Urine Specific Gravity and Other Urinary Indices

Inaccurate Tests for Dehydration

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Objective: Urine output, specific gravity, and ketones (urinary indices) are commonly used as an objective means to assess for dehydration and gastroenteritis severity; however, their utility has not been established. The study was designed to evaluate the accuracy of urinary indices as diagnostic tests to identify acute dehydration.

Methods: We completed a prospective cohort study in the Emergency Department of an urban pediatric hospital. Seventy-nine subjects ages 3 months to 36 months with gastroenteritis, clinically suspected moderate dehydration, and the need for intravenous rehydration were enrolled in the trial. Urine specific gravity and urine ketone levels were determined with bedside calorimetric (dipstick) testing, and urine output during rehydration and observation was measured by commonly used techniques. An internally validated, weight-based criterion standard for the percent dehydration on enrollment was used to identify the cohort of dehydrated subjects. Correlation statistics were calculated for urine output, specific gravity, and ketones. In addition, multilevel tables were created to determine the sensitivity, specificity, and likelihood ratio at varying test cutoff values to detect 3% and 5% dehydration.

Results: Urine specific gravity ($r = -0.06$, $P = 0.64$), urine ketones ($r = 0.08$, $P = 0.52$), and urine output during rehydration ($r = 0.01$, $P = 0.96$) did not correlate with the initial degree of dehydration present. Clinically useful cutoff values for urine specific gravity and ketones to increase or decrease the likelihood of dehydration at the time of enrollment could not be identified.

Conclusions: Urinary indices are not useful diagnostic tests to identify the presence of dehydration during the initial assessment of children with gastroenteritis.

Key Words: dehydration, gastroenteritis, diagnosis, urinalysis, specific gravity

Dehydration is one of the leading causes of morbidity and mortality in children throughout the world.[1–3] In the United States, more than 2 million office visits, 10% of hospital admissions, and 2 billion dollars in direct medical costs occur annually because of dehydration associated with gastroenteritis.[2–5] Dehydration is associated with many other pediatric illnesses and the ability to accurately assess hydration status is an important skill for all emergency department physicians and other pediatrics practitioners. Treatment guidelines for children frequently stress the importance of dehydration assessment, especially in the care of children with gastroenteritis.[2,6–8]

Clinicians caring for ambulatory pediatric patients assess hydration status primarily by physical examination, but historic details and laboratory values are also incorporated into the evaluation. Despite the importance of an accurate hydration assessment, a recent systematic review and meta-analysis found that most individual historic points, examination signs, and laboratory tests to detect dehydration lack accuracy and precision.[9]

Urine output and urine specific gravity are often used as tests to determine dehydration among patients in ambulatory settings. This practice is based on the physiologic principle that as children become dehydrated, renal compensation will decrease urine volume and increase the urine concentration.[10–13] In addition, many illnesses that cause dehydration have a concurrent decrease in oral carbohydrate intake leading to an increase in fatty acid oxidation and the presence of serum and urine ketones.[14] Although ketosis is not directly caused by dehydration, many clinicians use ketonuria as an indication of inadequate oral intake, severity of illness, and consider it suggestive of dehydration. Both urine ketones and urine specific gravity can be assessed quickly and inexpensively through the calorimetric or dipstick method by clinicians at the bedside. Pediatric textbooks and commonly used dehydration assessment scales reinforce the utility of these urinary indices in the evaluation of dehydration.[2,15–18]

Despite widespread use and physiological plausibility, the validity of urinary indices to assess dehydration has not been adequately studied. We designed this study to evaluate the utility of measuring urine specific gravity, urine ketone levels, and the urine output during rehydration to identify dehydration in children with gastroenteritis presenting to an emergency department.

METHODS

Study Design

This prospective cohort study enrolled a convenience sample of subjects with gastroenteritis, clinically diagnosed

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Dr. Steiner is currently working in the Department of Pediatrics at The University of North Carolina School of Medicine. He had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Extramural funding was not obtained for this study, and the hospital and university had no role in the design and conduct of the study.

