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## No need for routine glycosuria/proteinuria screen in pregnant women

### Practice recommendations

- Screening for gestational diabetes using urine dipsticks for glycosuria is ineffective with low sensitivities. False-positive tests outnumber true positives 11:1. A 50-g oral glucose challenge is a better test. Tests for glycosuria after this blood test are not useful (B).
- Proteinuria determined by dipstick in pregnancy is common and a poor predictor for preeclampsia with a positive predictive value between 2% and 11%. If the blood pressure is elevated, a more sensitive test should be used (B).
- After urinalysis at the first prenatal visit, routine urine dipstick screening should be stopped in low-risk women (B).

### Abstract

**Objective** More than 22 million prenatal visits occur in the US each year.<sup>1</sup> Each pregnant woman averages 7 visits. Most include urine testing for glucose and protein to screen for gestational diabetes and preeclampsia. Is there sufficient scientific evidence to support this routine practice?

**Methods** We searched Medline (1966–2004), the Cochrane review, AHRQ National Guideline Clearinghouse, the Institute for Clinical Systems Improvement, and Google, searching for studies on proteinuria or glycosuria in pregnancy. The reference list of each article reviewed was examined for additional studies, but none were identified. We found 6 studies

investigating glycosuria as a predictor for gestational diabetes mellitus, or proteinuria as a predictor for preeclampsia (1 examined both). Because every study used different dipstick methods of determining results, or definitions of abnormal, each was evaluated separately.

**Results** Glycosuria is found at some point in about 50% of pregnant women; it is believed to be due to an increased glomerular filtration rate.<sup>3</sup> The renal threshold for glucose is highly variable and may lead to a positive test result for glycosuria despite normal blood sugar. High intake of ascorbic acid or high urinary ketone levels may result in false-positive results. Four published studies assessed the value of glycosuria as a screen for gestational diabetes.<sup>4–7</sup> All used urine dipsticks. Three of the 4 most likely overestimate the sensitivity of glycosuria for predicting gestational diabetes.

**Conclusions** Routine dipstick screening for protein and glucose at each prenatal visit should be abandoned. Women who are known or perceived to be at high risk for gestational diabetes or preeclampsia should continue to be monitored closely at the discretion of their clinician.

**R**outine dipstick testing is time-consuming and expensive, especially when carried out over multiple visits. False-positive test results are frequent and often lead to further laboratory

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TABLE 1

## Accuracy of glycosuria for predicting gestational diabetes mellitus

DIAGNOSTIC TEST	STUDY QUALITY	N	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)	LR+ (95% CI)	LR- (95% CI)	PV+	PV-	PREVALENCE OF GDM	ODDS RATIO (95% CI)
≥2 determinations Urine dipstick glycosuria ≥100 mg/dL [trace] <sup>4</sup>	2b	500	27% (13%–48%)	83% (80%–87%)	1.6 (0.8–3.4)	0.87 (0.7–1.1)	7%	96%	4.4%	1.9 (0.7–5.0)
≥2 determinations Urine dipstick glycosuria ≥250 mg/dL [1+] <sup>5</sup>	2b	2745	7% (3%–15%)	98% (98%–99%)	4.5 (2.0–10.5)	0.94 (0.9–1.0)	13%	97%	3.1%	4.9 (2.0–11.8)
≤ 1 determination Urine dipstick glycosuria ≥100 mg/dL [1+] <sup>6</sup>	2b	607	36% (15%–64%)	98% (97%–99%)	20 (7.4–52.3)	0.65 (0.41–1.0)	27%	99%	1.8%	30.4 (7.8–119)
1 determination Urine dipstick glycosuria >75–125 mg/dL <sup>7</sup>	2b	766	11% (4%–25%)	93% (91%–95%)	1.5 (0.6–4.0)	.96 (0.9–1.1)	7%	95%	4.1%	1.6 (0.5–4.6)

LR+, positive likelihood ratio; LR-, negative likelihood ratio; PV+, probability of disease given a positive test; PV-, probability of disease given a negative test; GDM, gestational diabetes mellitus; CI, confidence interval.

examinations. Today, when our care of patients is squeezed by both time and monetary constraints, we have a rare opportunity to make office visits more productive and to save patients the burden of unnecessary work-ups.

