JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 1994, p. 1855–1859
0095-1137/94/$04.00+0
Copyright © 1994, American Society for Microbiology
Vol. 32, No. 8

Gas Chromatographic Determination of D-Arabinitol/L-Arabinitol Ratios in Urine: a Potential Method for Diagnosis of Disseminated Candidiasis

LENNART LARSSON,* CHRISTINA PEHRSON,[1] THOMAS WIEBE,[2] AND BERTIL CHRISTENSSON[3]

Department of Medical Microbiology,[1] Department of Pediatrics,[2] and Department of Infectious Diseases,[3] University Hospital of Lund, Lund, Sweden

Received 7 January 1994/Returned for modification 6 March 1994/Accepted 29 April 1994

A gas chromatographic procedure was developed to determine the relative amounts of D- and L-arabinitol in urine. Samples were filtered, diluted, purified through extractions, evaporated, and treated with trifluoroacetic anhydride; the arabinitol derivatives thus obtained were separated on a chiral stationary phase and registered by using an electron-capture detector. Urine samples from a patient with disseminated candidiasis had higher D-arabinitol/L-arabinitol ratios (referred to as D/L-arabinitol ratios)—up to 19.0—than samples from 96 study individuals with no signs of deep *Candida* infections (range, 1.1 to 4.5). D/L-Arabinitol ratios in urine samples from hospitalized patients without *Candida* infections were slightly higher than those in samples from healthy individuals; ratios in urine from children were slightly higher than those in adult urine samples. The D/L-arabinitol ratios in several urine samples culture positive for *Candida albicans*, but from patients without symptoms of disseminated candidiasis, did not differ from those in the urine of healthy individuals. The described gas chromatographic method is straightforward and can be implemented clinically to determine urine D/L-arabinitol ratios as a means of diagnosing disseminated candidiasis.

Disseminated candidiasis is a serious condition that mainly affects immunocompromised individuals, e.g., patients undergoing bone marrow transplantation or cancer treatment. Improved methods of diagnosing candidiasis are urgently needed since the blood cultures and antibody tests used today are considered highly unsatisfactory and alternative techniques (e.g., antigen detection and DNA amplification), although promising, are still in the developmental stages (9).

D-Arabinitol, a cyclic pentitol, is a major metabolite of several *Candida* species (1). In the late 1970s, elevated levels of arabinitol were found in the blood of patients with disseminated candidiasis (5); however, subsequent attempts to exploit this finding diagnostically were not fruitful because of the low specificity of arabinitol determination, i.e., high levels of arabinitol in blood were found not only in candidiasis patients but also in those suffering from renal dysfunction (4, 10). Subsequently, use of arabinitol/creatinine ratios was suggested to avoid false-positive results because of renal impairment (4, 15, 18). In an alternative approach, D- and L-arabinitol were separated chromatographically: elevated D-arabinitol/L-arabinitol ratios (referred to as D/L-arabinitol ratios) were found in connection with candidiasis but not with renal dysfunction (12). The D/L-arabinitol ratios in urine were found to be about the same as those in blood both in patients with deep-seated *Candida* infections and in healthy individuals (12, 13).

Gas chromatography (GC)-mass spectrometry (MS) and so-called multidimensional GC have been applied to determine D/L-arabinitol ratios in clinical specimens by separating halogenated derivatives of the arabinitol enantiomers on a chiral GC column (3, 11–13, 20). However, multidimensional GC is cumbersome, and clinical microbiological laboratories are only rarely equipped with the necessary equipment to perform GC-MS; hence, D/L-arabinitol ratio measurements have not been extensively applied in the diagnosis of *Candida* infections. The purpose of the present study was to develop a straightforward GC technique suitable for routine determination of D/L-arabinitol ratios in urine.

* Corresponding author. Mailing address: Dept. of Medical Microbiology, University of Lund, Sölvegatan 23, 223 62 Lund, Sweden. Phone: 4646-173289. Fax: 4646-189117.

MATERIALS AND METHODS

Urine samples. The collected urine samples (2-ml aliquots) were stored at −20°C before analysis. Samples were collected from patients at the Departments of Infectious Diseases and Pediatrics, Lund University Hospital, and from healthy controls.

