Bundle of documents for Oral hearings commencing from 19 August 2024 in relation to the Queen Elizabeth University Hospital and the Royal Hospital for Children, Glasgow

Bundle 21 – Volume 8

Substantive Core Participants responses to Cryptococcus Expert Report by Allan Bennett

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SCOTTISH HOSPITALS INQUIRY

REVIEW BY NHSGGC

OF

REPORT OF ALLAN BENNETT

REVIEW OF CRYPTOCOCCUS CASE INVESTIGATIONS AT QEUH/RHC

DATED 21 AUGUST 2024

1. INTRODUCTION

1.1. A report by Allan Bennett entitled *"Review of Cryptococcus Case Investigations at QEUH/RHC*" dated 21 August 2024 (the "**Report**") has been disclosed to Inquiry core participants.

1.2. This document contains NHSGGC's response to the Report. With reference to Scottish Hospitals Inquiry Direction 5, Appendix B at para 2.1, specific questions to be asked of the Report's author, and specific comments on the substance of the Report, are set out below. NHSGGC's questions and comments raise new matters or issues insofar as they relate to matters either not covered or not fully addressed in the report.

1.3. NHSGGC has provided general comments on the content of the Report, followed by more detailed comments on particular paragraphs. NHSGGC's review has been undertaken by, amongst others, those within NHSGGC who have expertise in infection prevention and control.

2. GENERAL COMMENTS

2.1. The author was asked to consider:

(i) Risk assessment and infection link – to identify whether there is an association between the QEUH/RHC and the cases of *Cryptococcus neoformans;*
(ii) Whether these cases were remarkable
(iii) Whether the methodology used by the subgroup to investigate the cases was adequate and should subsequent cases be included?

2.2. The author concludes that the instances of *CN* were between 5.4 and 7.2 times higher at the QEUH/RHC than would be expected. However, he suggests that there could be many explanations for this, of which the built environment could have been one. Alternative

explanations include (i) randomness; (ii) the QEUH/RHC being more likely to send samples to the reference laboratory; (iii) the QEUH/RHC patient groups being more susceptible to CN infection; and (iv) other NHS areas being more likely to do in house culture for CN. NHSGGC agrees that there could be many explanations. However, NHSGGC submits that the denominator used by Mr Bennett in order to calculate the rates of infection is incorrect. The RHC is a tertiary referral centre, so it is not appropriate to use the population of Greater Glasgow of 1.3million as the denominator to calculate the rate. The RHC takes cases from all over Scotland. As noted by the author, infections with *CN* are mainly in immunocompromised patients, who are particularly susceptible and vulnerable to infection. Wards 2A and B are a tertiary centre for immunocompromised patients, with a cohort from across Scotland. Given that the RHC treats such patients, and that such patients come from across Scotland, the author's assessment of *CN* being between 5.4 and 7.2 times more likely at the QEUH/RHC is unsafe

2.3. The author notes that he has not carried out any statistical analysis so cannot give any assessment of probabilities. However, he concludes that the number of cases reported in QEUH/RHC during 2018 was remarkable and definitely warranted further investigation. The Report acknowledges that people can develop an infection many years after exposure, which is usually a form of reactivation when the person develops a weakened immune system. This makes it very difficult to investigate sources of infection and to make any link between the hospital environment and the infections. Since exposure to *Cryptococc*us is common in the community, statistics should be applied to determine the probability of acquisition of infection in the months and years the individuals might have spent outside the hospital setting as opposed to a few days in the hospital.

2.4. The author comments that, had the patients been housed in HEPA filtered positive pressure rooms, the connection between the hospital environment and the patient could have been investigated and ruled out by demonstrating that the patient rooms conformed to best practise and guidance through validation. The author does not fully explain the basis for this assertion. Instead, the assertion is made in the abstract. In any event, NHSGGC's comments on HEPA filtration are contained in its response to Mr Bennett's initial report. NHSGGC invites the Inquiry to have regard to those comments in evaluating Mr Bennet's conclusion.