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ISSN: 0749-5161/07/2305-0298

dehydration, and the need for intravenous fluid rehydration. The study cohort was the subset of this group who had moderate (≥3% or ≥5%) dehydration confirmed by the weight-based criterion standard. The control subjects met all of the clinical enrollment criteria, but in actuality, were not moderately dehydrated based on the criterion standard.

The institutional review board at Childrens Hospital Los Angeles approved this study as part of a larger ongoing study to assess the safety and efficacy of ultrarapid intravenous rehydration in the emergency department. Assent was not obtained because of the young age of subjects; however, consent was obtained from parents or legal guardians.

Study Setting and Population

This study was conducted in the emergency department of an urban pediatric teaching hospital that has approximately 62,000 annual visits.

Children were included if they were 3 months to 36 months of age, had presumed viral gastroenteritis, and were estimated to have moderate dehydration as determined by a standard pediatric dehydration scale.[19] In addition, the treating physician had to decide that the child required intravenous rehydration due to the failure of oral rehydration therapy (refusal, recurrent emesis, or inadequate intake).

Children with an underlying chronic medical condition where rapid volume infusion could be injurious were excluded (eg, chronic lung disease, renal disease, or congenital heart disease). In addition, subjects were withdrawn if a new diagnosis requiring a change in therapy became evident during the study protocol.

Study Protocol

Upon entering the emergency department, subjects had a baseline weight obtained on an electronic scale by a standard protocol. After enrollment, a urine sample was collected primarily by catheterization or by spontaneous void if this occurred before intravenous fluid administration. Subjects were randomized to receive 50 mL/kg of isotonic sodium chloride solution over either 1 or 3 hours based on the protocol of the companion study. Vital signs, oral intake, urine and stool output, and physical examination were monitored every hour during therapy. After intravenous hydration, subjects were given an oral fluid challenge, and a repeat urine sample was collected by spontaneous void or rarely by catheterization. Subjects were then reweighed on the same scale and by the same protocol as initially used.

Subjects were considered rehydrated and discharged home if they tolerated oral fluids without emesis, had normal vital signs, capillary refill time, tears with crying, and moist mucous membranes after hydration. Subjects who failed to meet these criteria were admitted to the hospital for further observation and therapy. Study personnel contacted families the day after emergency department discharge to obtain clinical follow-up information.

Measurements

Body weight before and after intravenous hydration was recorded. Total urine volume after enrollment was documented, and the urine output in milliliters per kilogram of rehydrated weight per hour of protocol time was calculated. In addition, for children who were rehydrated over 3 hours, the number of subjects with increasing urine output during hydration was noted. A visual calorimetric analysis was carried out by the bedside nurse or the physician on both urine samples using Multistix-10 SG urinalysis strips (Bayer Healthcare Diagnostics Division, Tarrytown, NY). Urine specific gravity and urine ketone levels before and after rehydration were extracted from those results.

Criterion Standard

The criterion standard or gold standard for the initial degree of dehydration in each subject was determined by calculating the difference between the initial weight at enrollment and the final rehydrated weight, dividing that by the rehydrated weight, and transforming that into a percentage dehydrated.

A weight-based criterion standard calculated with an ill weight and a post-illness weight has been frequently used and validated in the literature.[9,20–29] However, this is one of the only studies to use an immediate posthydration weight instead of the post-illness weight as a well weight surrogate in that calculation.[30] To validate the posthydration weight as a surrogate for the well weight, we searched for previously documented well weights for all subjects using the method described by Gorelick et al.[20] Medical charts were reviewed for each subject enrolled. If a well weight was obtained within 10 days of this illness, then that weight was directly extracted. Other children had a well weight extrapolated if they had 3 or more weights documented within a year of study enrollment and those weights were all within 10 growth percentiles of each other. For children who met that criteria, the well weight was determined by calculating the mean of those consistent weight percentiles, and then an electronic growth chart was used to extrapolate the weight at the time of enrollment based on that percentile mean (STAT GrowthCharts, Austin Physician Productivity, 2000).