To study the reproducibility of the D/L-arabinitol ratio determinations, one urine sample from a child with acute myeloid leukemia and disseminated candidiasis (high D/L-arabinitol ratio) and one urine sample from a child with acute lymphatic leukemia without candidiasis (low D/L-arabinitol ratio) were prepared and analyzed on eight different occasions.

Sixty-one hospitalized patients (37 adults and 24 children) without *Candida* infection or colonization delivered one urine sample each.

To determine intraindividual variation over time, six urine samples were collected from each of 20 individuals (one sample every second day); 10 individuals were healthy adults and children (five of each), and 10 individuals were hospitalized adults and children (5 of each) with no signs of candidiasis; the children were between 2 and 10 years of age.

Ten patients without any clinical signs of deep-seated *Candida* infections delivered urine samples culture positive for *Candida albicans*: growth was rich (10^6 CFU/ml) in four samples, medium (10^5 CFU/ml) in four samples, and sparse ($<10^4$ CFU/ml) in two samples.

One urine sample each was collected from three females with *Candida* vaginitis and two AIDS patients with oral candidiasis.

Nine urine samples were collected from a 13-year-old girl with non-Hodgkin's lymphoma and disseminated candidiasis,

which was verified by growth of *C. albicans* in multiple blood cultures. Blood culturing was done in tryptic soy broth with a malt agar dip slide (Hoffmann-La Roche AG, Basel, Switzerland).

Cultivation. The following experiments were performed to further investigate whether local *Candida* colonization in the urinary tract influences D/L-arabinitol ratios in urine.

(i) Two 10-ml portions of a urine sample (culture negative for *Candida* spp.) from a healthy individual were used; *C. albicans* (6×10^5 CFU) was added to one portion. Both portions were then kept at 37°C for 3 days and thereafter at 4°C for 11 days. D/L-Arabinitol ratios were determined (in 1-ml aliquots) on days 0, 1, 2, 3, and 14.

(ii) Each of two urine samples culture positive for *C. albicans* (8×10^5 and 3×10^3 CFU) but collected from two individuals without symptoms of deep-seated *Candida* infections were divided into three 2-ml portions. Considering each sample separately, the three portions were treated as follows: one was immediately analyzed for its D/L-arabinitol ratio and the other two were incubated overnight at 20 and 37°C, respectively, and were then analyzed for their D/L-arabinitol ratios.

The production of D-arabinitol by different yeast species was studied. One loopful each of *C. albicans*, *Candida tropicalis*, *Torulopsis* (*Candida*) *glabrata*, *Candida parapsilosis*, *Candida krusei*, *Candida lusitaniae*, *Candida guilliermondii*, and *Saccharomyces cerevisiae* (clinical isolates) were incubated in 5 ml of liquid Sabouraud medium at 37°C for 48 h. After viable count determinations, the broth cultures were filtered and prepared for GC analysis as described below.

Chemicals. Trifluoroacetic anhydride was purchased from Janssen Chimica (Geel, Belgium), D- and L-arabinitol were purchased from Sigma (St. Louis, Mo.), and dichloromethane, diethyl ether, methanol, and *n*-hexane were purchased from Labscan (Dublin, Ireland). Solvents were of analytical grade and were used without further purification.

Preparation of samples for GC. Cultures and urine samples were filtered (0.45-μm-pore-size celluloseacetate filter from Schleicher & Schuell, Dassel, Germany) to remove solid material. A 0.1-ml aliquot of the filtrate was transferred to a separate test tube, and to this volume was added 0.9 ml of water, 2 to 4 drops of 0.1 M aqueous NaOH, and 0.1 to 0.2 g of solid NaCl; the remaining filtrate was stored in deep-freeze. Two milliliters of ether-hexane (1:1; vol/vol) was then added, and after shaking, the mixture was centrifuged (5 min, 1,000 × *g*). The lower phase was transferred to a new test tube, 4 to 6 drops of 0.1 M HCl was added (to pH < 4.0), and the extraction was repeated. Again, the lower phase was transferred to a new test tube and 6 to 8 drops of 0.1 M NaOH was added (pH 6 to 8); the sample was then evaporated to dryness under a stream of dry nitrogen. Methanol (2 ml) was added to the dried sample, and the test tube was shaken and centrifuged (5 min, 1,000 × *g*); the resulting supernatant was transferred to a new tube and was evaporated to dryness. Dichloromethane and trifluoroacetic anhydride (200 μl of each) were added, and the samples were then heated at 80°C for 10 min and were subsequently analyzed by GC.