### ■ Review methods

We searched Medline from 1966 to September 2004 for English language articles using keyword searching for “proteinuria” or “glycosuria” and “prenatal” or “pregnancy.” We explored the Cochrane review, AHRQ National Guideline Clearinghouse, the Institute for Clinical Systems Improvement, and Google. The reference list of each article reviewed was examined for additional studies, but none were identified.

All 6 identified studies that investigated glycosuria as a predictor for gestational diabetes mellitus or proteinuria as a predictor for preeclampsia are reviewed in this analysis. One study examined both. Because every study used different dipstick methods

of determining results, or definitions of abnormal, each was evaluated separately.

### ■ What the evidence shows

Found at some point in about 50% of women, glycosuria is believed to be due to an increased glomerular filtration rate.<sup>3</sup> The renal threshold for glucose is highly variable and may lead to a positive test result for glycosuria despite a normal blood sugar. High intake of ascorbic acid or high urinary ketone levels may result in false-positive results. There have been 4 published studies designed to assess the value of glycosuria as a screen for gestational diabetes mellitus.<sup>4-7</sup> All used urine dipsticks (TABLE 1).

#### Watson: Urine test a poor screening instrument

In an observational prospective study of 500 women, Watson evaluated glycosuria (trace, ≥100 mg/dL) detected on 2 separate prenatal visits (17% of women) as a predictor of gestational diabetes.<sup>4</sup> Gestational

### FAST TRACK

**High ascorbic acid intake or high urinary ketone levels can cause false-positive glycosuria results**

diabetes was defined as an abnormal 50-g glucose screen at 28 weeks gestation confirmed by an abnormal 100-mg 3-hour oral glucose tolerance test (OGTT).

He reported that glycosuria used as a screening test for gestational diabetes had a sensitivity of 27% and a specificity of 83% with a negative predictive value (PV-) of 96% and a positive predictive value (PV+) of 7% in a population with an unusually high prevalence of gestational diabetes of 4.4%. The high prevalence of gestational diabetes in this cohort increased the PV+ of urine screening for glycosuria. Women with severe glycosuria (>250 mg/dL, 2+) on 2 determinations during the first 2 trimesters had a 21% chance (PV+) of being diagnosed as having gestational diabetes.

The author concluded that urine testing for glucose was a poor screening test and was not worthwhile after the 28-week blood glucose challenge. He believed urine testing during the first 2 trimesters was indicated to early identify those 3.8% of women with severe (2+) glycosuria (sensitivity 18%, PV- 96%). However, the incidence of glycosuria was not increased in those women with gestational diabetes when compared with those with normal glucose screening values.

#### **Gribble: No evidence supports improved outcomes from earlier identification of gestational diabetes**

Gribble et al retrospectively examined 2745 charts of women at low risk for gestational diabetes in their first 2 trimesters of pregnancy.<sup>5</sup> Two urine dipstick screening determinations positive for glycosuria ( $\geq 250$  mg/dL) during the first 2 trimesters before a blood glucose screening test were 7% sensitive and 98% specific with a PV- of 97% and a PV+ of 13% in a population with a prevalence of gestational diabetes of 3.1%.<sup>5</sup>

Less than 1% had glycosuria on their first prenatal visit and were excluded from the study. Only 7% of women (6/85) who were subsequently diagnosed with gestational diabetes had glycosuria during the first 2 trimesters of their pregnancy. There was no statistically significant association

( $P < .05$ ) between glycosuria and maternal body mass index, age, history, multiparity, or birth weight of an infant greater than 4 kg. Many of these are considered risk factors for gestational diabetes. Over 8% of women with a normal 1-hour screen had glycosuria in the third trimester. Requiring 2 positive urine tests and analyzing data collected before the third trimester lowered sensitivity and the PV+.

