25-28].

For all the uncommon zoonotic pathogens, please also refer to the common animal associated infections quarterly reports (England and Wales) that can be found on the PHE gov.uk website.

Please note the numbers may differ slightly between these two reports as the common animal associated infections quarterly reports for England and Wales use data that are not limited to blood samples only.

Although bloodstream infections reported to the voluntary surveillance system for England and Northern Ireland should reflect only clinically significant disease, difficulties in blood culture sampling or contamination in laboratory processing may lead to inclusion of skin colonisers or contaminants [29].

If confirmation of unusual bacterial pathogens is required, isolates can be sent to the relevant laboratory within the Bacteriology Reference Department, National Infection Service, Colindale, Public Health England.

For confirmation of *Brucella* spp., isolates can be sent to the OIE/FAO Reference Laboratory for Brucellosis at APHA for culture confirmation and to the Brucella Reference Unit (BRU) in Liverpool for serology testing and molecular diagnostic service.

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References

1. PHE (2019). Polymicrobial bacteraemia and fungaemia in England, Wales and Norther Ireland, 2018. *Health Protection Report* **13** (33).

2. Al Akhrass F, Al Wohoush I, Chaftari AM, Reitzel R, Jiang Y, Ghannoum M, et al (2012). *Rhodococcus* bacteremia in cancer patients is mostly catheter related and associated with biofilm formation. PLoS ONE. **7**(3): e32945.

3. Kenna DTD, Fuller A, Martin K, Perry C, Pike R, Burns PJ, et al (2017). rpoB gene sequencing highlights the prevalence of an *E. miricola* cluster over other *Elizabethkingia* species among UK cystic fibrosis patients. *Diagn Microbiol Infect Dis*.

4. Brouqui P, Raoult D (2001). Endocarditis due to rare and fastidious bacteria. *Clin Microbiol Rev* **14**(1):177-207.

5. Ananthakrishna R, Shankarappa RK, Jagadeesan N, Math RS, Karur S, Nanjappa MC (2012). Infective endocarditis: a rare organism in an uncommon setting. *Case Rep Infect Dis* 2012: 307852.

6. Bale BF, Doneen AL, Vigerust DJ (2017). High-risk periodontal pathogens contribute to the pathogenesis of atherosclerosis. *Postgrad Med J* **93**(1098): 215-20.

7. PHE (2019). Common animal-associated infections quarterly reports (England and Wales): 2018.

8. Kenna DTD, Lilley D, Coward A, Martin K, Perry C, Pike R, et al (2017). Prevalence of *Burkholderia* species, including members of *Burkholderia cepacia* complex, among UK cystic and non-cystic fibrosis patients. *J Med Microbiol* **66**(4): 490-501.

9. Abdallah M, Abdallah HA, Memish ZA (2018). *Burkholderia cepacia* complex outbreaks among non-cystic fibrosis patients in the intensive care units: A review of adult and pediatric literature. *Infez Med* **26**(4): 299-307.

10. Chien YC, Liao CH, Sheng WH, Chien JY, Huang YT, Yu CJ, et al (2018). Clinical characteristics of bacteraemia caused by *Burkholderia cepacia* complex species and antimicrobial susceptibility of the isolates in a medical centre in Taiwan.
Int J Antimicrob Agents **51**(3): 357-64.

11. Rhodes KA, Schweizer HP (2016). Antibiotic resistance in *Burkholderia* species. *Drug Resist Updat* **28**: 82-90.

12. Alberti MO, Hindler JA, Humphries RM (2015). Antimicrobial susceptibilities of *Abiotrophia defectiva*, *Granulicatella adiacens*, and *Granulicatella elegans*. *Antimicrob Agents Chemother* **60**(3): 1411-20.

13. Le Tohic S, Montana M, Koch L, Curti C, Vanelle P (2019). A review of melioidosis cases imported into Europe. *Eur J Clin Microbiol Infect Dis* **38**(8): 1395-408.