Linearity. Amounts of 50, 75, 100, 150, 250, and 500 μg of D-arabinitol were added, respectively, to six solutions of L-arabinitol (50 μg) in water (2 ml). The samples were then derivatized for GC analysis as described above.

GC. A gas chromatograph (model 3700; Varian, Los Altos, Calif.) equipped with a solid-phase "falling needle" injector (Chromtech, Warsaw, Poland) and an electron capture detector (ECD) was used. The fused-silica column (30 m by 0.25 mm [inner diameter]) was coated with 0.25-μm-thick (film thickness) cyclodextrin (Beta Dex-120; Supelco Inc, Bellefonte, Pa.); the column temperature was programmed to rise 4°C/min from 70 to 120°C and then to rise 8°C/min to 190°C. The flow rate of the nitrogen carrier gas through the column was 2 ml/min. The temperature of the injector was 170°C, and that of the detector was 260°C. The chromatograms were evaluated by using a Chrompack Integration System with an IBM PS/2 model 30 computer and a Chrompack BD 70 printer and plotter.

A sample (2 μl) to be injected was placed on the tip of the glass rod of the solid-phase injector. After 1 min, when excess reagent and solvent had evaporated, the sample was introduced into the gas chromatograph.

D-Arabinitol and L-arabinitol were identified by GC-MS. A VG Trio-1S GC-MS system (Fisons, Manchester, United Kingdom) was used; the gas chromatograph was a Hewlett-Packard (Avondale, Pa.) model 5890 equipped with the same type of injector and chiral column used in the GC-ECD analyses (see above). The column temperature was programmed to rise from 90 to 150°C at 4°C/min. Helium was used as the carrier gas, and ammonia (10 lb/in^2) was used as the reagent gas in the negative ion-chemical ionization mode; the ion source temperature was 80°C. Analyses were performed in both the scanning and the selected ion monitoring modes.

RESULTS

GC-MS of arabinitol standard. No degradation of the D- or L-arabinitol trifluoroacetyl (TFA) derivatives was observed after several weeks of storage of the samples at room temperature in an excess of trifluoroacetic anhydride. The GC system enabled baseline resolution of the enantiomer derivatives which eluted from the column after approximately 11 (ECD) and 6 (GC-MS) min. The sensitivity of the ECD was adjusted so that a full-scale response was obtained when approximately 300 pg of the arabinitol TFA derivative was injected (attenuation of detector signal, 640). The calibration curve was linear over the range studied.

The negative ion-chemical ionization mass spectra of the D- and L-arabinitol TFA derivatives were identical. In the high-mass region, ions of mass-to-charge ratio (*m/z*) 518 (loss of trifluoroacetic acid) and *m/z* 632 (molecular ion) dominated (Fig. 1); *m/z* 518 was used for selected ion monitoring.

Analysis of urine samples. The reproducibilities of the D/L-arabinitol ratio determinations were studied. The two urine samples with low and high D/L-arabinitol ratios, respectively, were extracted and analyzed by GC-ECD eight times, resulting in mean (range) ratios of 1.6 (1.5 to 1.9) and 5.9 (5.1 to 6.2). Calculated interassay imprecision (coefficient of variation) percentages for the two samples were 7.7 and 7.6, respectively. As examples, Fig. 2 illustrates GC-ECD chromatograms that were obtained and also shows that the results of GC-MS and GC-ECD analyses of the same samples were very similar.

Thirty-seven hospitalized adult control patients without *Candida* infection or colonization had a mean ± standard deviation (SD) (range) D/L-arabinitol ratio in urine of 1.8 ± 0.4 (1.0 to 2.9). The corresponding values for 24 hospitalized control children with cancer were 2.1 ± 0.7 (1.1 to 4.5) (Table 1). This difference in ratios between adults and children was, however, not significant ($P = 0.097$ by Student's unpaired two-tailed *t* test).