2.5. The author notes that the connection between the QEUH/RHC environment and the cases of *CN* is unlikely to be proved or disproved at this distance of time. However, NHSGGC submits that the extensive investigations undertaken at the time ought to be given weight in assessing any link between *CN* and the built environment. NHSGGC established the IMT sub-group to review and advise on all potential sources including

instructing a review of the full ventilation system. Extensive air sampling was undertaken. *CN* was not identified in any of the over 3,000 samples taken. *Cryptococcus diffluens* was identified in samples but is prevalent in the community which would explain its identification in samples.

3. ANALYSIS OF HYPOTHESES

3.1. The Report reviews the individual hypotheses in the IMT sub-group's report and largely agrees with the conclusions in respect of hypotheses 2, 3, 4, 6 and 7. The exceptions are Hypothesis 1 – Plant Room Air and Hypothesis 5 – Helipad.

Hypothesis 1: Plant Room Air

3.2. The view of the NHSGGC Sub-Group was that this hypothesis was **UNFEASIBLE** due to the lack of route for plant room air to reach a patient room. Mr Bennett concludes that this hypothesis is **POSSIBLE.**

3.3. At the Sub-Group meeting on 6 June 2019, Dr Hood, who chaired the meeting, hypothesised that air entering the AHUs within the plant rooms on Level 12 was not likely to be the source of the *CN* infection. Mr Bennett disagrees with this conclusion. In paragraph 8.15, Mr Bennett makes reference to a one inch hole in the AHU and the reader may be of the impression that this hole is a direct route from the plant room into the internal chambers of the AHU and, as a result, would provide a route for potentially contaminated air within the plant room to be drawn into the ventilation system and dispersed in the patient areas. The one-inch hole is by design and its purpose is to allow a mechanically driven spindle to be operated either manually and/or by a motorised valve to drive the damper mechanism to a closed or opened position. It is an essential component of the system and does not provide a route onto the airflow as suggested by the author.

3.4. It is not clear if the author has visited the plant room or indeed seen images of the "one inch hole" he references and therefore NHSGGC has provided images of an example of an AHU within plantroom 123. Mr Hugh Brown, Lead Ventilation AP on the QEUH site, arranged for images to be captured on 10 Sept 2024 to confirm that the external hole on the AHU is sealed internally within a designed chamber. Image 1 shows the spindle external to the unit and image 2 shows the AHU internally where the spindle is connected to the damper mechanism. It is sealed in relation to the outside of the unit.

Image 1: External view of actuator drive showing one inch hole for mechanism	**Image 2: Internal view of actuator drive**
	

3.5. The author suggests that smoke tests ought to be undertaken to establish whether air from the plantroom was present in patient areas. Such tests were undertaken by NHSGGC. As noted in the Sub-Group minutes of 22 February 2019 (bundle 9 page 13), Mr Steele advised that the action taken was to smoke test and to verify there was no infiltration. The minute notes that:

> Discussion took place around the 'plant room' as the possible source. Peter Hoffman commented that the plant room could be the source if the spores are getting into the air handling unit after the final filter or bypassing filtration via gaps between or around the filters. It had previously been confirmed that the relative positions of the fan and final filter preclude ingress after the final filter, so air bypassing filtration remains a possibility. This is in addition to ingress of unfiltered air into rooms not under positive pressure (see JH statement below). Tom Steele advised that the first action taken was to smoke test and to verify that there was no infiltration. Peter Hoffman stated that it is difficult to look under the air handling units. Eddie McLaughlan advised that we know there is a one inch hole on the AHU intake damper actuator spigot on the suction side of the fan (before the primary [F4] and secondary [F7] filters and if the AHUs are not sealed then the plant room could be the source, if the bird droppings have been disturbed.

3.6. In paragraph 8.16, the author makes a further suggestion that there exists a possibility to remove panels in the AHU in times of extreme low temperatures to prevent the unit closing down. There is no evidence to suggest this is or was a practice undertaken by staff at QEUH/RHC. A review of the Building Management System for November and December 2018 confirms that during that timeframe there were no occasions when the air intake dampers were closed due to external air temperatures being too cold. Indeed, a review of

temperatures in Glasgow from November 2018 until 31 December 2018 illustrates there were no occasions where extreme low temperatures were reached. Furthermore, the Sub-Group 22 February meeting was advised by estates staff at the that "*the units had not been opened since last September*" suggesting that no maintenance activity took place which would involve a planned opening of access panels in the unit (bundle 9 page 12).

