

Letter to the Editor

Contamination by Cardboard Particles as a Cause of False-Positive Results for *Aspergillus* Galactomannan Enzyme Immunoassays[∇]

Galactomannan (GM) detection by the Platelia *Aspergillus* enzyme immunoassay is widely used for diagnosing invasive aspergillosis. A major problem with the detection of circulating GM is the occurrence of false-positive results due to the cross-reactivity of the test with antigens other than *Aspergillus* GM. In the clinical setting, cross-reactivity with antibiotics, in particular piperacillin-tazobactam, and other opportunistic fungi represent the two major causes of false-positive results (3, 5). Gastrointestinal translocation of GM from food is also a presumed cause of false positivity for antigenemia (5). Recently, solutions containing gluconate, which is usually produced by fermentation of glucose in mold cultures, have been shown to be another cause of false-positive GM assay reactivity (4, 6).

At our institution, GM assay is routinely used in the diagnosis of invasive aspergillosis in patients with hematologic malignancies. In March 2007, in two consecutive experiments, all serum samples (32 samples total) showed very high indexes of reactivity (indexes of >4) with normal reactivity to negative, positive, and standard serum controls provided by the manufacturer. Considering that most of these results were not consistent with the clinical findings for the patients and that the patients had no specific clinical characteristic in common (they were adult and pediatric inpatients and outpatients with various underlying diseases and conditions), we hypothesized that Platelia *Aspergillus* positivity may have been due to a cross-reaction related to an abnormal laboratory procedure. Initially, no particular handling practice during assay performance potentially leading to the contamination of samples was identified. Finally, we found out that while the tubes (1.5-ml Eppendorf microcentrifuge tubes) we use for serum sample storage in our laboratory are usually taken from a plastic box, in the two above-described experiments the laboratory technician erroneously used the same type of tubes but took them from a cardboard box (the control samples had previously been stored in tubes from the plastic box). The tubes, not plugged as provided by the manufacturer, had been placed in the cardboard box and the box in a laboratory cupboard several months before, and some cardboard particles were visible. We performed the GM assay with sterile distilled water using tubes taken from the cardboard box and with cardboard homogenate, and all gave high indexes of reactivity. Multiple cultures of tubes and cardboard were negative for fungi.

Polysaccharides containing mannopyrosyl residues, such as mannans, glucomannans, and GMs, are commonly found as

plant cell wall components (1). Considering that paper and paper products are made from plants, it seems reasonable to hypothesize that cardboard particles contain GM antigen cross-reacting with the Platelia *Aspergillus* assay. Similar cross-reaction was also reported for cotton swabs (2). Therefore, we think that the false-positive GM results we observed in the above-described experiments were related to the prior contamination of the tubes by cardboard particles before their use for serum sample storage. Although enzyme immunoassay procedures usually do not require particular sterility precautions, considering that GMs are polysaccharides widely distributed in the environment, improper laboratory practices possibly allowing contamination and false-positive results should be known and carefully avoided.

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Corrado Girmenia*

Daniele Ballarò

Pietro Martino

Dipartimento di Biotecnologie Cellulari ed. Ematologia
University “La Sapienza” of Rome

Via Benevento 6
00161 Rome, Italy

*Phone: 39-06-857951

Fax: 39-06-44241984

E-mail: girmenia@bce.uniroma1.it

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