The authors recommended continuing glycosuria testing in the first two trimesters and then stop testing after the blood screen for gestational diabetes at 24 to 28 weeks although they noted that there was no evidence to support an improved pregnancy outcome because of earlier identification in gestational diabetes.

#### **Hooper and Buhling: Urine glucose screening should be abandoned**

In a retrospective study by Hooper of 610 patients who did not have glycosuria at the first prenatal visit, I calculated a sensitivity of 36%, specificity of 98%, a NPV of 99%, and a PPV of 27% using a single glycosuria value of  $\geq 100$  mg/dL in a population with a prevalence of gestational diabetes of 1.8%.<sup>6</sup> The author advised that urine screening for gestational diabetes and preeclampsia be abandoned.

In a prospective German study, 1001 women were followed throughout their pregnancy.<sup>7</sup> Glycosuria was detected in 8.2% of patients. Twenty-seven percent (267/1001) had an abnormal 50-g (>140 mg/dL) glucose screening test result, 178 (67% of them) completed a 3-hour 75-g glucose diagnostic test and 37 (4.1%) had gestational diabetes.

Of the 729 patients with a normal 50-g screening test, 52 (7%) had glycosuria while of the 37 with gestational diabetes, 4 (11%) had glycosuria. Sensitivity was 11% with a PV- of 95%. The 50-gram glucose screening test was done at  $33.8 \pm 3$  weeks gestation, later than the 28 weeks recommended in this country. Also the cutoff values for the diagnosis of gestational diabetes were lower than those of the American Diabetes Association. Both changes would

### **FAST TRACK**

**Testing for gestational diabetes before 28 weeks, as might be prompted by urine test results, does not change pregnancy outcomes**

increase the incidence of gestational diabetes and the sensitivity of urine glucose screening. The authors recommended against screening for glycosuria.

### Summary of the studies

Three of the 4 studies most likely overestimate the sensitivity of glycosuria for predicting gestational diabetes. All but Gribble et al included urine testing results collected in the third trimester, after the gold standard oral glucose screening test and diagnostic test were completed. Furthermore, most urine tests were probably done in the third trimester when prenatal visits occur more frequently and when glycosuria is more prevalent.<sup>7</sup> Both of these factors would tend to falsely elevate the sensitivity of testing for glycosuria in the first and second trimesters, when it is theoretically most useful. Gribble et al reported that including third-trimester data did not change the predictive values of glycosuria for gestational diabetes; the other investigators did not.

### Recommendations from professional societies

The American Diabetes Association recommends blood glucose testing as soon as possible in high-risk women and routinely at 24 to 28 weeks gestation in those at lower risk.<sup>8</sup> The American College of Obstetricians and Gynecologists (ACOG) does not address urine testing for glucose.<sup>9</sup> The Institute for Clinical Systems Improvement (ICSI) considers urine dipsticks for glycosuria unreliable.<sup>10</sup>

Abandoning all but the initial urinalysis may miss a few women with true but unrecognized diabetes mellitus. None of the studies presented above address this problem although screening for diabetes mellitus using urine test strips is not an ideal screening test, identifying only between 30% and 59% of a predominately middle-aged nonpregnant group.<sup>11</sup>

There is no evidence that testing for gestational diabetes before 28 weeks, as might be prompted by urine testing, changes pregnancy outcome. Screening for gestational

diabetes by glycosuria is not effective with low sensitivities and low positive predictive values. False-positive tests outnumber true positives 11:1, leading to unnecessary further testing. Based on the information available, it appears safe to abandon routine urine testing for glucose at every prenatal visit. This recommendation stands regardless of the debate over the value of screening for gestational diabetes by 50-g glucose challenge followed by an OGTT if indicated.<sup>12</sup>