3.7. NHSGGC therefore maintains that this hypothesis is unfeasible and, in light of the above information, asks that the author review his assessment of hypothesis 1.

Hypothesis 5: Helipad

3.8. The view of NHSGGC Sub-Group was that this hypothesis was **REJECTED**. Mr Bennett concludes that this hypothesis is **POSSIBLE.**

3.9. Mr Bennett criticises the computer fluid dynamic study due to limited modelling at lower air speeds. However, NHSGGC does not consider that this is a valid criticism. The sub-group report used variations of wind speeds based on weather data which is sufficiently reliable to reject the hypothesis.

3.10. In any event, NHSGGC undertook extensive testing in relation to this hypothesis.

The report concluded as follows:
The CFD simulations undertaken demonstrate that the air arriving at the AHU intake locations does not originate in the region beneath the helipad for any of the scenarios considered. It is therefore, unlikely that debris from the helipad area is being carried into the hospital ventilation system so anything drawn into the AHU will come from the wider environment. Whilst it is not possible to determine how far away potential contamination will originate, it should be noted that anything carried in the flow will be lightweight, since heavier matter will fall out due to gravity.
Additionally, the simulations show that with the maximum wind from the prevailing direction (south-west) and when there is no helicopter in the area, the air speed around the front entrance of the main hospital should be under 6 m/s, which would not be excessive for pedestrian comfort for walking or standing. However, when a helicopter is approaching, gusts of over 20 m/s may be experienced in the area.

With wind from the second most frequent direction (east-north-east) at the maximum average wind speed of 18.7 m/s, wind speeds over 10 m/s are present around the front entrance, which is above the Lawson's comfort criterion for any activity. However, this is a higher wind speed than the average recorded for this direction.

At the more likely speed of 5.5 m/s, the wind in the area is more acceptable, below 7 m/s. This would be uncomfortable for sitting or standing but acceptable for walking. However, at the maximum wind speed form this direction (9 m/s) the wind speed in the area would be higher and likely to be above the Lawson comfort criteria of 10 m/s It is understood that remedial work is being undertaken to add canopies in the area to protect against falling debris, but these have not been included in the model. Further work would be required to evaluate how these will influence the flow in the area.

4. EXPERTISE OF THE AUTHOR

4.1. It is essential to appreciate that no hospital can be a fully sterile environment. Pathogens can enter the environment from a range of sources. Accordingly, it is necessary to consider all steps taken to mitigate against risk of infection, not just ventilation in isolation.

4.2. NHSGGC note that Mr Bennett acknowledges that he has no clinical expertise and no experience of day-to-day working in a hospital environment. Whilst the Report is of assistance to the Inquiry this limitation must be recognised. Steps taken to manage risk within the QEUH include but are not limited to: use of single en-suite rooms, prophylaxis, PPE, air filtration, air pressure differential, limiting access to patients, staff vaccination, cleaning regime, screening, testing and monitoring. Infection control is multifactorial. The combined impact of these features in a hospital environment, particularly one used to treat neutropenic patients, must be understood.

4.3. NHSGGC notes that Mr Bennett recognises that he cannot comment on the approach to managing pigeons and the prevalence of pigeons in hospitals sites.

5. DETAILED COMMENTS

5.1. Additional comments on certain paragraphs of the Report are provided below:

Report Reference	**Comments**
5.7	The data cited have been obtained from UKHSA Mycology Reference Laboratory in Bristol but some laboratories may be sending their isolates to the Mycology Reference Centre located in Manchester. These numbers may have been missed when estimating the baseline rate of infection and so the Report utilises data that are an underestimate.

