Prognostic Value of 24-Hour Blood Pressure in Pregnancy

Gianni Bellomo, MD
Pier Luca Narducci, MD
Francesco Rondoni, MD
Giovanni Pastorelli, MD
Gabriela Stangoni, MD
Giulio Angeli, MD
Paolo Verdecchia, MD

White coat hypertension (WCH) is generally defined by a persistently elevated office blood pressure (BP) with normal BP outside the medical setting.1 Like any other category of hypertension, the definition is arbitrary. A diagnosis of WCH is established by 24-hour BP monitoring, and its prevalence has been estimated at 5% to 60%, depending on the clinical characteristics of the population studied and the diagnostic criteria used.2-6 Whether WCH is a benign condition7-9 or carries a definitely increased cardiovascular risk is not known.10-13

White coat hypertension is common among young, nonobese women of childbearing age.5 At present, there is little information regarding prevalence and prognostic significance of WCH in pregnancy, although WCH has been reported to be as frequent or even more frequent among pregnant women5 compared with nonpregnant women.14-16

If this is the case, then a number of pregnant women may be subjected to expensive diagnostic procedures and even drug treatment for a hypertensive condition that might actually prove to be limited to the clinical visit.

We used 24-hour BP monitoring to evaluate a group of 148 clinically hypertensive pregnant women in their third trimester of pregnancy and compared the findings with those of a group of 106 clinically normotensive pregnant women at the same gestational age. We followed up all subjects to completion of pregnancy to establish prevalence and prognostic value of WCH in the third trimester of pregnancy. The main evaluation criteria were duration of pregnancy, incidence of transient gestational hypertension, preeclampsia and eclampsia, incidence of cesarean delivery, and maternal and neonatal hospital stays for those with and without elevated office BP.

Results

After application of exclusion criteria, data for 7 women were removed from the analysis. For the remaining subjects, in the group with elevated BP, prevalence of WCH was 29.2% (42/144). Duration of pregnancy was similar in the normotensive and WCH groups (39.6 vs 39.8 weeks; P = .50), but shorter (38.3 weeks; P < .001) in the true hypertension group. Incidence of preeclampsia was similar in the normotensive and WCH groups (5.8% vs 7.1%; P = .86) but higher in the true hypertension group (61.7%; P < .001). Frequency of cesarean delivery was lower in the normotensive (12.4%) than in the WCH group (14.5%; P = .098) and true hypertension (41.1%; P < .001). Neonatal weight was lower (P < .001) in the true hypertension (mean, 2911 g) than in the normotensive (3336 g) and WCH (3435 g), which did not differ (P = .50). The duration of neonatal hospital stay did not differ between the normotensive and the WCH groups (45.2 days; P = .47). The duration of hospital stay stayed the same for the normotensive group (12.3 days; P < .001). The duration of hospital stay stayed the same for the normotensive group (12.3 days; P < .001).

Conclusions

In women with elevated BP during their third trimester of pregnancy, 24-hour BP was superior to office BP (distinguishing true hypertension from WCH) for prediction of the outcome of pregnancy. Outcomes in the normotensive and WCH group were comparable, but the increased incidence of cesarean delivery in the WCH group may reflect decision-making processes influenced by office BP.

Context

Elevated blood pressure (BP) measured at the physician’s office may reflect true hypertension or white coat hypertension (WCH). The prognostic value of WCH among pregnant women is unknown.

Objective

To assess the prognostic value of WCH in pregnancy.

Design

Prospective cohort study conducted between September 1994 and October 1997.

Setting

Community hospital.

Patients

Women without preexisting hypertension and not treated with antihypertensive drugs and with high (n = 148) or normal (n = 106) office BP (high office BP was defined as $≥140$ mm Hg systolic and/or $≥90$ mm Hg diastolic) matched for gestational age during their third trimester of pregnancy. All women underwent 24-hour noninvasive BP monitoring, and women without hypertension on 24-hour monitoring (125/74 mm Hg or less for average 24-hour BP) with office hypertension were classified as having WCH. Women were followed up through the end of pregnancy.