### Proteinuria as a predictor for preeclampsia

Proteinuria in pregnancy is common. One study of 913 women reported that 3.8% of them had proteinuria by automated dipstick testing on their first antenatal visit and 40.8% had dipstick-positive ( $\geq 1+$ ) proteinuria at least once during the course of their pregnancy.<sup>13</sup> In another study of 3122 otherwise healthy women with a single gestation, 9.8% of the women had at least 1 episode of dipstick proteinuria  $\geq 30$  mg/dL ( $\geq 1+$ ).<sup>5</sup>

Detection of proteinuria in hospitalized hypertensive pregnant women by visual reading of dipsticks, as is the usual office practice, has a high false-positive rate for true proteinuria ( $\geq 300$  mg/L) with a PV+ (true positives/true plus false positives) of 24% for 1+, 53% for 2+, and 93% for 3+ or 4+.<sup>14</sup> Another study reported a PV+ of 38% for  $\geq 1+$  proteinuria.<sup>15</sup> A recent literature review concluded that the accuracy of 1+ proteinuria in pregnant women by dipstick was “poor and therefore of limited usefulness.”<sup>16</sup> In a busy office with a number of healthy nonhypertensive women, the false-positive rate is high due to contamination with vaginal secretions, previous exercise, high specific gravity of urine, or other benign causes.<sup>17-19</sup> In contrast to the high false-positive rates noted in the previous studies, Meyer et al reported a negative predictive value of only 34% for trace or negative proteinuria in hospitalized women with hypertension in pregnancy.<sup>20</sup> Proteinuria detected by dipstick using visual or automated testing alone is a poor indicator for

### FAST TRACK

**When testing for proteinuria to detect preeclampsia, a random protein:creatinine ratio is better than dipstick**

TABLE 2

## Accuracy of proteinuria for predicting preeclampsia

DIAGNOSTIC TEST	STUDY QUALITY	N	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)	LR+ (95% CI)	LR- (95% CI)	PV+	PV-	PREVALENCE OF PREECLAMPSIA	ODDS RATIO (95% CI)
Automated read urine dipstick proteinuria $\geq 1+$ <sup>13</sup>	2b	913	63% (43%–79%)	62% (59%–65%)	1.7 (1.2–2.3)	0.60 (0.4–1.0)	5%	98%	2.8%	2.7 (1.2–6.3)
Visually read urine dipstick proteinuria $\geq 30$ mg/dL [H] <sup>6</sup>	2b	610	71% (47%–87%)	84% (80%–86%)	4.3 (3.0–6.2)	0.35 (0.17–0.74)	11%	99%	2.8%	12.3 (4.2–35.6)
Visually read urine dipstick proteinuria $\geq$ trace (30 mg/dL) <sup>5</sup>	2b	2802	5% (2%–11%)	90% (89%–91%)	0.5 (0.2–1.1)	1.1 (1.0–1.1)	2%	96%	9.7%	0.5 (0.2–1.1)

LR+, positive likelihood ratio; LR-, negative likelihood ratio; PV+, probability of disease given a positive test; PV-, probability of disease given a negative test; CI, confidence interval.

## FAST TRACK

### Pregnancy outcomes were similar in proteinuria and no-proteinuria groups

true proteinuria although the automated method is the more accurate of the 2.<sup>14</sup> When the measurement of proteinuria is indicated for the early identification of preeclampsia, then a random protein:creatinine ratio is a better test choice.<sup>14,15,21</sup>

Three studies have addressed the question: Is proteinuria an accurate predictor for preeclampsia?<sup>6,15,16</sup> Preeclampsia is defined as an elevated blood pressure with either proteinuria or edema or both.<sup>15</sup>