The intraindividual variation of D/L-arabinitol ratios over time was determined by analyzing 120 urine samples from a total of 20 both healthy and hospitalized (non-*Candida*-infected) individuals. The ratios varied between 1.1 and 3.9, with a mean ratio of 2.0. The mean D/L-arabinitol ratio was 2.0 for the

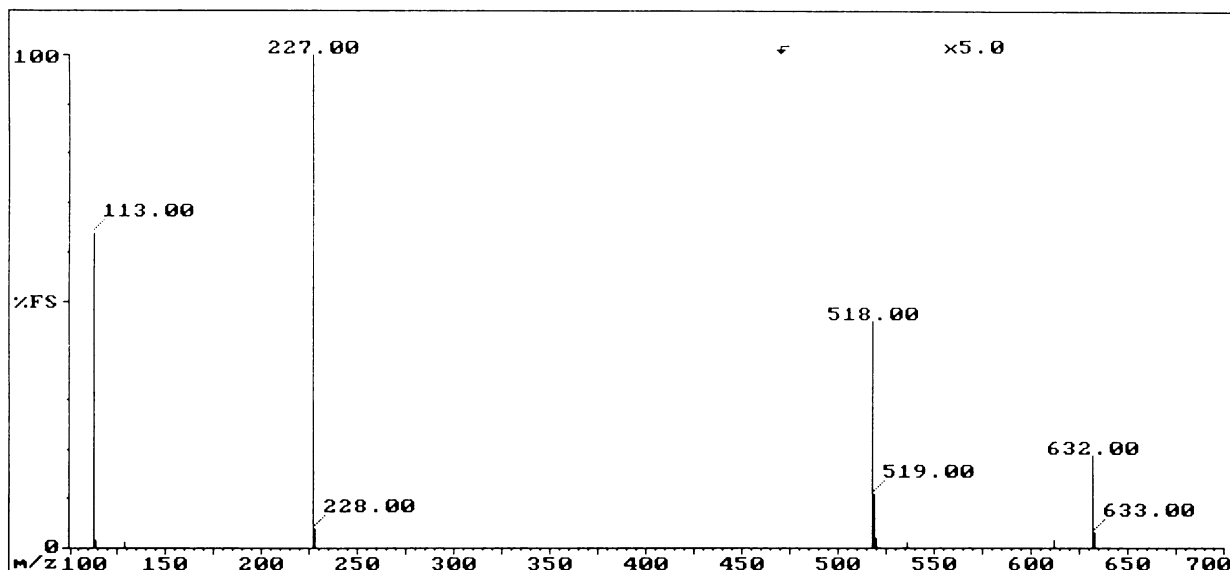

FIG. 1. Negative ion-chemical ionization mass spectrum of trifluoroacetylated D-arabinitol.

healthy children, 2.2 for the hospitalized children, 1.6 for the healthy adults, and 2.0 for the hospitalized adults (Table 1). The individual range varied from 0.2 to 1.4, with the mean of the range being 0.9.

The 10 urine samples that were culture positive for *C. albicans*, although collected from patients without any signs of disseminated candidiasis, had D/L-arabinitol ratios of between 1.3 and 2.5. The five urine samples from patients with vaginitis and oral candidiasis had ratios of between 1.8 and 3.3.

The urine of the patient with non-Hodgkin's lymphoma and disseminated *C. albicans* infection showed a significant increase in D/L-arabinitol ratios during the course of infection (Fig. 3). On days 6 to 12, while the patient was febrile, multiple blood cultures were negative and no antifungal treatment was given. On day 15, oral steroids were instituted and were subsequently continued for 5 days. Fever recurred on day 24, and on day 27 amphotericin B was given as an empiric antifungal treatment. Later, it was revealed that blood cultures were positive for *C. albicans* on days 28, 33, 35, and 36. The patient did not respond to antifungal treatment but died from multiorgan failure on day 52. Retrospectively, D/L-arabinitol ratios were analyzed, showing a significant increase several days before the patient again became febrile and blood cultures were positive.

Analysis of *Candida* cultures. Incubation of *C. albicans* in the culture-negative urine sample for 3 days at 37°C and then for 11 days at 4°C did not affect the D/L-arabinitol ratio; i.e., the value was constant at 1.6.

