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# When the Galactomannan Test "Lies" : False Positives Are Not Analytical Errors but a Clinical Responsibility

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## Editorial

The *Aspergillus* galactomannan (GM) antigen test is one of the principal mycological approaches to diagnosing invasive aspergillosis (IA). It is recognized as a mycological assessment endorsed by the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) guidelines (1). A serum or plasma cutoff of 0.5 was established in the 2008 EORTC/MSG guidelines (2), and this threshold was revised to 1.0 for a single serum or plasma specimen in the 2020 update (3). In the literature, false-positive GM results are commonly attributed to various interfering factors, including piperacillin-tazobactam, certain other antibiotics, blood products, and cross-reactive fungi. This list continues to grow, and its increasing length may obscure a more important question: whether the laboratory has the capacity and willingness to recognize false-positive results and intervene when they occur.

A 2024 case-control study (4) identified dextrose-containing intravenous fluids as a strong independent predictor of false-positive GM results (Adjusted OR up to 18.60). Some fluid samples themselves tested positive for GM because of *Aspergillus niger*-derived glucoamylase used in manufacturing. The study traced an anomalous signal through clinical data and the product supply chain, prompting a change in the manufacturer's process; following this change, GM false-positive rates declined immediately and remained low. The same principle extends to respiratory specimens: blood contamination in bronchoalveolar lavage (BAL) samples can also produce false-positive GM results (5). This observation indicates that specimen quality, rather than the numerical result alone, should be considered when interpreting BAL GM positivity. Such an approach constitutes a laboratory-driven patient safety intervention rather than merely conventional quality control.

In 2025, Lee et al. (6) developed a web-based tool grounded in GM pharmacokinetics that analyzes patterns of change in the GM index over time. The tool aims to distinguish false-positive results related to fluid contamination from true IA within 24 hours. Its significance lies in addressing a common clinical dilemma: when a patient receiving dextrose-containing fluids has a positive GM result, should the clinician initiate antifungal therapy immediately or await repeat testing? Existing guidelines do not provide a satisfactory answer, whereas the kinetic model offers a practical intermediate approach. External validation is required before routine adoption; nevertheless, this approach points to a valuable direction: the longitudinal pattern of GM provides more information than a binary interpretation based on a single cutoff value.

Other sources of false-positive GM results are less readily apparent and require greater interdisciplinary awareness within the laboratory. Nebulized colistin was identified as an independent risk factor for false-positive GM results in ICU patients (Adjusted OR 35.68). The key question is whether the laboratory routinely collects information on nebulized treatments and flags it in respiratory specimen reports. Among patients with multiple myeloma, the false-positive GM rate reached 25.5%, and optical density indices were generally below 3.0, further reducing the specificity of low-level positive results. Including this association in the report would substantially improve clinical decision-making. A case report of Rhodococcus peritonitis causing a false-positive GM result in peritoneal dialysis fluid (7) demonstrates that false-positive results are not confined to serum and BAL. In peritoneal dialysis fluid, a false-positive result may be misinterpreted as evidence of fungal peritonitis, leading to unnecessary antifungal therapy in patients who actually have bacterial peritonitis.

Taken together, these observations support a clear argument: The focus of managing GM false positivity should shift from compiling lists of interfering substances to providing contextual information in laboratory reports. In common practice, the laboratory enters a value into the laboratory information system and labels it positive if it exceeds the cutoff, leaving clinicians with an isolated result. This model may be acceptable for serological tests with manageable false-positive rates. For the GM assay, however, whose limited specificity has been repeatedly demonstrated, a "report the number, ignore the context" approach is inappropriate.

The laboratory can intervene at three levels. Pre-analytically, known high-risk exposures (Dextrose-containing fluids, nebulized colistin, and specific antimicrobials) can be incorporated into an alert system for GM orders or, at a minimum, flagged during result review. Analytically, for results near the cutoff, repeat testing and kinetic trend analysis can be proactively recommended instead of issuing a single definitive interpretation. Post-analytically, a brief interpretive comment can be added to positive reports to contextualize the likelihood of a false-positive result based on medication history and underlying disease. These measures require neither approval of new technology nor a large-scale overhaul of information systems. Rather, they require a redefinition of the laboratory's role, from a producer of data to an integrator of diagnostic information.

The limitations of this approach must be acknowledged. Not all laboratories have access to complete medication records, and not every institution has the capacity to manually review every positive GM result. For this reason, the lessons from the 2025 pharmacokinetic tool and the 2024 dextrose-fluid study are particularly valuable: they demonstrate the feasibility of structured interventions based on a small number of key variables. A history of exposure to dextrose-containing fluids is a binary variable, and assessing temporal changes in the GM index requires only two data points for a preliminary judgment. The barrier to implementation is therefore lower than it may appear.

The problem of false-positive GM results will not disappear. As new drugs, formulations, and clinical scenarios emerge, the number of interfering factors will only increase. A laboratory's competence becomes evident when it encounters an assay known to be imperfect: Does it simply issue the report without comment, or does it give the result actionable meaning? In the former case, a false-positive result remains an error; in the latter, it becomes an opportunity for improvement.

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