

Urinary Markers of Intestinal Yeast
Letter to the editor of
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Editor:

The detection of clinically significant intestinal yeast growth is challenging. Because of the serious life-threatening nature of invasive candidiasis for immunosuppressed individuals, there is strong interest in markers that reveal early stages of this condition. [1] Evidence from a series of recent studies has led to a recommendation that urinary levels of the sugar alcohol, D-arabinitol, be used as a reliable biomarker for invasive candidiasis. [2] The enantiomeric L-arabinitol is not associated with intestinal yeast, and some investigators report the D-/L-arabinitol ratio as a marker. Invasive candidiasis is detected, for example, by such measures of D-arabinitol in newborn infants, and it is reported to be more sensitive than fungal blood cultures. [3] D-arabinitol is five-carbon sugar alcohol produced from dietary carbohydrates when yeasts are rapidly growing in the reducing environment of the small intestine. Claims have been made that urinary arabinose, an aldopentose with chiral centers similar to arabinitol, is a marker of intestinal yeast growth. Several lines of existing evidence contradict these claims.

Arabinose is a five-carbon sugar produced in plants. [4] Arabinose polymers are found in tomatoes and many other foods. [5] A relationship between intestinal yeast and urinary arabinose (steroisomer unspecified) has been claimed in a patent, particularly in reference to the diagnosis of autism. [6] The patent is based on a report of compounds found in the urine of two autistic brothers. [7] Other than this report by the inventor of the patent, however, there is no evidence of such an association. Evidence from many reports demonstrates that yeasts utilize arabinose as a substrate for growth, thus destroying the sugar. [8, 9] The fungal pathway for utilization of arabinose consists of five enzymes, and the dehydrogenase enzyme responsible for the reduction of arabinose to arabinitol has been characterized in *Saccharomyces cerevisiae*. [10, 11] Several species of yeast and bacteria have the capacity to metabolize arabinose. [12, 13] A study of arabinose excretion in chickens reached a conclusion of lowered arabinose digestibility following ileostomy. [14] Cecal microflora of the rat efficiently degrade over 90% of arabinose in the media. [5] Profound human L-arabinosuria has been found as a result of an inherited defect in pentose metabolism. [15] Thus, not only is there no evidence that arabinose is produced by any strain of yeast, the extant evidence favors the conclusion that any available

arabinose in their environment would be consumed by yeast. Furthermore, any of the sugar present in the intestine undergoes rapid fermentation by a variety of microbial species, and that which is absorbed is efficiently metabolized in human tissues.

Anecdotal reports of urinary arabinose correlating with the administration and withdrawal of anti-fungal medications are sometimes circulated. Medications that have powerful anti-fungal effects are known for their hepatotoxic effects. [16] Therefore, any apparent correlation of urinary arabinose with anti-fungal administration must rule out alteration of hepatic arabinose metabolism before a conclusion regarding intestinal yeast populations can be made.

Analytical difficulties also cloud the use of urinary arabinose as a marker compound. The method that is cited in support of the autism diagnosis patent involves ethyl acetate extraction of acidified urine. [7] In our laboratory, similar methods using ethyl acetate and several other organic extraction solvents demonstrated very poor recoveries for arabinose. This finding is not surprising due to the high water solubility of small molecular weight polyalcohols and their lack of solubility in non-polar organic solvents. In summary, arabinose is a common component of carbohydrate-rich foods. It is metabolized by intestinal microbial populations and by human hepatocytes. It has never been reported to be a metabolic by-product of any strain of yeast or fungus. Finally, the sugar is poorly extracted using standard procedures of sample preparation for measurement of organic acids in urine. These several lines of evidence lead to a conclusion that urinary arabinose should be rejected as a marker for the assessment of intestinal yeast overgrowth. Urinary D-arabinitol remains the standard for detection of early stages of invasive candidiasis.

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