Impact of negative air pressure in ICU rooms on the risk of pulmonary aspergillosis in COVID-19 patients

Philippe Ichai*1, Faouzi Saliba1, Patricia Baune2, Asma Daoud1, Audrey Coilly1 and Didier Samuel1

From the start of the COVID-19 epidemic, one recommendation regarding the intensive care management of COVID-19 patients concerned the infrastructure in intensive care units (ICU) and particularly the air pressure system in ICU rooms [1]. Under normal circumstances and mainly in ICUs hosting immunocompromised patients, ICU rooms are equipped with positive air room pressure in order to protect patients against infections from the surrounding environment and particularly those due to Aspergillus fumigatus (AF). This link between positive pressure rooms and a reduction in Aspergillus infection rates has been demonstrated during several studies [2]. However, these studies included numerous other associated preventive measures. The relationship between the fungal levels in the air of neutral pressure rooms and those in positive pressure rooms has not been established [3].

During the current COVID-19 pandemic, on the contrary, the recommendations have been to place intensive care rooms under negative or even normal pressure so as to protect the staff and patients healthcare. Two recent studies reported a high incidence (26.3–33%) of pulmonary aspergillosis in COVID-19 infected patients [4, 5]. This high risk of pulmonary aspergillosis was also seen in patients with severe influenza (19%). Thevissen et al. reported that the rate of influenza-associated pulmonary aspergillosis (IAPA) varied according to country and that variation in IAPA prevalence might be related to underdiagnosis due to lower use of galactomannan testing on broncho-alveolar lavage or serum in some areas [6].

In line with these recommendations, the 15 rooms of our ICU were placed under negative pressure to receive COVID-19 patients. During this change, all filters in the air conditioning unit were replaced. Two months earlier, routine air sampling had not revealed the presence of any fungal agents and our annual incidence of aspergillosis was lower than 2%. Between 23 March and 4 May 2020, 26 COVID-19 patients were admitted to our ICU (Table 1). Six of the 26 (23.1%) developed probable or proven pulmonary aspergillosis, while two were colonized by AF.

Air cultures from the rooms occupied by the first four infected patients revealed the presence of AF. No colonies of AF were found on the surfaces in rooms or in the air of stepdown rooms (same building, same geographical orientation, two floors up) that were sampled.

| Table 1 Principal characteristics of patients with probable or proven pulmonary aspergillosis |
|---------------------------------|
| Mean age (SD): 64 ± 9 years |
| Gender (n males): 18 M |
| ARDS due to COVID-19, n = 21 |
| Delay between admission and the diagnosis of aspergillosis: 6.5 ± 4.2 days |
| Antifungal therapy: 6/6 |
| - Isavuconazole, n = 5 |
| - Voriconazole, n = 1 |
| Alive: 4/6 patients (67%) |

* Correspondence: philippe.ichai@aphp.fr
| 1Liver Intensive Care Unit, Centre Hépato-Biliaire, AP-HP, Hôpital Paul-Brousse, Université Paris-Saclay, Inserm U1193, 12 Avenue Paul Vaillant Couturier, F-94804 Villejuif, France |
| 2Full list of author information is available at the end of the article |

© The Author(s). 2020 Open Access. This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.
at the same time and were being operated under unventilated rooms. During the crisis, no building projects were being carried out anywhere near the ICU. Checks on accessible sections of the room ventilation circuits did not identify any reservoir of contamination.

After surface disinfection, the negative air pressure in the rooms was raised on two successive occasions, ultimately reaching a pressure of 1.2 ± 1.5 Pa. From that time on, the levels of AF in room air fell in spectacular fashion (0–2 CFU/m³) (Fig. 1).

All infected patients received antifungal therapy and 4 out of 6 are alive. Prophylactic antifungal therapy was administered to all other patients. Since then, no further cases of aspergillosis have been recorded.

Our results demonstrate that implementing negative pressure in ICU rooms could be the source of air contamination by Aspergillus and thus increase the risk of opportunistic infections. A switch to neutral or slightly positive pressure in the rooms, combined with standard environmental cleaning protocols and prophylactic antifungal treatments, enabled the eradication of aspergillus from the air in these rooms. One hypothesis regarding contamination was a spread of dust from the plenum spaces in false ceilings which “might” have been moved during successive adjustments to high/low/neutral pressure and could have infiltrated via unsealed parts of the ceiling.

Close mycological screening of COVID-19 infected patients (biomarkers and mycological diagnosis) and regular controls of air quality are highly recommended.

Acknowledgements
Not applicable

Authors’ contributions
PI conceived and wrote the first draft of the paper. PI and FS analyzed the data. PI, FS, PB, AD, AC, and DS participated in the critical review of the manuscript. All authors read and approved the final manuscript.

Funding
Not applicable

Availability of data and materials
If necessary, data could be transmitted to the Editor.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable in this study.

Competing interests
Not applicable

Author details
1Liver Intensive Care Unit, Centre Hépato-Biliaire, AP-HP, Hôpital Paul-Brousse, Université Paris-Saclay, Inserm U1193, 12 Avenue Paul Vaillant Couturier, F-94804 Villejuif, France. 2Infection Control Team, AP-HP Hôpital Paul-Brousse, F-94800 Villejuif, France.

Received: 3 July 2020 Accepted: 3 August 2020
Published online: 01 September 2020

References
1. Phua J, Weng L, Ling L, Egi M, Lin CM, Dviveta J, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med. 2020;8(5):506–17.
2. Humphrey H. Positive-pressure isolation and the prevention of invasive aspergillosis. What is the evidence? J Hosp Infect. 2004;56(2):93–100 quiz 63.
3. Ryan L, O’Mara N, Tansey S, Slattery T, Hanahoe B, Vellinga A, et al. A 2-year comparative study of mold and bacterial counts in air samples from neutral and positive pressure rooms in 2 tertiary care hospitals. Am J Infect Control. 2018;46(5):590–3.

4. Alanio A, Delliere S, Fodil S, Bretagne S, Megarbane B. Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Lancet Respir Med. 2020;8(e48–e9.

5. Koehler P, Cornely OA, Bottiger BW, Dusse F, Eichenauer DA, Fuchs F, et al. COVID-19 associated pulmonary aspergillosis. Mycoses. 2020;63(6):528–34.

6. Thevissen K, Jacobs C, Holtappels M, Toda M, Verweij P, Wauters J. International survey on influenza-associated pulmonary aspergillosis (IAPA) in intensive care units: responses suggest low awareness and potential underdiagnosis outside Europe. Crit Care. 2020;24(1):84.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.