5.8	It would be unlikely for laboratories to refer multiple isolates from the same patient to the reference laboratories. Also, some laboratories may be sending isolates to Mycology Reference Centre in Manchester and these numbers would need to be taken into account when estimating baseline rates of infection. The Report utilises data that are an underestimate.
5.12 – 5.14	The Report estimates the theoretical incidence in the UK compared with NHSGGC and gives potential reasons why NHSGGC exceeds the expected annual case numbers. It is essential to recognise that the RHC is a tertiary referral centre so it is not appropriate to use the population of Greater Glasgow of 1.3m as the denominator to calculate the rate as the hospital takes cases from all over Scotland. The report suggests that the expected number of cases in NHS GGC would be 1.94 per annum. When analysing small numbers, it is very difficult to comment on any uptick. The percentage rise in number of cases would be magnified if the estimated baseline is low. Statistically, there will be standard deviation to take into account. NHSGGC agrees that there may be multiple explanations for detection. It cannot therefore be said with any degree of certainty that there is something linked to the QEUH/RHC, such as the built environment, that caused a higher rate than other healthcare areas.
8.3	The minimum incubation period of 7 days is at the very low end when the report itself cites that the incubation period is weeks to months. Relapse of a latent infection may happen after years of acquiring infection.
8.6 - 8.9	*Cryptococcus diffluens* was isolated on a number of plates. It is expected that at least one colony of *CN* would have grown on at least one of the 13 plates that were not overgrown with other organisms. This was not the case. Indeed, *CN* was never detected in any of the over 3,000 samples taken. This is significant. *C. diffluens* is ubiquitous in the environment and its isolation from plant room and ward areas might reflect its wide ecological presence.

8.19	It is not clear how a possible mode of acquisition is more likely to be a probable mode of acquisition merely based on the 200 times likelihood of potential exposure. The numerical likelihood is not a correlate of the statistical probability unless a certain baseline value has been found to be associated with an outcome.

6. CONCLUSIONS

6.1. NHSGGC established an IMT sub-group to investigate cases of C*N* and the hypotheses relating to the incidences of *CN*. The Report largely agrees with the sub-group's assessment. In respect of hypotheses 1 and 5, NHSGGC invites the author to have regard to the additional information presented in this response and asks that he reevaluate his conclusions.

6.2. NHSGGC submits that it is not possible to link exposure to *CN* with the built environment. As noted, there are a number of factors which may explain the instances of *CN* that are entirely unrelated to the built environment. Exposure in the community is likely and, due to the lengthy incubation period, exposure cannot be definitively linked to the hospital.

6.3. In any event, the denominator used by the author to conclude that QEUH/RHC had a higher incidence of infection is incorrect as it fails to recognise that the QEUH/RHC is a tertiary centre with patients from across Scotland, not just the Greater Glasgow area.

Andrew McWhirter, Advocate
17 September 2024

SCOTTISH HOSPITALS INQUIRY

RESPONSE

TO THE

"REVIEW OF CRYPTOCOCCUS CASE INVESTIGATIONS AT QEUH/RHC"

PREPARED BY ALLAN BENNETT

DATED 21 AUGUST 2024

SUBMITTED ON BEHALF OF DR CHRISTINE PETERS

A. INTRODUCTION

1. This response to the expert report titled "Review of Cryptococcus Case Investigations at QEUH/RHC" prepared by Allan Bennett and dated 21 August 2024 (the "Cryptococcus Report") is submitted on behalf of Dr Christine Peters.

2. Overall Dr Peters welcomes the report with regard to the hypothesis that Cryptococcal aerosol transmission to inpatients can be plausibly linked to the excessive pigeon guano contamination of the QEUH premises with clear routes of ingress from the ventilation plant room and helipad. Mr Bennett's expertise in relation to the movement of infectious aerosols and air movements is invaluable in assessing these routes.

3. However, Dr Peters submits that a comprehensive approach to the analysis of the environmental sources, routes of ingress and a link to the specific cases observed requires a clinical epidemiological approach. Such a report requires to be prepared by a person with an expertise in the epidemiology of infectious diseases such as Sid Mookerjee and in outbreak investigation with diagnostic clinical expertise such as Dr Mumford.

B. RESPONSE

4. In Dr Peters' opinion Mr Bennett misunderstands the diagnostic process in paragraph 5.3. It important to understand that a CRAG positive is adequate evidence of the organism even without culture positivity (*see* Reference 1: "*Cryptococcal antigen in cerebrospinal fluid or blood confirms cryptococcosis*" and "*we also recognize cryptococcal infection among individuals in high-risk host groups who have few, if any, symptoms and only a positive serum cryptococcal antigen test (asymptomatic cryptococcal antigenemia). This condition may be*

more common than symptomatic disease, and patients may develop clinical cryptococcal disease unless treated and so are now included in these definitions"). Lack of culture positivity does not exclude the diagnosis and, therefore, while it is preferable to obtain a culture positive, this does not always occur, *see, e.g.,* in this published case https://www.sciencedirect.com/science/article/pii/S1876034117302496.