Main Outcome Measures

Duration of pregnancy, gestational hypertension, preeclampsia or eclampsia, cesarean delivery, placental and neonatal weight, and length of maternal and neonatal hospital stays for those with and without elevated office BP.

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ery, placental and neonatal weight, Apgar score, and length of hospital stay of mother and newborn.

**METHODS**

The study began in September 1994 and ended in October 1997. The study population consisted of 148 women with office hypertension in their third trimester of pregnancy, between 26 and 28 weeks of gestation, and a control group composed of 106 normotensive women at the same stage of pregnancy. At entry to the study, BP was obtained on 2 separate occasions in a quiet environment with the subject seated at an angle of approximately 60° to the horizontal. A physician on the hospital staff measured BP with a standard mercury sphygmomanometer. In our institution, all mercury sphygmomanometers are calibrated every 3 months against an electronic pressure generator. Diastolic BP was taken at Korotkoff phase 5, which has been shown to correspond more closely to intra-arterial measurement and be less dependent on the examiner’s skill than Korotkoff phase 4.17,18 Three measurements were taken, 5 minutes apart, and the average was recorded: the mean of the averages recorded on the 2 occasions was considered the actual BP. Blood pressure values equal to or greater than 140 mm Hg systolic or 90 mm Hg diastolic were considered abnormal and used for diagnosis of hypertension. Known heart disease, nephropathy, or hypertension preceding pregnancy were reasons for exclusion from the study. None of the subjects were treated with antihypertensive drugs on entry. All the women participating in the study were informed about its purpose and the procedures involved and gave their consent. The study was approved by the hospital ethics committee.

All the participating women were admitted to the hospital on the day preceding ambulatory BP monitoring, blood samples were taken, and a 24-hour urine collection was started for determination of proteinuria.

A pressurometer validated for use in pregnant women (TM2420, A&D Company, Tokyo, Japan) was used to measure 24-hour BP.19 Device accuracy was checked in every session against a mercury sphygmomanometer, and a difference greater than 5 mm Hg was reason for exclusion from the study. The pressurometer takes systolic BP at Korotkoff phase 1 and diastolic BP at Korotkoff phase 5 with a microphone. Blood pressure was recorded at 15-minute intervals both during the day and night for 25 hours, starting between 9 and 11 AM. Cuffs of appropriate size were used, always applied to the left arm. The subjects were free to move around in the hospital and encouraged to engage in social activities with friends and relatives. We chose to perform 24-hour BP monitoring within a hospital setting to ensure a more controlled and homogeneous environment for all subjects in terms of meal schedules, sleeping times, and physical activity. Moreover, in our experience the number of artifacts and missing values tends to be lower in a hospital setting than in an outpatient setting when using an auscultatory method for BP recording (G.B., unpublished data).

All BP recordings from the first hour of monitoring were removed from analysis because they might be influenced by an alarm reaction.1,20 All the readings with a pulse pressure lower than 20 mm Hg, a diastolic BP greater than 140 mm Hg or lower than 40 mm Hg, or a systolic BP greater than 250 mm Hg or lower than 60 mm Hg were automatically rejected. The quality of 24-hour BP monitoring was judged satisfactory when at least 70% of the readings passed the editing criteria and at least 1 recording per hour was obtained. Daytime was defined as 6 AM to 10 PM. Our upper normal limits for 24-hour BP monitoring were 125/74 mm Hg for average 24-hour BP, 128/78 mm Hg for average daytime BP, and 121/70 mm Hg for average night-
time BP. These reference values mark the 90th percentile of the distribution of 24-hour BP monitoring in a population of 132 normotensive pregnant women (72 primipara and 60 multipara) of mean age 29 years (range, 18-41 years) attending our hospital between 1991 and 1994, whose office BP was persistently below 140 mm Hg systolic and 90 mm Hg diastolic during the entire pregnancy and puerperium. In all these women, 24-hour BP monitoring was carried out during the third trimester of pregnancy (26-40 weeks of gestation) in the hospital. Their mean daytime 24-hour BP was 113 mm Hg (range, 92-136 mm Hg) systolic and 72 mm Hg (range, 57-84 mm Hg) diastolic.