Overnight incubation of the two urine samples culture positive for *C. albicans* gave divergent results. In one sample (containing 8×10^5 CFU), the D/L-arabinitol ratio was constant at 1.6; in the other sample (containing 3×10^3 CFU), the ratio increased from 2.0 to 2.3 (incubation at 20°C) or 2.8 (incubation at 37°C).

D-Arabinitol was detected in the broth cultures of all strains studied except *S. cerevisiae* and *T. glabrata*; *C. krusei*, however, produced only trace amounts. Absolute quantifications were not made.

DISCUSSION

Considerable efforts have been made to improve current diagnostic techniques for deep-seated *Candida* infections. Lysis-centrifugation blood culturing was reported to improve the detection of fungemia in comparison with the use of biphasic medium. In one study, samples from 73% of patients with histologically proven cases of disseminated candidiasis were positive by the lysis-centrifugation method and the mean time for recovery of *Candida* spp. was 3.8 days (range, 1 to 21 days) (16). Of the non-culture-based methods, antibody tests are of limited value because most cases of fungal infection occur in immunocompromised individuals. Improved methods for the detection of marker antigens and amplified DNA are being developed, although at present, the sensitivities and specificities of these procedures are unsatisfactory (9).

Although the "arabinitol method" was first suggested almost 15 years ago, it has seldom been routinely applied in clinical laboratories. One reason for this was the low diagnostic specificity because total arabinitol was measured (without separation of the optical enantiomers) and because of interference by renal dysfunction. To increase the specificity of the method, the method was improved in two ways: (i) arabinitol levels were related to renal function, as roughly estimated by creatinine levels in serum (4, 18), and (ii) the D-enantiomer of arabinitol was selectively measured by analyzing total arabinitol levels both before and after sample incubation with a strain of *C. tropicalis* that specifically consumed D-arabinitol (2). An automated enzymatic method with D-arabinitol dehydrogenase from *C. tropicalis* was described recently (15), but again, the results must be related to renal function. In the late 1980s, chromatographic separation of D- and L-arabinitol was achieved. The advantage of chiral separation of the two enantiomers is that internal (or external) standardization for quantitation is not required because only the ratios of the D/L-arabinitol enantiomers are measured. In addition, D/L-arabinitol ratios are not influenced by renal dysfunction (12). Unfortunately, not even in very recent studies on arabinitol in