Data Analysis

Spearman coefficient of rank correlation was used to establish the correlation between urine specific gravity, ketones, output, and the degree of dehydration present. Before statistical analysis, urine ketone descriptive values were transferred to a commonly used numerical scale of 0 (no ketones), 1 (slight or trace ketones), 2 (moderate ketones), and 3 (large ketones). The Centers for Disease Control and Prevention gastroenteritis management guideline that has been adopted by the American Academy of Pediatrics uses 3% as the lower limit of clinically important dehydration.[2] Previous research and other commonly taught pediatric dehydration assessment scales use greater than 5% as the cutoff limit for moderate dehydration.[15,16,20,21,24,26] Therefore, we created multilevel tables to calculate sensitivities, specificities, likelihood ratios (LRs), and confidence intervals (CIs) for varying cutoffs of the urine specific gravity and urine ketones to detect both 3% and 5% dehydration. All statistical analyses were carried out using Microsoft Excel spreadsheet programs (Microsoft Corp, Redmond, Wash) and STATA 8.0 (Stata Corp, College

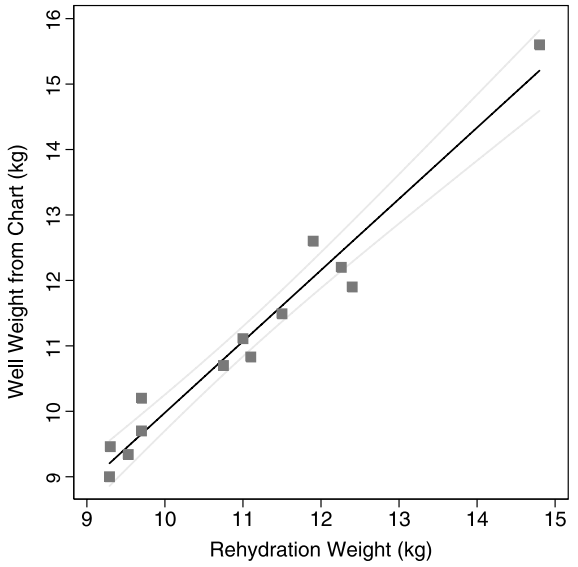

FIGURE 1. Scatter plot and regression line for rehydration weight and corresponding well weight from chart.

Station, Tex). Confidence intervals for the LRs were calculated in the method recommended by Simel et al.[31]

RESULTS

Subject Characteristics

Seventy-nine subjects were enrolled in this study. Four of these subjects were eventually excluded, leaving 75 for full analysis. The mean age of included subjects was 17.3 months. Three subjects had a history of diarrhea without vomiting, 11 had vomiting without diarrhea, and 61 of 75 subjects had both vomiting and diarrhea before enrollment.

The range of dehydration in our subjects was 0.1% to 7.9%. Fifty of 75 included subjects were at least 3% dehydrated, and 16 of the subjects were at least 5% dehydrated by the weight-based criterion standard.

Two of the subjects were excluded from analysis because of refractory hypokalemia, and 1 child was excluded because of hypernatremia. The treating physicians believed that these children needed specific therapy beyond the study protocol, and therefore they were withdrawn from the study. A fourth subject had excessive ongoing stool losses necessitating a change in therapy and exclusion. No children were admitted to the hospital solely because of failure to meet the clinical rehydration criteria. There was no statistically significant difference between the 4 excluded subjects and the included sample with regard to age (17.3 and 18.4 months, respectively, $P = 0.94$), percent dehydration (3.5% and 3.9%, $P = 0.98$), urine output during hydration (4.7 and 5.3 mL/kg per hr, $P = 0.91$), initial urine specific gravity (1.024 and 1.025, $P = 0.56$), or initial degree of ketonuria (1.5 plus and 1.6 plus, $P = 0.77$).

Validity of Criterion Standard

Thirteen of the enrolled subjects or 16% of the sample had well weight information available from the medical record. Eight subjects had a well weight obtained within 10 days of enrollment, and we were able to extrapolate a well weight from 5 other subjects.