For the purpose of this study, WCH was defined as the presence of office hypertension (office BP ≥140 mm Hg systolic and/or 90 mm Hg diastolic) and mean 24-hour, daytime, and nighttime systolic and diastolic BP below the reference values. The women with higher 24-hour BP were classified as having true hypertension.

Ambulatory BP reports were accessible to gynecologists and patients, but these data were unlikely to influence therapeutic decisions because they were considered experimental findings unsupported by specific guidelines.

All women were followed up at our hospital until the end of pregnancy and regularly up to 1 month after delivery, unless their clinical conditions dictated otherwise. According to standard criteria,21,22 preeclampsia was diagnosed as the presence of office BP greater than 140/90 mm Hg and proteinuria greater than 300 mg/24 h. Transient late gestational hypertension was defined as the presence of normal office BP (<140 mm Hg systolic and <90 mm Hg diastolic) 4 weeks after delivery in untreated women who had hypertension without preeclampsia during the third trimester of pregnancy.

Statistical analysis was carried out using 1-way analysis of variance and the Scheffe test or the $x^2$ test with Yates correction, as appropriate. Results are expressed as mean (SD), unless otherwise indicated.

## RESULTS

The 24-hour BP monitoring values from 4 women in the hypertensive group and 3 in the normotensive group did not pass the inclusion criteria, and the data relative to these subjects were not included in the analysis. On average, 91.8% of readings were valid (range, 75%-100%). Among the 144 remaining women with clinic hypertension, 42 (29.2%) were classified as having WCH according to the criteria defined in the “Methods” section. The relevant clinical, laboratory, perinatal, and 24-hour BP monitoring data in the normotensive group, WCH group, and true hypertensive group are summarized in Table 1 and Table 2. The indications for cesarean delivery and the treatments received by the patients are shown in Table 3 and Table 4. In particular, duration of pregnancy ($P = .50$) and neonatal weight ($P = .68$) did not differ between the normotensive and WCH group.

Prevalence of pregnancy-induced hypertension (ie, transient late gestational hypertension and preeclampsia combined) was greater in the WCH than in the normotensive group (19.1% [8/42] vs 12.6% [13/103]; $P = .02$), but lower than in the true hypertensive group (95% [97/102]; $P < .001$).

The incidence of preeclampsia alone did not differ significantly between the WCH and the normotensive groups (7.1% [3/42] vs 5.8% [13/103]; $P = .86$), while it was considerably higher in the true hypertensive group (61.7% [63/102]; $P < .001$).

At entry into the study, none of the women in the normotensive and WCH group had 24-hour proteinuria greater than 300 mg; whereas in the true hypertensive group, 34 women had 24-hour proteinuria greater than 300 mg.

### Table 2. Perinatal Data*

<table>
<thead>
<tr>
<th></th>
<th>Normotensive Group (n = 103)</th>
<th>Hypertensive Group (n = 42)</th>
<th>White Coat Hypertensive Group (n = 29)</th>
<th>True Hypertensive Group (n = 102)</th>
<th>P†</th>
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</thead>
<tbody>
<tr>
<td><strong>Entire Population (N = 247)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Preeclampsia, %</td>
<td>5.8</td>
<td>7.1</td>
<td>61.7</td>
<td>&lt;.001</td>
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<tr>
<td>Gestational hypertension, %</td>
<td>6.8</td>
<td>11.9</td>
<td>33.3</td>
<td>&lt;.001</td>
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<tr>
<td>Week at delivery</td>
<td>39.8 (0.9)</td>
<td>39.6 (1.5)</td>
<td>38.3 (2.3)</td>
<td>&lt;.001</td>
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</tr>
<tr>
<td>Neonatal weight, g</td>
<td>3336 (96)</td>
<td>3435 (540)</td>
<td>2911 (766)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Placental weight, g</td>
<td>665 (106)</td>
<td>669 (121)</td>
<td>588 (141)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Apgar score, 1 min</td>
<td>9.8 (0.5)</td>
<td>9.4 (1.0)‡</td>
<td>9.1 (1.6)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Cesarean delivery, No. (%)</td>
<td>13 (12.4)</td>
<td>19 (45.2)§</td>
<td>42 (41.1)</td>
<td>&lt;.001§</td>
<td></td>
</tr>
<tr>
<td>Hospital stay of mother, d</td>
<td>4.6 (1.4)</td>
<td>5.9 (1.9)†</td>
<td>7.6 (3.6)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Hospital stay of newborn, d</td>
<td>5.3 (6.0)</td>
<td>6.9 (6.4)</td>
<td>12.3 (14.6)</td>
<td>&lt;.001</td>
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### Table 3. Cesarean Delivery Group (n = 72)