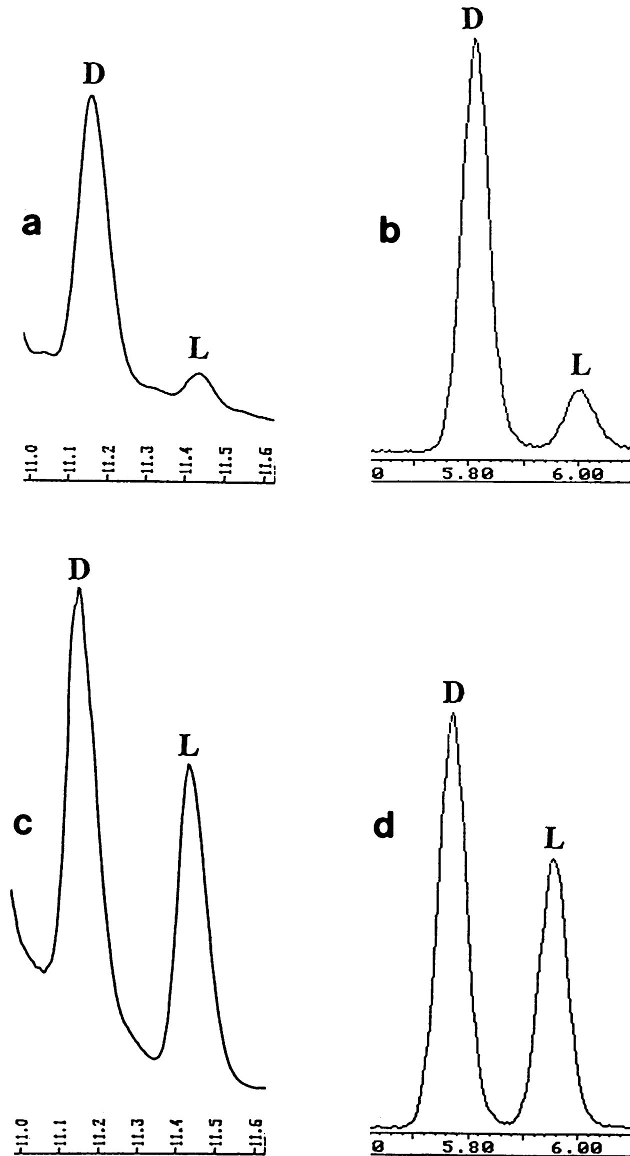

FIG. 2. Separation of D- and L-arabinitol in two urine samples analyzed by GC-ECD (a and c) and GC-MS with selected ion monitoring at m/z 518 (b and d). One sample came from a patient with disseminated *C. albicans* infection (a and b; D/L-arabinitol ratio, 5.9) and the other came from a healthy individual (c and d; D/L-arabinitol ratio, 1.6).

relation to candidiasis has chiral separation been extensively applied (7, 8, 17).

To date, GC-MS and the so-called multidimensional GC have been used to determine D/L-arabinitol ratios in clinical specimens. When using the latter technique, the sample is first separated on a precolumn, and a selected fraction is thereafter transferred to a cold trap which is then heated to introduce the fraction into the analytical column; thus, an efficient on-line sample purification is achieved. We have previously applied multidimensional GC to detect specific hydroxylated and branched-chain bacterial fatty acids in clinical samples (6, 14), but in comparison, the GC method used in the present study is more straightforward and far better suited for routine application since standard GC instrumentation is sufficient. The

TABLE 1. D/L-Arabinitol ratios for various groups of non-*Candida*-infected or colonized controls

Group[a]	Mean (range) D/L-Arabinitol ratio
Hospitalized adults (n = 37/1)	1.8 (1.0–2.9)
Hospitalized children (n = 24/1)	2.1 (1.1–4.5)
Hospitalized adults (n = 5/6)	2.0 (1.7–2.4)
Nonhospitalized adults (n = 5/6)	1.6 (1.1–2.7)
Hospitalized children (n = 5/6)	2.2 (1.2–3.6)
Nonhospitalized children (n = 5/6)	2.0 (1.3–3.9)

[a] n equals the number of individuals in the group/number of urine samples obtained from each individual.

results of the GC-ECD and GC-MS analyses were similar, although a drift in the baseline did appear when using GC-ECD (Fig. 2), which may lower the precision of the integration of peak areas. Clearly, because of its superior inherent specificity, GC-MS is the preferred method for the clinical determination of D/L-arabinitol ratios, provided that it is available for routine application.

The GC system described here was designed to minimize the risk of contaminating the chiral column. This was accomplished in several ways: (i) by using TFA derivatization with ECD, thus ensuring that only a minimal amount of sample is required for analysis, since this detector is highly sensitive to halogenated compounds; (ii) by using a solid-phase injector to prevent excess reagents and solvents from entering the column and being exposed to the ECD; (iii) by increasing the column temperature to 190°C after each run to remove compounds eluting late, and thus prevent the coelution of the arabinitol TFA derivative with compounds carried over from earlier injections; and (iv) by purifying the urine samples, i.e., performing extractions with organic solvents at both high and low pHs, before analysis. The principal potential advantage of analyzing urine instead of blood is that the amounts of arabinitol are about 60 times higher in the former (12, 13). The GC method described here is not suitable for analyzing blood