There was a high degree of correlation between the rehydrated weights and the well weights (Spearman $\sigma = 0.97$, $P < 0.001$). Linear regression of the well weights and the rehydrated weights are displayed in Figure 1. The slope of the regression line was 1.09 ($P < 0.001$; 95% CI, 0.94 to 1.24) and the y intercept was -0.91 ($P = 0.26$, 95% CI, -2.58 to 0.76). Six subjects had well weights that were higher than their rehydrated weights; 7 subjects had well weights that were lower than their rehydrated weights.

As an additional evaluation for the accuracy of the rehydration weight as a well weight surrogate, sample calculations for test characteristics of urine were carried out for the children with available well weight information. Two subjects would have been reclassified with greater than 5% dehydration using the well weight, and 1 subject would no longer have been considered dehydrated. These alterations would not have caused important changes in the underlying test characteristics.

Diagnostic Test Characteristics

Urine specific gravity of enrolled subjects was not significantly correlated with their degree of dehydration

TABLE 1. The Test Characteristics of Urine Specific Gravity to Detect 3% Dehydration

Specific Gravity Values	Subjects (≥3% Dehydration)	Controls (<3% Dehydration)	Total	Sensitivity	Specificity	LR Positive
1.030	32	16	47	64.0 (49.2, 77.1)	40.0 (21.1, 61.3)	1.1 (0.7, 1.6)
1.025	4	3	7	72.0 (57.5, 83.8)	28.0 (12.1, 49.4)	1.0 (0.7, 1.4)
1.020	7	2	9	86.0 (73.3, 94.2)	20.0 (6.8, 40.7)	1.1 (0.9, 1.4)
1.015	4	4	8	94.0 (83.5, 98.8)	4.0 (0.1, 20.4)	0.98 (0.87, 1.12)
1.010	1	0	1	96.0 (86.3, 99.5)	4.0 (0.1, 20.4)	1.0 (0.9, 1.1)
1.005	2	1	3	100	0	1
Total	50	25	75			

Sensitivity, specificity, and LR positivity are expressed as % and/or CI.

TABLE 2. The Test Characteristics of Urine Specific Gravity to Detect 5% Dehydration

Specific Gravity Values	Subjects (≥5% Dehydration)	Controls (<5% Dehydration)	Total	Sensitivity	Specificity	LR Positive
1.030	6	41	47	37.5 (15.2, 64.6)	30.5 (19.2, 43.9)	0.54 (0.30, 1.04)
1.025	2	5	7	50.0 (24.7, 75.4)	22.0 (12.3, 34.7)	0.64 (0.41, 1.07)
1.020	3	6	9	68.8 (41.3, 89.0)	11.9 (4.9, 22.9)	0.78 (0.58, 1.01)
1.015	3	5	8	87.5 (61.7, 98.5)	3.4 (0.4, 11.7)	0.91 (0.76, 1.10)
1.010	0	1	1	87.5 (61.7, 98.5)	1.7 (0.04, 9.1)	0.90 (0.75, 1.07)
1.005	2	1	3	100	0	1
Totals	16	59	75			

Sensitivity, specificity, and LR positivity are expressed as % and/or CI.

($r = -0.06$, $P = 0.64$). Tables 1 and 2 demonstrate that after the creation of multilevel tables, we were unable to identify clinically useful test characteristics for urine specific gravity. No cutoff level increased or decreased the likelihood of either 3% or 5% dehydration to a statistically significant degree. As expected, the urine specific gravity of individual subjects did decrease after rehydration (1.025 and 1.018, respectively, Wilcoxon signed rank test, $P < 0.001$).

Because of concern that young children may not be able to maximally concentrate their urine, we carried out subset analysis based on age. There was no correlation between the urine specific gravity and the degree of dehydration in the subset of subjects 18 months of age or older ($r = 0.08$, $P = 0.64$).

