



Letter to Editor



Post-Mortem Sepsis and Post-Mortem Diagnostic Anti-Microbial Stewardship

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ABSTRACT

Post-mortem sepsis (PMS) represents a crucial yet underexplored dimension of infectious disease diagnostics, particularly in cases where infections are undiagnosed antemortem. This paper explores the concept of post-mortem diagnostic antimicrobial stewardship (D-AMS), emphasising the value of post-mortem microbiology (PMM) in guiding evidence-based assessments of infection-related deaths. By analysing tissue and fluid samples after death, PMM can uncover occult pathogens, clarify clinical ambiguities, and refine the understanding of antimicrobial resistance trends. Despite its potential, PMS is challenged by diagnostic variability, resource limitations, and the difficulty of distinguishing true pathogens from contaminants. The absence of standardised protocols further hampers the clinical utility of PMM. We highlight instances where post-mortem findings provided critical insights into unsuspected infections in diagnosis and treatment. We put forward integration of PMM into broader antimicrobial stewardship frameworks to bridge the gap between clinical and post-mortem. As diagnostic technologies advance, particularly with the inclusion of rapid molecular tools and artificial intelligence, PMM stands poised to enhance precision medicine and public health surveillance. The incorporation of PMM findings into clinical feedback loops can ultimately influence empirical therapy guidelines, detect lapses in diagnostic protocols, and contribute to more rational use of antimicrobials. This paper advocates for greater recognition of PMS and structured implementation of D-AMS as essential components of future health systems, combining forensic insight with clinical impact.

KEYWORDS: Post-mortem microbiology; Sepsis; Antimicrobial stewardship

BACKGROUND

Post-mortem sepsis (PMS) refers to the detection of infections at autopsy that may have caused or contributed to death. Although this area holds clinical and public health importance, it is still not explored. PMS involves identifying infections using post-mortem microbiology (culture and sensitivity) and other parameters like biomarkers of infection (procalcitonin). In recent years, the idea of post-mortem diagnostic anti-microbial stewardship

(D-AMS) has emerged. This concept focuses on using microbiological findings from autopsy samples to support and improve diagnostic antimicrobial stewardship efforts. By integrating such data, it may help clarify uncertain diagnoses, better identification of cause of death, judicious use of antibiotics, and even track microbial resistance patterns.

Post-mortem microbiological investigations serve as a critical adjunct in the identification of infections that frequently remain undiagnosed during life, often due to

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atypical clinical manifestations, diagnostic limitations, or underlying immunosuppression. Autopsy based detection of infections, co-existing pathogens, and antimicrobial resistance provides valuable insights that extend beyond individual case assessment to inform broader public health and antimicrobial stewardship efforts. The integration of post-mortem microbiological data into Antimicrobial Stewardship Program (AMSP) holds potential for enhancing diagnostic accuracy, informing targeted antimicrobial therapies, and reducing the reliance on empiric broad-spectrum antibiotics¹. Such evidence-driven approaches can contribute to the refinement of therapeutic strategies, better identification of cause of death and the surveillance of emerging resistance trends. This in turn will ultimately reinforce the integrated AMSP.

THE NEED FOR IDENTIFYING POST-MORTEM SEPSIS

Post-mortem microbiology (PMM) plays an important role in detecting infections that were missed or not properly diagnosed before death. PMM helps in identifying the undiagnosed microorganisms that were present at the time of death by examining tissue samples, body fluids, and cultures collected after death, although it is believed that the post-mortem changes can influence results, proper sampling techniques and modern diagnostic tools can still provide reliable information². These results are particularly useful in detecting hidden infections that may have caused sudden deaths, confirming suspected infections that were not proven / suspected during life³. By identifying previously unrecognised infection, PMM may also contribute in identifying possible medical errors and health care associated infection. Microbiome of the gut in the dead body (thanatobiome) can give useful clues about the time since death⁴.

SAMPLE COLLECTION FOR POST-MORTEM SEPSIS

A positive bacterial growth detected on post-mortem samples can be a sign of antemortem infection where the isolated microbe is the causative agent or a contributing factor of death. The main concerns for the sample collection in post-mortem microbiology are post-mortem translocation and contamination⁸. It is generally accepted in recent literatures that post-mortem bacterial translocation does not have significant impact if the samples are obtained within a maximum 48 hours after death^{7,8,9}. This is provided that the corpse has been maintained refrigerated at 4° C^{10,11}. To avoid contamination, PMM is proven useful when aseptic measures are taken at autopsy by using sterile conditions like routine and pre-sampling sterilisation of

instrument, trays etc by rectified spirit, hypochlorite solutions⁷. In 2019, ESCMID (European Society for Clinical Microbiology and Infectious Diseases) incorporated in the International Guidelines that for post-mortem blood sample collection, the subclavian vein is the most appropriate sampling site for peripheral blood, rather than the jugular or femoral veins¹¹. For tissue sample collection the most frequently cited approach is the searing the organ's surface with a hot spatula before obtaining the tissue samples, using sterile instrumentation^{7,8}. Use of these techniques result in significant reduction of translocation and contamination.