5. There is also a misunderstanding of the diagnostic pathway in paragraphs 5.9 and 5.11 of the Cryptococcus Report where it would appear that Mr Bennett has been told isolates at the QEUH/RHC are grown in Bristol. This is incorrect. All the *Cryptococcus neoformans* isolates are primarily grown on agar at the QEUH/RHC labs and are identified locally. They are sent to Bristol only for secondary tests. The isolate, not the sample, is sent for resistance testing. Occasionally samples are sent for molecular testing such as 18 S, but the cases discussed in the report were all grown in Glasgow laboratories. This nullifies the idea that the sending to Bristol differentiates the QEUH/RHC from other labs in terms of culture.

6. It is also important to note that *Cryptococcus neoformans* grows readily on media commonly used in all labs for blood cultures and, therefore, it is unlikely cases of fungaemia are being missed very often across the UK.

7. At paragraph 5.14 of the report, Mr Bennett suggests four possible explanations for excess in numbers in Glasgow. Dr Peters disagrees with the suggested explanations:

a) Randomness producing a 5-7 fold increase is unlikely but needs some statistical analysis regarding the likelihood of all of the excess cases having a link to one building;
b) The QEUH/RHC data set is based on the hospital's in-house diagnostics - no cases were picked up by Bristol that had not already been picked up by the local lab so this explanation is invalid;
c) It seems unlikely that in one year a susceptibility profile would alter 5-7 fold uniquely across the Glasgow population and nowhere else. There would need to be a plausible susceptibility factor shared by the four cases that is different from previous years and other populations. None have been suggested to date.
d) Unlikely as culture does not require special equipment or agar plates.

8. While Mr Bennet correctly identifies the large range in incubation periods, it is notable that large doses of inoculation or inhalation are linked to rapid acute infections. Cases linked to known exposures in contrast to reactivation are well reported. *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8461368/. This is vital to understand in the context of the QEUH/RHC linked cases.

9. While Mr Bennet quotes a paper on the reactivation of Cryptococcus, this is very much in keeping with the presentation of cases where the earlier exposures occurred in high incident countries. The important aspect of this is to be able to differentiate between imported reactivation epidemiology and local epidemiology. Reactivation in Haemato-oncology patients or children is not recognised in Scotland pre-2018. This is new.

10. As far as Dr Peters is aware, the 5% antibody rates in New York have not been replicated in the UK. Dr Peters has previously suggested that antibody prevalence of QEUH/RHC workers versus other populations would be a very worthwhile study. However, even taken at this level in a higher incidence setting - 95% have not been exposed, suggesting that "it's in the air everywhere" is not a risk factor for latent Cryptococcus.

11. While Dr Peters agrees with Mr Bennett's assessment in paragraph 8.4 of the Cryptococcus Report of a key period in late November 2018 that would link the two initial patients, there is no further information regarding what would constitute such a link. Dr Peters raised these exact timeframes with John Hood and drew a timeline on paper reflecting that those days were the key if there was to be a "single incident" of exposure. John Hood simply stated that it was impossible for air to get from the plant room to the bedrooms.

12. In light of Darryl Conner's evidence to the Inquiry that pigeon ingress was noted by H+V workers in late November 2018, it is important to have a full assessment of the records of the nature of that work and which areas/ AHUs were involved. Dr Peters suggested to John Hood at the time that the spraying of the floors to clear up the mess could have presented an "aerosolisation event" (*see* photograph 4 provided in the annex hereto). The spraying, combined with issues such as door seals being inadequate and the presence of a gap around the spigot, could have resulted in an increase in ingress of infectious spores into the AHU which in turn were transported to the patients. This could have increased the concentration delivered to patients and, thus, increased the probability of infection.

13. In paragraph 8.8 of his report, Mr Bennett references air sampling data that is unavailable for Core Participants including the routine samples - it would be helpful to make this available. Dr Peters would highlight that the normal practice of air sampling is not to identify yeast species and so unless there was a specific effort to find Cryptococcal sp., these would not have been expected to be reported in routine sampling.