In these children with gastroenteritis, urine ketone levels were not correlated with the parental report of emesis frequency ($r = 0.16$, $P = 0.16$), length of illness ($r = -0.03$, $P = 0.82$), or degree of dehydration ($r = 0.08$, $P = 0.52$). Similarly to specific gravity, no degree of ketonuria increased the likelihood of 3% or 5% dehydration (LR positive point estimate range, 0.94 to 1.12). The amount of urine ketones did not decrease after rehydration ($P = 0.67$).

Urine output after enrollment and during the period of rehydration and observation did not correlate with the degree of dehydration that had been present when the subjects were enrolled ($r = 0.01$, $P = 0.96$). Thirty-one of 37 subjects randomized to the 3-hour rehydration group had increasing urine output during therapy. This characteristic had a sensitivity of 89% to detect 5% dehydration at presentation (95% CI, 51.8 to 99.7). However, an increase in urine output had a specificity of only 18% (95% CI 6.1 to 36.9) and likelihood ratios that did not statistically change the odds that dehydration had been present (LR positive 1.1, 95% CI, 0.84 to 1.44; LR negative 0.62, 95% CI, 0.08 to 4.65).

Although no subjects were anuric during the period of treatment, 7 subjects had oliguria (<0.5 mL/kg per hr) from the time of enrollment until discharge. None of these children were greater than 5% dehydrated; however, 3 (43%) of 7 returned to the emergency department for further therapy later in the course of their illness. Only 8 (12%) of 68 children with normal urine output returned to the emergency department during their illness. That difference was statistically significant (Mann-Whitney U test, $P = 0.03$).

DISCUSSION

Common clinical teaching suggests that an elevated urine specific gravity and decreased urine output are helpful to identify children with dehydration.[12,15,16,18] This observation has largely been based on our understanding of renal physiology instead of the evaluation of these diagnostic tests in clinical settings where they are used. Based on the results of our study, an elevated urine specific gravity and elevated levels of urine ketones determined with bedside dipstick testing are not helpful diagnostic tests to determine whether children with gastroenteritis are dehydrated. In addition, a low urine output during rehydration did not accurately predict dehydration severity at the time of presentation.

Previous research into the relationship between urinary indices, urine volume, and the degree of dehydration in acutely ill children has produced results similar to this study. English et al[23] and Teach et al[24] did not find an association between the urine specific gravity and the degree of dehydration in acutely ill ambulatory children. Neither of those authors evaluated cutoff values for specific gravity that could be replicated by clinicians and used as tests for dehydration. A recently published study by Neville et al[32] also documented a wide range of urine osmolalities in children presenting with gastroenteritis and clinically determined dehydration. Our study is the first to present dehydration data at varying cutoff levels of urine specific gravity. These findings reinforce all of the previously published data and demonstrate that urine specific gravity values are broadly distributed in mild and moderate dehydration, and in addition, that there is no specific gravity cutoff level with clinically useful test characteristics.[23,24,32]

We are unaware of previous studies that have directly assessed the presence of urine ketones as a test for gastroenteritis severity and dehydration. Teach et al[24] assessed serum anion gap as a diagnostic test for dehydration. Serum ketones and other unmeasured anions such as lactic acid could contribute to an elevated anion gap in the serum. As a test for dehydration in children with gastroenteritis, an elevated anion gap did not increase the odds of dehydration.[24]

Our findings for urine ketone levels mirror the previous negative findings for serum anion gap by Teach et al.[24]

Three different authors have included the parental report of urine output in the clinical assessment of dehydration.[20–22] A meta-analysis of their findings demonstrated that a reported history of low urine output did not accurately predict dehydration.[9] Although we did not assess parental report of prior urine output, we did objectively quantify urine output during clinical treatment and its relationship to dehydration at the time of presentation. We are unaware of previous studies that have examined the diagnostic use of this procedure in this clinical setting. Our study suggests that measuring urine output by the commonly used, but often inaccurate, combination of adhesive urine bag, diaper weight, and spontaneous elective void does not have clinical utility to assist with the identification of dehydrated children. However, based on the high rate of return to the emergency department in children with low urine outputs, ongoing oliguria may be a marker for other aspects of disease severity and suggestive of the need for more intense or ongoing therapy.