In a prospective observational study carried out in Australia, 866 non-hypertensive women were tested using an automated dipstick method for proteinuria on their first prenatal visit and 35 were  $\geq 1+$  positive.<sup>13</sup> Twenty-five (71%) of these women had proteinuria detected during subsequent visits, and 2 (6%) of them developed preeclampsia. Of the 833 women who did not have proteinuria on the first visit, 316 had it on subsequent dipstick testing, and 15 of these women developed preeclampsia. Of the 512 who never had proteinuria, 9 developed preeclampsia (sensitivity=63%, PV- =98%). Proteinuria at the first visit may be a risk factor for subsequent preeclampsia (relative risk=2.2; 95% CI, 0.49–9.6). Of the 8 women who developed proteinuria before hypertension developed, 5 could be considered at high risk: 2 had proteinuria at their first prenatal visit, 2 had multiple gestations,

and 1 had a history of preeclampsia. Pregnancy outcomes were similar in the proteinuria and no proteinuria groups. The authors recommended discontinuing urine protein testing except in high-risk women (TABLE 2).

A retrospective study of 3104 low-risk American women which excluded those at high risk (multiple gestations, diabetes mellitus, preexisting hypertension, renal disease, or  $\geq 30$  mg/dL [1+] proteinuria at the first prenatal visit) found routine visually evaluated dipstick determination for proteinuria of no value in the prediction of preeclampsia.<sup>22</sup> In this study for the 6.1% of woman who had a blood pressure of greater than 140/90 mm Hg, a weight gain of 3 pounds a week or more, or greater than 1+ edema, testing for proteinuria was considered to be for diagnostic reasons. When the remaining 2802 patients were evaluated throughout their pregnancy, 90.3% had no proteinuria, 7.6% were 1+, and 2.2% were  $\geq 2+$ . The sensitivity and PV+ of proteinuria for preeclampsia in routine patients were 5% and 96% respectively.

The presence of proteinuria was increased in younger women and those with a greater pre-pregnant body mass index but not with pregnancy-associated hypertension–preeclampsia, fetal distress, abruptio, low birth weight, prematurity,

stillbirth, or Apgar scores less than 7 at 5 minutes. The authors concluded that there is no evidence supporting routine urine dipstick protein determinations during uncomplicated prenatal visits.

In another retrospective study of 610 women, 18 % had  $\geq 1+$  proteinuria during at least one prenatal visit and 17 (3%) developed preeclampsia.<sup>6</sup> Three women with preeclampsia (17%) developed proteinuria before hypertension. But the timing of the appearance of proteinuria was not otherwise specified, and it may have been remote from the hypertension. The sensitivity of proteinuria detected prior to the onset of hypertension for preeclampsia was 71% with a PV- of 99%. The author advised against routine dipstick testing.

## ■ Recommendations and practices of others

Routine testing at antenatal visits for proteinuria is not helpful in predicting preeclampsia and should be targeted at women with an increased blood pressure or acute weight gain. ACOG advises that there is no reliable predictive test for preeclampsia.<sup>23</sup> The US Preventive Services Task Force advises urine testing for protein only after abnormalities in blood pressure appear.<sup>24</sup> The Canadian Task Force on the Periodic Health Examination<sup>25</sup> and other groups in Australia<sup>26</sup> advise against testing, as does a standard textbook of obstetrics.<sup>27</sup> ICSI suggests that prenatal care would be improved by discontinuing routine urine dipstick testing.<sup>10</sup>

Most groups support further evaluation of proteinuria<sup>21,26,30</sup> or glycosuria<sup>26</sup> found on the initial urinalysis at the first prenatal visit although there is little evidence to support this course of action.<sup>31</sup> Based on the results of these studies and the recommendations of other groups, it is reasonable to reserve urine protein testing (using a more accurate method than a dipstick) for women with an elevated blood pressure. ■

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## CONFLICT OF INTEREST

The author has no conflicts of interest to declare.

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## FAST TRACK

**Target routine testing for proteinuria at women with increased BP or acute weight gain**

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