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<tr>
<th></th>
<th>Normotensive Group (n = 30)</th>
<th>Hypertensive Group (n = 12)</th>
<th>White Coat Hypertensive Group (n = 10)</th>
<th>True Hypertensive Group (n = 52)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal weight, g</td>
<td>3301 (575)</td>
<td>3308 (666)</td>
<td>2637 (844)</td>
<td>&lt;.001</td>
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<tr>
<td>Placental weight, g</td>
<td>661 (126)</td>
<td>667 (142)</td>
<td>541 (143)</td>
<td>&lt;.001</td>
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<tr>
<td>Apgar score, 1 min</td>
<td>9.5 (1.2)</td>
<td>9.2 (2.4)</td>
<td>8.4 (2.2)</td>
<td>&lt;.001</td>
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<td>Hospital stay of mother, d</td>
<td>7.4 (1.4)</td>
<td>7.8 (1.1)</td>
<td>10.4 (3.1)</td>
<td>&lt;.001</td>
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<tr>
<td>Hospital stay of newborn, d</td>
<td>11.3 (11.2)</td>
<td>11.0 (5.7)</td>
<td>20.2 (7.4)</td>
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### Table 4. Vaginal Delivery Group (n = 175)

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<th>Normotensive Group (n = 53)</th>
<th>Hypertensive Group (n = 12)</th>
<th>White Coat Hypertensive Group (n = 10)</th>
<th>True Hypertensive Group (n = 112)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal weight, g</td>
<td>3341 (365)</td>
<td>3469 (585)</td>
<td>3103 (561)</td>
<td>.001</td>
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<tr>
<td>Placental weight, g</td>
<td>667 (97)</td>
<td>670 (123)</td>
<td>606 (142)</td>
<td>.004</td>
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<tr>
<td>Apgar score, 1 min</td>
<td>9.9 (0.5)</td>
<td>9.8 (0.9)</td>
<td>9.7 (1.4)</td>
<td>.42</td>
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<tr>
<td>Hospital stay of mother, d</td>
<td>4.2 (0.9)</td>
<td>4.2 (0.8)</td>
<td>6.1 (1.7)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Hospital stay of newborn, d</td>
<td>4.4 (4.7)</td>
<td>4.5 (4.8)</td>
<td>6.6 (5.5)</td>
<td>.001</td>
<td></td>
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</table>

*Data expressed as mean (SD) unless otherwise indicated.

†P value is comparison between true hypertensive group vs normotensive group and between true hypertensive group vs white coat hypertensive group unless otherwise indicated.

§P = .0001 for white coat hypertensive group or true hypertensive group vs normotensive group both number and percentage.
In the true hypertensive group, among the 68 women who did not have significant proteinuria at entry, 29 developed preeclampsia later in the course of pregnancy. Three women in the WCH group and 6 in the normotensive group whose proteinuria values were less than 300 mg/24 h at entry later developed preeclampsia.

Sensitivity and specificity of office hypertension, 24-hour BP monitoring, and 24-hour proteinuria values for diagnosis of pregnancy-induced hypertension and preeclampsia alone are shown in Table 5.

At the follow-up visit 1 month after delivery, none of the women in the normotensive group had office BP greater than 140 mm Hg systolic or 90 mm Hg diastolic, compared with 3 women in the WCH group (P = .04) and 26 women in the true hypertensive group (P < .001). Five women in the true hypertensive group still had 24-hour urine protein values greater than 300 mg 1 month after delivery.