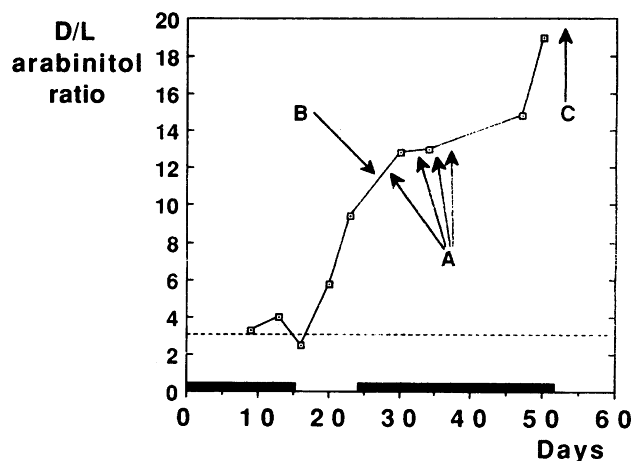

FIG. 3. D/L-Arabinitol ratios in urine from a 13-year-old girl with disseminated candidiasis. (A) Blood cultures positive for *C. albicans*; (B) onset of antifungal chemotherapy; (C) death of the patient. The horizontal black bar indicates a body temperature of >38.3°C. The interrupted line at 3.0 corresponds to the mean + 3 SD D/L-arabinitol ratio of hospitalized adult controls without disseminated *Candida* infection.

or serum because of interference from coeluting compounds (data not shown).

The mean ± SD (range) D/L-arabinitol ratio in the 37 adult control patients was 1.8 ± 0.4 (1.0 to 2.9). This agrees well with the results of Roboz et al. (12), who found that the corresponding ratios for 13 urine samples from healthy subjects were 1.75 ± 0.4 (1.31 to 2.43). In 23 control children, the mean ± SD (range) ratios were slightly, but not significantly, higher, i.e., 2.1 ± 0.7 (1.1 to 4.5). The reproducibility of the method was satisfactory (coefficient of variation, $<8\%$), but because of normal biological variation, D/L-arabinitol ratios could increase or decrease by up to 1.4 units over time.

Many antibiotic-treated hospitalized patients, especially those with urinary catheters, often develop urinary tract *Candida* colonization. Therefore, we attempted to determine whether local D-arabinitol production could lead to a false diagnosis of disseminated candidiasis. This was not, however, found to be the case, since these patients, as well as those with oral and vaginal candidiases, showed D/L-arabinitol ratios similar to those of healthy controls. Also, there was no significant increase in D/L-arabinitol ratios upon incubation of *Candida* spp. in urine.

Using a rat model, Wong et al. (19) were unable to show that gastrointestinal colonization with *C. albicans* had any effects on arabinitol levels in serum or urine. However, when the rats were given intragastric antibiotics, minor and transient increases in urinary arabinitol levels were detected; D/L-arabinitol ratios were not determined. The authors speculated that antibiotics caused increased arabinitol excretion by suppressing gastrointestinal tract bacteria that are capable of consuming dietary arabinitol.

In summary, we showed that a straightforward GC method can be conveniently used to determine D/L-arabinitol ratios in urine, and this method is therefore suitable for routine application. The data presented here indicate that disseminated candidiasis can be diagnosed before blood cultures become positive, especially when serial samples are used. Local colonization of *C. albicans* in the urinary tract did not interfere with the test result. The test should be widely applicable since most clinically important *Candida* spp. produce D-arabinitol. A prospective study of a large number of patients at risk for candidiasis is in progress to determine the predictive value of this method for diagnosing disseminated candidiasis.

ACKNOWLEDGMENTS

This study was supported by grants from The Children Cancer Foundation of Sweden, The Medical Faculty of Lund University, and the Royal Physiographic Society in Lund.

Elke Delfs, Åsa Hjort, and Srinivas Alugupalli are gratefully acknowledged for expert technical assistance.