The use of a definitive criterion standard is crucial for studies of diagnostic tests.[33,34] Although debate exists, the generally accepted criterion standard for the degree of dehydration is the difference between the ill weight and the well weight for the child expressed as a percentage of the well weight.[9,20,35] One potential limitation of our article is the use of an immediate rehydration weight instead of an established well weight to calculate the initial percent dehydration. A previous study by Friedman et al[30] also used a weight obtained soon after aggressive rehydration as a surrogate for the well weight. Because of the importance of the criterion standard and the lack of validation of the rehydration weight in the Friedman study, we attempted to validate the rehydration weight as a well weight surrogate. The rehydrated weights in this study were directly compared with previously documented well weights for a subset of subjects. The weights demonstrated a high degree of correlation, and the point estimate of the *y* intercept was not statistically different from zero. The *y* intercept did display a trend suggestive of potential systematic overhydration. This risk of overhydration if excess intravenous fluid was infused should have been minimized by rapid renal adjustment and increased urine output. The potential risk of systematic underhydration was mitigated by the study protocol that used the normalization of clinical examination findings, such as moist mucous membranes and a normal capillary refill time to assure adequate hydration after intravenous fluid administration. The high degree of correlation between well and rehydrated weights and the lack of statistically significant unidirectional bias suggests that meeting the clinical criteria in this protocol prevents underhydration and that overhydration also did not occur. Because of our small sample size, further studies should confirm this criterion standard before it is widely adopted in dehydration research.

Another limitation of our study is that all subjects were thought to be dehydrated based on initial clinical assessment. In reality, many were not truly dehydrated based on our criterion standard; however, spectrum bias can occur when a diagnostic test is evaluated in a population preselected for the presumed presence of the underlying disease (in this case, dehydration).[36] This phenomenon can produce test characteristics that seem better than if the test was applied to an unselected population. Because the test characteristics of urinary indices were not helpful to predict dehydration in our preselected population, it is very unlikely that the tests will be useful in children solely at risk for dehydration.

Limitations in the timing and collection of urine samples might explain the discrepancy between urine specific gravity results and volume status. For example, rapid blood loss in a child would stimulate an immediate increase in free water absorption and urine concentration, however, the urine in the bladder at that instant would still be dilute. It is unlikely that rapid volume changes similar to this scenario produced a sampling error in the setting of a protracted dehydrating process such as diarrhea and vomiting.

Urine specific gravity measured by refractometry is highly correlated with urine osmolality in most clinical settings.[37–40] However, the accuracy of bedside calorimetric assessment used in this study and elsewhere has been questioned.[40,41] Measurement inaccuracy might have contributed to the lack of correlation between urinary indices and dehydration in our study. Urine dipsticks are often used for assessment because they are quick, inexpensive, and easy to use. Future dehydration research could use refractometer-determined specific gravity or osmolality measurement to assess urine concentration. However, the relatively high cost, time, and effort associated with performing those tests decrease their practical use in ambulatory clinical settings, even if they demonstrated diagnostic effectiveness.

The clinical literature on urine specific gravity in the assessment of dehydration seems to be different than our understanding of the basic mechanisms of renal adaptation to hypovolemia. Ongoing research in renal physiology may help explain why urinary indices have not demonstrated accuracy in predicting dehydration in clinical studies. For example, previous research has elegantly demonstrated that even isonatremic fluid deficits in gastroenteritis cause a decrease of intravascular volume that is proportional to the degree of dehydration.[42] This intravascular component of the fluid deficit should quickly elicit renal compensatory mechanisms including sodium retention.[10,11] However, Neville et al[32] recently demonstrated surprisingly high urinary sodium concentrations and fractional sodium excretions in children with gastroenteritis and dehydration. The dysfunction of sodium retention during dehydration and nonosmotic causes of antidiuretic hormone release predisposed their subjects to dilutional hyponatremia during rehydration. The clinical data on urinary indices in dehydration may help to stimulate further basic science research into the complex interaction between dehydration, gastroenteritis, neurohormonal activation, and renal physiology.