We evaluated separately the perinatal data for the women who gave birth by cesarean delivery and those who delivered vaginally (Table 2). No significant differences were observed between the normotensive group and the WCH group for Apgar score at 1 minute (cesarean delivery, 9.5 [1.2] vs 9.2 [2.4]; P = .24; vaginal delivery, 9.9 (0.5) vs 9.8 [0.8]; P = .76) and maternal hospital stay (cesarean birth, 7.4 [1.4] vs 7.8 [1.1] days; P = .16; vaginal delivery, 4.2 [0.9] vs 4.2 [0.8] days; P = .85).

One maternal and 1 neonatal death occurred in the hypertensive group, 1 stillbirth occurred in the WCH group (attributed to umbilical cord strangulation), and 1 stillbirth in the normotensive group (due to placental insufficiency caused by multiple infarcts). The maternal death occurred suddenly 36 days after delivery, when the patient was at home, in apparent good health. An autopsy did not show abnormalities. Death was attributed to “sudden death, probably due to ventricular arrhythmia.” The neonatal death in the hypertensive group resulted from hyaline membrane disease and sepsis in a premature neonate, who was born at 28 weeks of gestation and weighed 918 g.

Overall, 24-hour BP monitoring was well tolerated. Four women (1.6%) were not able to complete the recording session because of excessive discomfort caused by the procedure, and 74 (29.1%) complained of sleep disturbances caused by cuff inflation. Five women (2.0%) presented with minor local allergic reactions secondary to the contact of the skin with the microphone, and in 18 women (7.1%) a slight swelling or bruising of the hand and/or forearm was observed.

**COMMENT**

Prevalence of WCH was 29.2% in our population of women with high BP measured in an office during their third trimester of pregnancy. This number is comparable, though slightly higher, with that observed in a nonpregnant population of similar age. To the best of our knowledge, few data exist on the clinical value of WCH in pregnancy, and none of these studies provided a comprehensive assessment of the prognostic impact of this condition.

The only 2 available studies found a higher prevalence of WCH than ours. However, only a subset of the pregnant women actually underwent 24-hour BP monitoring in 1 study, while in the other study, the dividing line between WCH and true hypertension was set to 85 mm Hg diastolic for average 24-hour ambulatory blood pressure, regardless of systolic BP, with a reported prevalence of WCH greater than 60%. The criteria used in our study for diagnosis of WCH are more restrictive, in line with the criteria currently used in nonpregnant populations.

We studied hospitalized patients and used normal reference values derived from hospitalized subjects: these values appear to be lower than those found in other studies. However, we derived the cutoff point for true hypertension from a population evaluated in a hospital setting, and a 1996 study showed that 24-hour BP monitoring values in hospitalized subjects tend to be slightly lower than in outpatients, probably due to a reduction of environmental stress and physical activity. In the other studies, BP was recorded every 30 minutes by means of...
an oscillometric method. We used 15-minute recording intervals and an auscultatory method. Moreover, in 2 of the studies, the average 24-hour systolic and diastolic BP was higher than the office BP, and in 1 study, the auscultometer was shown to systematically overestimate both systolic and diastolic BP. According to Clark et al, this is avoided when an auscultatory method is used. Finally, 2 of the studies included women who developed pregnancy-induced hypertension, and 1 study included only primigravidas.

Our study shows that office systolic and diastolic BP were significantly higher in the WCH group than in the normotensive group, although their 24-hour BP values were almost identical. The women with true hypertension had 24-hour BP significantly higher than the women in either the WCH or normotensive group. Office BP in the true hypertensive group was considerably higher than in the normotensive women, but only marginally increased in comparison with the women in the WCH group.

Laboratory testing showed that the women in the true hypertensive group had significantly higher 24-hour urine protein values, higher serum creatinine, and uric acid values, and a lower platelet count compared with the other 2 groups. Such an observation is consistent with the greater proportion of women who developed preeclampsia in the group with true hypertension. Of note, none of these parameters differed between the normotensive and the WCH groups; these 2 groups appeared to differ only in their office BP.