14. Ellis J, Oyston PC, Green M, Titball RW (2002). Tularemia. *Clin Microbiol Rev* **15**(4): 631-46.

15. Hestvik G, Warns-Petit E, Smith LA, Fox NJ, Uhlhorn H, Artois M, et al (2015). The status of tularemia in Europe in a one-health context: a review. *Epidemiol Infect* **143**(10): 2137-60.

16. Zellner B, Huntley JF (2019). Ticks and Tularemia: Do We Know What We Don't Know? *Front Cell Infect Microbiol* **9**: 146.

17. Epstein DJ, Ernst K, Rogers R, Carmody E, Aguero-Rosenfeld M (2017). The Brief Case: *Anaerobiospirillum succiniciproducens b*acteremia and pyomyositis. *J Clin Microbiol* **55**(3): 665-9.

18. Ding X, Yu Y, Chen M, Wang C, Kang Y, Li H, et al (2017). Bacteremia due to *Gordonia polyisoprenivorans*: case report and review of literature. *BMC Infect Dis* **17**(1): 419.

19. Chotikanatis K, Backer M, Rosas-Garcia G, Hammerschlag MR (2011). Recurrent intravascular-catheter-related bacteremia caused by *Delftia acidovorans* in a hemodialysis patient. *J Clin Microbiol* **49**(9): 3418-21.

20. Takahashi N, Shinjoh M, Tomita H, Fujino A, Sugita K, Katohno Y, et al (2015). Catheter-related blood stream infection caused by *Dermacoccus barathri*, representing the first case of *Dermacoccus* infection in humans. *J Infect Chemother* **21**(8): 613-6.

21. Negishi T, Matsumoto T, Saito S, Kasuga E, Horiuchi K, Natori T, et al (2016). Catheter-Related bacteremia due to *Gordonia sputi* in a patient with acute lymphocytic leukemia: a case report. *Jpn J Infect Dis* **69**(4): 342-3.

22. Pedersen H, Senneby E, Rasmussen M (2017). Clinical and microbiological features of *Actinotignum bacteremia*: a retrospective observational study of 57 cases. *Eur J Clin Microbiol Infect Dis* **36**(5): 791-6.

23. Miller AO, Buckwalter SP, Henry MW, Wu F, Maloney KF, Abraham BK, et al (2017). *Globicatella sanguinis* osteomyelitis and bacteremia: review of an emerging human pathogen with an expanding spectrum of disease. *Open Forum Infect Dis* **4**(1): ofw277.

24. Yagupsky P (2015). *Kingella kingae*: carriage, transmission, and disease (2015). *Clin Microbiol Rev* **28**(1): 54-79.

25. Tankovic J, Timinskas A, Janulaitiene M, Zilnyte M, Baudel JL, Maury E, et al (2017). *Gardnerella vaginalis* bacteremia associated with severe acute encephalopathy in a young female patient. *Anaerobe* 47: 132-4.

26. Johnson AP, Boustouller YL (1987). Extra-vaginal infection caused by *Gardnerella vaginalis*. *Epidemiol Infect* **98**(2): 131-7.

27. Amaya RA, Al-Dossary F, Demmler GJ (2002). *Gardnerella vaginalis* bacteremia in a premature neonate. *J Perinatol* **22**(7): 585-7.

28. Babics A, Roussellier P (2015). *Gardnerella vaginalis*: an overlooked pathogen in male patients? *Med Mal Infect* **45**(10): 423-4.

29. Melish M, Campbell KA (1998). Coagulase-positive staphylococcal infections. In: Feigin RD, Cherry JD (editors). *Textbook of Paediatric Infectious Diseases* 1998: 1039-65.

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Health Protection Report is a national public health bulletin for England and Wales, published by Public Health England. It is PHE's principal channel for the dissemination of laboratory data relating to pathogens and infections/communicable diseases of public health significance and of reports on outbreaks, incidents and ongoing investigations.

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