There were some clinical measurements in our study that did reinforce standard physiological principles of renal filtration and reabsorption. The urine specific gravity decreased after subjects were rehydrated. Similarly, most subjects with a 3-hour rehydration period had an increase in

urine output. These 2 findings suggest that as individual children are rehydrated, their urine output increases and urine specific gravity decreases. Despite individual trends, initial values are inconsistently dispersed which makes them invalid tools for dehydration assessment.

This study demonstrates that urine specific gravity, ketone levels, and measurements of urine output during hydration are not valid methods to determine the degree of dehydration in children with gastroenteritis. In fact, the validity of using these measures to assess the hydration status of previously well ambulatory children has never been confirmed in a clinical trial. Therefore, we recommend that bedside urinary indices not be used to assess hydration status in these settings.

ACKNOWLEDGMENTS

The authors thank Susan Wu, MD, for her thoughtful manuscript review and Anne Z. Steiner, MD, MPH, for the provision of statistical expertise.

REFERENCES

1. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet*. 2003;361:2226–2234.
2. King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm Rep*. 2003;52:1–16.
3. American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics*. 1996;97:424–435.
4. McConnochie KM, Conners GP, Lu E, et al. How commonly are children hospitalized for dehydration eligible for care in alternative settings? *Arch Pediatr Adolesc Med*. 1999;153:1233–1241.
5. Glass RI, Lew JF, Gangarosa RE, et al. Estimates of morbidity and mortality rates for diarrheal disease in American children. *J Pediatr*. 1991;118:S27–S33.
6. Gove S, Tamburlini G, Molyneux E, et al. Development and technical basis of simplified guidelines for emergency triage assessment and treatment in developing countries. WHO Integrated Management of Childhood Illness (IMCI) Referral Care Project. *Arch Dis Child*. 1999;81:473–477.
7. Bergman DA, Baltz RD, Cooley JR. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. *Pediatrics*. 1999;103:843–852.
8. Armon K, Stephenson T, MacFaul R, et al. An evidence and consensus based guideline for acute diarrhoea management. *Arch Dis Child*. 2001;85:132–141.
9. Steiner MJ, Dewalt DA, Byerley JS. Is this child dehydrated? *JAMA*. 2004;291:2746–2754.
10. Ichikawa I. *Pediatric Textbook of Fluid and Electrolytes*. Baltimore, MD: Williams & Wilkins; 1990.
11. Narins RG. *Clinical Disorders of Fluid and Electrolyte Metabolism*. 5th ed. San Francisco, CA: McGraw-Hill, Inc; 1994.
12. Wallach J. *Interpretation of Diagnostic Tests*. 6th ed. New York, NY: Little Brown and Company; 1996.
13. Henry JB, Lauzon RB, Schumann GB. Basic examination of the urine. In: Henry JB, ed. *Clinical Diagnosis and Management by Laboratory Methods*. 19th ed. Philadelphia, PA: WB Saunders Company; 1996: 411–434.
14. McClatchey KD. *Clinical Laboratory Medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002.
15. Behrman RE, Kliegman RM, Arvin AM. *Nelson Textbook of Pediatrics*. 15th ed. Philadelphia, PA: WB Saunders Company; 1996.
16. Gunn VL, Nechyba C. *The Harriet Lane Manual*. 16th ed. Philadelphia, PA: Mosby; 2005.
17. Zitelli BJ, Davis HW. *Atlas of Pediatric Physical Diagnosis*. 4th ed. Philadelphia, PA: Mosby; 2002.
18. McMillan JA, DeAngelis CD, Feigin RD, et al. *Oski's Pediatrics*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