For outcome of pregnancy, the incidence of preeclampsia or eclampsia was much greater in the women with true hypertension, whereas no differences were noted between the WCH and normotensive groups.

Analysis of perinatal data (Table 2) showed that the duration of pregnancy and neonatal and placental weights did not differ between the normotensive and WCH groups. However, the women from the latter group had a higher incidence of cesarean delivery, with a slightly lower Apgar score at 1 minute and a longer hospital stay for both the mother and the newborn, although not as long as in the true hypertension group. These observations indicate that WCH has an intermediate prognostic impact on some variables, between that of normotension and true hypertension. However, subgroup analysis (Table 2) showed that the differences between the normotensive and WCH groups are mostly explained by the different rate of cesarean deliveries. In fact, when the data from the women who underwent cesarean delivery and those who delivered vaginally are evaluated separately, the differences between the 2 groups disappear.

It is difficult to provide a definite explanation for the higher incidence of cesarean delivery in the women with WCH compared with the normotensive women. However, it is possible that the attitude of the physicians caring for the women with increased office BP in their third trimester of pregnancy may have played a role. Such speculation is supported by the lack of biochemical or clinical abnormalities in the women in the WCH group. Moreover, many women with WCH were treated with antihypertensive agents, including nifedipine, which may depress uterine contractility and is also used as a tocolytic agent. It is worth noting that 6 women in this group underwent cesarean delivery because of dystocia due to uterine inertia. The lower Apgar score at 1 minute and the longer hospital stay of women in the WCH group may have been direct consequences of an increased tendency to perform cesarean delivery in these women, as suggested by the lack of differences between the normotensive group and the WCH group when the 2 subsets with vaginal delivery and cesarean delivery are analyzed separately.

Sensitivity of 24-hour BP for the diagnosis of transient late gestational hypertension and preeclampsia was marginally lower than that of office hypertension, but its specificity was considerably higher. Such a finding is in accordance with the data provided by 2 recent studies, which show that 24-hour BP is superior to office BP in predicting occurrence of severe hypertension in pregnancy. Furthermore, a recent study showed that fetal growth is inversely associated with 24-hour BP but not with office BP. A study by Hermida and Ayala showed sensitivity and specificity values lower than those we observed for diagnosis of pregnancy-induced hypertension. However, in that study BP was measured with an oscillometric method every 30 minutes during daytime and every 60 minutes during the night.

### Table 5. Sensitivity and Specificity of Test Results of 24-Hour Blood Pressure (BP) Monitoring, Office BP Measurement, and 24-Hour Proteinuria for Prediction of Pregnancy-Induced Hypertension and Preeclampsia

<table>
<thead>
<tr>
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<th>24-Hour BP Monitoring</th>
<th>Office BP Measurement</th>
<th>24-Hour Proteinuria†</th>
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<tbody>
<tr>
<td></td>
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<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Test results abnormal</td>
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<td>129</td>
<td>118</td>
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<table>
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<th></th>
<th>24-Hour BP Monitoring</th>
<th>Office BP Measurement</th>
<th>24-Hour Proteinuria†</th>
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<tbody>
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<td></td>
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<td>Yes</td>
</tr>
<tr>
<td>Test results abnormal</td>
<td>63</td>
<td>39</td>
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<tr>
<td>Total</td>
<td>72</td>
<td>175</td>
<td>72</td>
</tr>
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</table>

*All data are numbers of subjects.
†Measurement of greater than 300 mg/24 h.
‡Sensitivity and specificity for 24-hour BP monitoring are 82.2% and 96.1%; for office BP measurement, 88.9% and 69.7%; and for 24-hour proteinuria, 28.8% and 100%, respectively.
§Sensitivity and specificity for 24-hour BP monitoring are 87.5% and 77.7%; for office BP measurement, 91.6% and 65.4%; and for 24-hour proteinuria, 47.2% and 100%, respectively.