REFERENCES

1. **Bernard, E. M., K. J. Christiansen, S. Tsang, T. E. Kiehn, and D. Armstrong.** 1981. Rate of arabinitol production by pathogenic yeast species. J. Clin. Microbiol. **14:**189–194.
2. **Bernard, E. M., B. Wong, and D. Armstrong.** 1985. Stereoisomeric configuration of arabinitol in serum, urine, and tissues in invasive candidiasis. J. Infect. Dis. **151:**711–715.
3. **Christensson, B., and J. Roboz.** 1991. Arabinitol enantiomers in cerebrospinal fluid. J. Neurol. Sci. **105:**234–239.
4. **Gold, J. W. M., B. Wong, E. M. Bernard, T. E. Kiehn, and D. Armstrong.** 1983. Serum arabinitol concentrations and arabinitol/creatinine ratios in invasive candidiasis. J. Infect. Dis. **147:**504–513.
5. **Kiehn, T. E., E. M. Bernard, J. W. M. Gold, and D. Armstrong.** 1979. Candidiasis: detection by gas-liquid chromatography of d-arabinitol, a fungal metabolite, in human serum. Science **206:** 577–580.
6. **Larsson, L., J. Jimenez, A. Sonesson, and F. Portaels.** 1989. Two-dimensional gas chromatography with electron capture detection for the sensitive determination of specific mycobacterial lipid constituents. J. Clin. Microbiol. **27:**2230–2233.
7. **Lehtonen, L., A. Rantala, P. Oksman, E. Eerola, and O. P. Lehtonen.** 1993. Determination of serum arabinitol levels by mass spectrometry in patients with postoperative candidiasis. Eur. J. Clin. Microbiol. Infect. Dis. **12:**330–335.
8. **McSharry, C., C. Lewis, G. Cruickshank, and M. D. Richardson.** 1993. Measurement of serum arabinitol by gas-liquid chromatography: limitations for detection of systemic candidia infections. J. Clin. Pathol. **46:**475–476.
9. **Reiss, E., and C. J. Morrison.** 1993. Nonculture methods for diagnosis of disseminated candidiasis. Clin. Microbiol. Rev. **6:**311–323.
10. **Roboz, J., D. C. Kappatos, and J. F. Holland.** 1987. Role of individual serum pentitol concentrations in the diagnosis of disseminated visceral candidiasis. Eur. J. Clin. Microbiol. **6:**708–714.
11. **Roboz, J., and R. N. Katz.** 1992. Diagnosis of disseminated candidiasis based on serum D/L-arabinitol ratios using negative chemical ionization mass spectrometry. J. Chromatogr. **575:**281–286.
12. **Roboz, J., E. Nieves, and J. F. Holland.** 1990. Separation and quantification by gas chromatography-mass spectrometry of arabinitol enantiomers to aid the differential diagnosis of disseminated candidiasis. J. Chromatogr. **500:**413–426.
13. **Roboz, J., Q. Yu, and J. F. Holland.** 1992. Filter paper sampling of whole blood and urine for the determination of D/L arabinitol ratios by mass spectrometry. J. Microbiol. Methods **15:**207–214.
14. **Sonesson, A., L. Larsson, R. Andersson, N. Adner, and K.-G. Tranberg.** 1990. Use of two-dimensional gas chromatography with electron capture detection for the measurement of lipopolysaccharide in peritoneal fluid and plasma from rats with induced peritonits. J. Clin. Microbiol. **28:**1163–1168.
15. **Switchenko, A. C., C. G. Miyada, T. C. Goodman, T. J. Walsh, B. Wong, M. J. Becker, and E. F. Ullman.** 1994. An automated enzymatic method for measurement of D-arabinitol, a metabolite of pathogenic *Candida* species. J. Clin. Microbiol. **32:**92–97.
16. **Telenti, A., and G. D. Roberts.** 1989. Fungal blood cultures. Eur. J. Clin. Microbiol. Infect. Dis. **8:**825–831.
17. **Tokunaga, S., M. Ohkawa, M. Takashima, and H. Hisazumi.** 1992. Clinical significance of measurement of serum D-arabinitol levels in candiduria patients. Urol. Int. **48:**195–199.
18. **Wong, B., E. M. Bernard, J. W. M. Gold, D. Fong, and D. Armstrong.** 1982. The arabinitol appearance rate in laboratory animals and humans: estimation from the arabinitol/creatinine ratios and relevance to the diagnosis of candidiasis. J. Infect. Dis. **146:**353–359.
19. **Wong, B., K. L. Brauer, J. R. Clemens, and S. Beggs.** 1990. Effects of gastrointestinal candidiasis, antibiotics, dietary arabinitol, and cortisone acetate on levels of the *Candida* metabolite D-arabinitol in rat serum and urine. Infect. Immun. **58:**283–288.
20. **Wong, B., and M. Castellanos.** 1989. Enantioselective measurement of the *Candida* metabolite D-arabinitol in human serum using multidimensional gas chromatography and a new chiral phase. J. Chromatogr. **495:**21–30.