19. Duggan C, Santosham M, Glass RI. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 1992;41:1–20.
20. Gorelick MH, Shaw KN, Murphy KO. Validity and reliability of clinical signs in the diagnosis of dehydration in children. *Pediatrics*. 1997;99:E6.
21. Porter SC, Fleisher GR, Kohane IS, et al. The value of parental report for diagnosis and management of dehydration in the emergency department. *Ann Emerg Med*. 2003;41:196–205.
22. Mackenzie A, Barnes G, Shann F. Clinical signs of dehydration in children. *Lancet*. 1989;2:605–607.
23. English M, Waruiru C, Mwakesi R, et al. Signs of dehydration in severe childhood malaria. *Trop Doct*. 1997;27:235–236.
24. Teach SJ, Yates EW, Feld LG. Laboratory predictors of fluid deficit in acutely dehydrated children. *Clin Pediatr (Phila)*. 1997;36: 395–400.
25. Yilmaz K, Karabocuoglu M, Citak A, et al. Evaluation of laboratory tests in dehydrated children with acute gastroenteritis. *J Paediatr Child Health*. 2002;38:226–228.
26. Duggan C, Refat M, Hashem M, et al. How valid are clinical signs of dehydration in infants? *J Pediatr Gastroenterol Nutr*. 1996;22:56–61.
27. Vega RM, Avner JR. A prospective study of the usefulness of clinical and laboratory parameters for predicting percentage of dehydration in children. *Pediatr Emerg Care*. 1997;13:179–182.
28. Amin SS, Jusniar B, Suharjono. Blood urea nitrogen (B. U. N.) in gastroenteritis with dehydration. *Paediatr Indones*. 1980;20:77–82.
29. Saavedra JM, Harris GD, Li S, et al. Capillary refilling (skin turgor) in the assessment of dehydration. *Am J Dis Child*. 1991;145:296–298.
30. Friedman JN, Goldman RD, Srivastava R, et al. Development of a clinical dehydration scale for use in children between 1 and 36 months of age. *J Pediatr*. 2004;145:201–207.
31. Simel DL, Samsa GP, Matchar DB. Likelihood ratios with confidence: sample-size estimation for diagnostic-test studies. *J Clin Epidemiol*. 1991;44:763–770.
32. Neville KA, Verge CF, O'Meara MW, et al. High antidiuretic hormone levels and hyponatremia in children with gastroenteritis. *Pediatrics*. 2005;116:1401–1407.
33. Sackett DL, Haynes RB, Tugwell P. *Clinical Epidemiology: A Basic Science for Clinical Medicine*. 1st ed. Boston, MA: Little Brown and Company; 1985.
34. Sackett DL, Straus SE, Richardson WS, et al. *Evidence-Based Medicine: How to Practice and Teach EBM*. 2nd ed. New York, NY: Churchill Livingstone; 2000.
35. Leung AK, Robson WL. Clinical signs of dehydration in children. *Lancet*. 1989;2:1038
36. Mulherin SA, Miller WC. Spectrum bias or spectrum effect? Subgroup variation in diagnostic test evaluation. *Ann Intern Med*. 2002;137:598–602.
37. Edelmann CM Jr, Barnett HL, Stark H, et al. A standarized test of renal concentrating capacity in children. *Am J Dis Child*. 1967;114: 639–644.
38. Leech S, Penney MD. Correlation of specific gravity and osmolality of urine in neonates and adults. *Arch Dis Child*. 1987;62:671–673.
39. Voinescu GC, Shoemaker M, Moore H, et al. The relationship between urine osmolality and specific gravity. *Am J Med Sci*. 2002;323:39–42.
40. Roessingh ASD, Drukker A, Guignard JP. Dipstick measurements of urine specific gravity are unreliable. *Arch Dis Child*. 2001;85:155–157.
41. Rumley A. Urine dipstick testing: comparison of results obtained by visual reading and with the Bayer CLINITEK 50. *Ann Clin Biochem*. 2000;37:220–221.
42. Czaczkes JW. Plasma volume as an index of total fluid loss. *Am J Dis Child*. 1961;102:190–193.