14. In paragraph 8.9 of his report, Mr Bennett states that the failure to find *Cryptococcus neoformans* in 3000 samples is significant but does not state how. Dr Peters thinks it is significant as the methodology was not quality tested with known positives and so there is no reason to believe it would pick up the organism if it was there. If one does accept that the methodology used could have picked up *Cryptococcus neoformans* - the negative samples suggest that the idea of a steady state of widespread air contamination is wrong. Dr Peters would further suggest that the plant room provides the perfect environment for excessive amounts of aerosolised Cryptococcus given the lack of UV light and water ingress evidenced in the photographs and witnessed by her (*see* photograph provided in the annex hereto), all of which encourage the replication of Cryptococcus.

15. Reference is made to: https://link.springer.com/article/10.1007/bf02050749 and also to https://www.walshmedicalmedia.com/open-access/review-on-cryptococcus-disease.pdf in relation to survival in desiccated pigeon excreta for more than 20 years in the dark. In particular, in this last source the authors state: *"It is estimated that 1 gram of dry pigeon excreta may contain up to 50 million viable cells of C. neoformans. Such natural sites may become a point source of infection to man and animals [6]. The zoo attendants, pet bird keepers, bird enthusiast, pigeon breeder and persons engaged in the cleaning of historical buildings, old monuments etc. are more likely to expose to cryptococcal infection [7].*"

16. In paragraph 8.15 of his report, Mr Bennett suggests that the negative pressure end of the AHU could allow ingress of air from the plant room. Dr Peters agrees and this was a hypothesis which she also suggested at the time. Along with Mr Powrie, Dr Peters conducted smoke testing but the results were minimal (*see* photos provided in the annex hereto). Dr Peters was never made aware that the spigot gap accessed the inside of the AHU. The explanation given to her was that this was under the AHU (*see* photo provided in the annex

hereto), if this is the spigot referred to by Mr Bennett. Air did go into it but it was thought to be under the AHU.

17. In paragraph 8.18 of his report, Mr Bennett suggests "naturally occurring CN" in the outside air is "feasible". It is important to note that CN grubii is a particularly fastidious organism and its primary environmental niche is bird guano (*see* https://journals.asm.org/doi/full/10.1128/ec.00097-07). This is different from the other species which can be found in soil uncontaminated with bird faeces including C. gatti. Interpretation of environmental sampling needs to take into account this important difference. Dr Peters considers this to be "unlikely" - not impossible. She also considers it to be unlikely as the dose is likely to be very low indeed, due to dilution, and less likely to cause infection, and consistent over years, exposing many, many immune compromised patients and the epidemiology to date does not support this.

18. In contrast, ingress of outside contaminated air, if the source, would much more likely be from the helipad due to less chance of dilution and the possible very heavy levels of contamination.

19. In paragraph 8.24 of his report, Mr Bennett suggests some weather conditions may be associated with a potential source of pigeon derived material from the helipad. Has Mr Bennett obtained or been provided with any data on the weather conditions in late November 2018 as well as any records of helicopter landings in that 9 day window period?

20. In paragraph 8.26 of his report, Mr Bennett suggests that removal of Fluconazole could have allowed reactivation in case A. This is possible, but equally it would allow a current exposure to establish as an acute infection. Once again, people from a non highly endemic place such as Scotland do not frequently reactivate. Any co-existence with the other cases makes this less likely, though clearly not impossible.

21. Mr Bennett states that this case is "sporadic especially as they tested negative for CN". Dr Peters disagrees as the clinical history and response to treatment in addition to the multiple CRAG positive samples both at QEUH/RHC and at Bristol makes this a case. The soundness of the diagnosis is separate from the epidemiology. Dr Peters submits that it should be considered a case but agrees that its timing appears to be sporadic. However, Dr Peters believes that this can only be finally assessed with a full, open transparent account of all

pigeon ingress incidents, and a close attention to the emerging epidemiology over the years in Glasgow. This has not been done.

