

Brian Kelleher
Sean O'Broin*
Dept. of Haematol.
St. James's Hosp.
Dublin 8, Ireland

* Corresponding author.

Spokespersons for Bio-Rad Labs. comment:

To the Editor:

The commercially available Lyphocheck Whole-Blood Control from Bio-Rad Labs. is supplied in lyophilized form and may conveniently be stored at refrigerated temperatures over its shelf life. The product is neither designed nor recommended to be stored frozen for longer than 30 days; further, no claims are made for storage of the control material under ascorbated conditions. By contrast, in the study above, the control material was both ascorbated and stored frozen in excess of 30 days. Those specimens stored at -70°C performed identically to their previously reported behavior (above ref. 1).

Freezer space being at a premium in the clinical laboratory, one cannot expect that clinical chemists will want to spend additional time in ascorbating, aliquoting, and freezing control material. The format of Lyphocheck Whole-Blood Control provides clinicians with a material for quality control of folate test procedures along with the convenience of long-term refrigerated storage and simplified reconstitution.

Brian Passkiewicz
Cynthia French
Bio-Rad Labs., ECS Division
3726 E. Miraloma Ave.
Anaheim, CA 92806

Screening for Sulfite Oxidase Deficiency with Urinary Thiosulfate/Sulfate Ratios Determined by Anion Chromatography

To the Editor:

Detection of sulfite oxidase deficiency by urine screening tests is hampered by the rarity of the disorder and the complex chemical character of the excreted compounds [1]. False negatives are well recognized, both with use of the commercial urine test strip and the various "screening" assays for sulfite and thiosulfate [2-5]. False positives are also not uncommon [6]. However, several novel analytical methods have recently been reported, including a robust assay for urinary *S*-sulfocysteine [7] and a reliable method for quantifying total sulfite in serum [8]. In their original description of the commercial assay, Wadman et al. [9] referred to the potential utility of quantitative ion chromatography. However, urine is a complex matrix precluding simple separation and conductimetric detection of trace anions, as we discovered in attempting to establish a normal reference range for thiosulfate. We found anion-chromatographic separation of urinary thiosulfate satisfactory if a "heart-cut" method [10] was used, directing the void volume fraction (with abundant anions such as chloride) and the tailing fraction to waste.

We have recently reported our method [11], with which we determined a reference range modestly lower than previously published [12]. We believe this difference may reflect a positive bias introduced by background urinary thiocyanate in the commonly used cyanolysis procedure. In our utilization of anion

chromatography to help detect sulfite oxidase deficiency, we normalized the thiosulfate excretion data with respect to urinary sulfate rather than to creatinine [13] for two reasons: (a) excretion of the sulfite oxidase product, inorganic sulfate, is limited in affected patients [14], so the ratio is likely to be more efficient in detecting the inborn error; and (b) sulfate and thiosulfate can both be quantified by using the same chromatographic conditions.

Table 1 shows the results for clean, early-morning urines from controls and two patients (courtesy of A. Feigenbaum, Hospital for Sick Children, Toronto, ON): one with molybdenum cofactor deficiency and the other with isolated sulfite oxidase deficiency (confirmed by J. Johnson, Duke University, Durham, NC). Preliminary studies of the obligate heterozygote parents revealed no overlap of values with those in the affected children (data not shown). Thus, ion chromatography continues to be an important alternative method for assay of inorganic sulfur ions. The method may be a useful adjunct for studies of sulfite sensitivity and for clinical referral laboratories charged with screening for sulfite oxidase deficiency.

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Table 1. Urinary thiosulfate and sulfate in sulfite oxidase-deficient patients and controls.

Subjects	Age, years	n	Thiosulfate (S_2O_3), ^a $\mu\text{mol/L}$	Sulfate (SO_4), ^b mmol/L	$\text{S}_2\text{O}_3/\text{SO}_4$ ratio, $\mu\text{mol/mmol}$
Isolated sulfite oxidase deficiency	2.4	1	2197	3.80	578
Molybdenum cofactor deficiency	4.3	1	1220	1.92	635
Controls: Infants	<2	8	7.14 ± 1.63 (0.3-18.3) ^c	5.75 ± 0.81 (2.7-8.9)	1.66 ± 0.59 (0.27-2.94)
Children	2-10	21	8.46 ± 2.04 (0.3-39.2)	10.8 ± 0.6 (4.7-24.4)	0.83 ± 0.08 (0.04-2.98)
Children	10-18	14	10.78 ± 3.81 (0.8-26.2)	14.8 ± 1.6 (1.5-27.2)	0.54 ± 0.11 (0.01-1.27)
Adults ^d	>18	20	9.41 ± 1.16 (0.4-27.3)	17.1 ± 1.8 (5.0-36.1)	0.49 ± 0.09 (0.03-1.94)

^a Assayed in duplicate by ion chromatography, with intraassay CV = 4.5% and interassay CV = 11.7% [11].

^b Analyzed in duplicate with intraassay CV = 3.5% and interassay CV = 5.5%, under conditions identical to those used for thiosulfate assay.

^c Mean \pm SE (and range).

^d Taken from ref. 11. In that study, the difference between 24-h urines and early-morning specimens was much smaller than the interindividual variation.

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David E. C. Cole*

Jovan Evrovski

*Depts. of Clin. Biochem., Med., and
Genetics
Univ. of Toronto
and Dept. of Clin. Chem.
The Toronto Hospital
Toronto, ON M5G 1L5, Canada*

* Address for correspondence: Rm. 415,
Department of Clinical Biochemistry, Banting
Institute, 100 College St., Toronto M5G 1L5.