CHALLENGES FACED BY POST-MORTEM SEPSIS AND STEWARDSHIP

1. Diagnostic Accuracy in Complex Cases

One of the challenges of using PMM and detecting sepsis after death (PMS) is to ensure their application in living patients. PMM very often delineates the pathogen responsible for atypical presentation in post-mortem findings, and these may have repercussions in simulative ante-mortem cases⁵. However, to connect such insights effectively, clinicians have to interpret their findings within the context of living patients with non-specific symptoms. This calls for defined diagnostic alignments and strict communication between post-mortem investigators and clinicians.

2. Variability in Protocols and Resource Constraints

Lack of standard protocols in the performance of PMM results in variability in the quality and generalizability of the findings. Differences in sampling techniques, processing, and reporting also prevent the integration of PMM data into clinical and public health practice⁶. In this context, PMM requires specialized expertise and infrastructure, which are not always available in resource-limited settings, thus constraining its wider application⁷.

3. Distinguishing True Infections from Contaminants

An important challenge is in distinguishing between the pathogens that have caused infection prior to death and those that translocated or multiplied after death occurred during or post-mortem. This distinction would be important to generate meaningful data to inform both clinical and stewardship practices. In the absence of standardized methodologies in interpreting PMM results, risks of misidentification and over-interpretation remain. There is a paucity of global literature on this. However, some scientists working on PMS believes that significant PMM in automated culture systems with corroborative findings can suggest PMS.

OPPORTUNITIES FOR POST-MORTEM SEPSIS AND POST-MORTEM STEWARDSHIP

1. Refining Empirical Therapy Guidelines:

The post-mortem microbiology (PMM) provides exceptional opportunities to fine-tune empiric therapy recommendations in critical care. By documenting pathogens associated with specific clinical syndromes (which standard management protocols may have failed to detect), PMM has the potential to offer a real-world pathogen data set with wider implication. The impending change in clinical practice through PMM guided sepsis or presence of micro-organisms, will be of at most useful in integrated AMSP.

2. Identify Gaps in Diagnostic:

PMM plays a crucial role in identifying diagnostic blind spots, such as infections that were not diagnosed during life but have emerged pathogenic over the time¹². For instance, invasive fungal infections and many bacteremia are usually not detected due to improper diagnostic stewardship protocol (improper techniques / sample / media / machine)¹³. PMM identifies such missed opportunities to include improved diagnostic tools, such as rapid PCR and metagenomic sequencing, in ante-mortem practice. Hence PMM has the potential to test the diagnostic stewardship and further optimizing efforts in integrated AMSP.

3. Contributing to Public Health Surveillance:

PMM findings are a valuable resource for public health surveillance. PMM involves samples obtained directly from organs intended and clear visualisation of organs on gross autopsy examination, internal abscesses and their extent and liberty of multiple samples without harm to person concerned is possible in PMM¹⁴. The identification of rare or emerging pathogens in deceased individuals can signal outbreaks or the introduction of new microbial strains into the community. This information is critical for epidemiological monitoring and tailoring infection control strategies to evolving pathogen prevalence and resistance patterns. In this context, PMM will help improve infection prevention and community-wide public health initiatives.

CASE REPORTS AND IMPLICATIONS FOR POST-MORTEM STEWARDSHIP

Various case studies clearly show how post-mortem microbiological findings are beneficial for infectious diseases. For instance, in the case of a patient with acute lymphoblastic leukemia who acquired persistent candidemia and pulmonary aspergillosis during their stay in the hospital, it was found, on post-mortem

analysis, that the patient had severe right-sided endocarditis, which acted as the cause of the refractory candidemia. This identified the extent of infection and gave direction to further understand similar cases¹⁵. Another case involved a college student who experienced sudden death; the autopsy revealed purulent meningitis caused by *Neisseria meningitidis*¹⁶. This highlights the critical role of post-mortem microbiological identification in detecting and managing fulminant infections. These cases emphasize how autopsy data can refine clinical approaches and inform antimicrobial stewardship efforts, particularly in identifying causative pathogens and guiding appropriate treatments.

ADVANCING PRECISION MEDICINE AND STEWARDSHIP:

A robust PMM surveillance system if in place, can more accurately diagnose sepsis. With adequate number of PMM pooled meta data set, artificial intelligence can be applied for machine learning. PMM with artificial intelligence and machine learning has the potential for evolution of precision medicine in this field.

CONCLUSIONS

Post-mortem microbiology (PMM) has significant clinical implications such as in detecting cause of death and time since death. Post-mortem diagnostic anti-microbial stewardship includes careful handling, control of contamination, and best practices in sample collection to address this issue. PMS and post-mortem D-AMSP has the potential for never felt before health care indices such as medical negligence, improper management protocols in critical care settings, poor D-AMSP and health care associated infections. We strongly believe, the advancement of PMS and D-PMS will be critical in time to come for innumerable medico legalities.

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTION

EP: Initial drafting of the manuscript, literature review.

AC: Conceptualization of the study

DC: Analysis and interpretation.

AA: Conceptual guidance, supervision, and final manuscript approval.

SK: Critical review and intellectual input for clinical correlation.

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