22. In paragraph 9.2 of his report, Mr Bennett states that:

> "*The lack of this assurance has, in my opinion, led to suspicion, loss of reputation and a great deal of effort in this investigation.*"

23. Dr Peters would suggest that there is no question that the protective measures usually expected in this cohort were not present in either Ward 6A or 4C and so assurance could not be given and, if given, was false. The source of the Cryptococcus is different from the breaching of the final protection. In this regard also there can be no assurance given as there was undeniably huge quantities of the main risk factor for the presence of Cryptococcus in the environment - pigeon guano, coupled with the lack of protection and poor air quality, added to the previously unheard of case in Scotland in a child. The situation calls for more than suspicion, it calls for a careful follow up and monitoring of the rates of infection in vulnerable cohorts treated in this building over years to come.

24. In summary, Dr Peters suggests that the recommended epidemiological assessment needs to take into account:

- the unusual patient group - in this group the rate compared to previous years is by definition very high as it has never been noted in this group before in Scotland where the historical epidemiology is very different to other parts of the world.
- What the likelihood is of two reactivations within 3 weeks at one hospital, two floors apart, in a country where reactivations/ acute infections have not been described in children <u>at all</u>, and reactivations never in haemato- oncology patients to Dr Peters' knowledge.
- The climate of Scotland presenting a different ecological dynamic in that countries that are dry and warm have higher rates of Crytpotcoccal infections.
- The epidemiology globally being related to the HIV pandemic and therefore comparison to HIV epidemiology, particularly with *C gattii* needs to be carefully assessed regarding relevance to this incident.

- The clinical history and course of illness that would give a window of exposure should the QEUH/RHC be the source, *e.g.*, a delay in diagnosis would date onset differently to the positive result date - this is relevant to the other 3 cases.
- This would mean a case definition of "Cryptococcal disease presenting within 2 years of a visit to the QEUH" for example which should include all cases to September 2024.
- This could be compared with all Cryptococcal cases with no previous exposure to the QEUH/RHC.
- A second study could do a case comparison of haematology oncology patents, and renal patients cryptococcal rates in QEUH/RHC versus similar patient cohorts in London/ other centres.
- Detailed assessment of all cryptococcal cases to identify how often a pigeon exposure is elicited - to test the "cryptic, all of the outdoors is a risk" hypothesis.

C. CONCLUSION

25. In relation to the above and the Cryptococcus Report more generally, Dr Peters would be happy to provide further input, information and/or clarification as required.

Helen Watts KC and Leigh Lawrie, Advocate

On behalf of Dr Christine Peters

16 September 2024

References:

1. J Peter Donnelly, Sharon C Chen, Carol A Kauffman, et all Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and ReConsortium, Clinical Infectious Diseases, Volume 71, Issue 6, 15 September 2020, Pages 1367–1376,

ANNEX

PHOTOGRAPHS

The following photographs were all taken by Dr Peters in 21 January 2019.

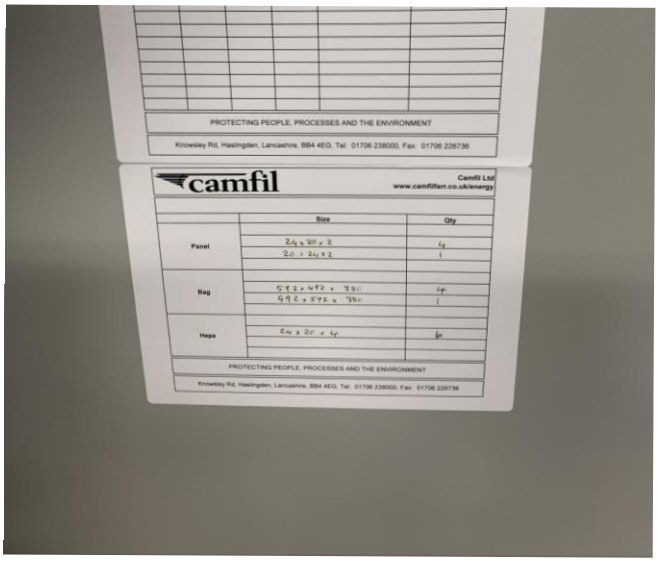
Index of photographs:

1.Spigot at base of AHU

2. Records of filter changes

3. Smoke testing inside AHU

4. Wetness on floor of plant room - water ingress

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