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ing the night, 24-hour BP parameters were derived by mathematical modeling rather than actual BP readings, and sensitivity and specificity were computed separately for systolic and diastolic BP. The sensitivity of 24-hour urine protein values for the diagnosis of pregnancy-induced hypertension was low in our study (less than 50%), with, however, a 100% specificity. This latter figure is probably overestimated, as we excluded women with known nephropathy or hypertension.

In summary, the results of this study show that 29.2% of women with high office BP in the third trimester of pregnancy have WCH and that this condition carries a diagnostic impact that, as far as the outcome of pregnancy is concerned, differs from the normotensive women only for a greater probability of undergoing cesarean delivery, a slightly lower Apgar score at 1 minute, and a higher incidence of transient late gestational hypertension. Taken together, these findings indicate that 24-hour BP is superior to office BP for prediction of the outcome of pregnancy. Twenty-four hour BP monitoring may be considered a valuable diagnostic procedure in pregnant women with hypertension, particularly in uncomplicated cases in which a therapeutic decision appears to be most difficult. On the basis of our data, it is also possible to speculate that a significant proportion of women diagnosed as having transient gestational hypertension may actually have WCH. The higher incidence of cesarean delivery in the group of women with WCH probably reflects decision-making processes based on office BP. These data suggest the utility of a randomized study of the effects of therapeutic decisions based on office BP vs 24-hour BP in women with uncomplicated hypertension during their third trimester of pregnancy.

REFERENCES


response protective effect, and patients with MS have lower levels of uric acid than controls.\(^5\) To further assess this possible inverse relationship between nitric oxide and uric acid, we performed a circadian analysis of these 2 substances in a series of subjects without a history of either MS or gout.

**Methods.** In 1979, 11 healthy male volunteers, then aged 32 to 57 years, were selected from a military reserve unit on the basis of good venous access. In 1979, and again in 1988, 1993, and 1998, blood was obtained at 3-hour intervals over a 24-hour period, and the uric acid concentration of each sample was measured. Nitric oxide levels were also measured in the 1998 samples. Five of the subjects developed type 2 diabetes during the study period, but no other chronic diseases were reported. Data were analyzed for circadian characteristics by population multicomponent analysis.\(^6\)

**Results.** The mean uric acid levels at the 4 successive measurement years were 0.40 mmol/L (95% confidence interval [CI], 0.33-0.46 mmol/L), 0.40 mmol/L (95% CI, 0.36-0.43 mmol/L), 0.39 mmol/L (95% CI, 0.33-0.45 mmol/L), and 0.38 mmol/L (95% CI, 0.35-0.42 mmol/L), respectively. This stability of uric acid over time allowed us to pool the values for the analysis. A significant circadian rhythm was obtained for a harmonic model with 2 components (with periods of 24 hours and 8 hours) for both uric acid (\(P<.001\)) and nitric oxide (\(P=.004\)). The timing of uric acid peak and nitric oxide trough concentrations is virtually cosynchronous, at 5:08 and 5:32, respectively (FIGURE).

**Comment.** The temporally reciprocal relationship between uric acid and nitric oxide in these men suggests that their concentrations are physiologically related. This observation supports previous results of the protective effects of uric acid in nitric oxide–mediated diseases, such as MS.

Eugene L. Kanabrook, PhD
Jane L. H. C. Third, MD
May D. Ryan, RN, MS
Bernard A. Nemchausky, MD
Parvez Shirazi, MD
Lawrence E. Scheving, PhD
Edward Hines Jr Hospital
Hines, Ill
James B. McCormick, MD
Swedish Covenant Hospital
Chicago, Ill

Ramon C. Hermida, PhD
Universidade de Vigo
Vigo, Spain
W. Fraser Brenner, MD, PhD
MacNeal Cardiology Group
Berwyn, Ill
Debbie A. Hoppensteadt, PhD
Jawed Farreed, PhD
Loyola University Medical Center
Maywood, Ill
John H. Olwin, MD
Vascular Disease Research Foundation
Skokie, Ill


**CORRECTIONS**

**Inaccurate Statement:** In the Original Contribution entitled “Health Consequences of Religious and Philosophical Exemptions From Immunization Laws: Individual and Societal Risk of Measles” published in the July 7, 1999, issue of *The Journal* (1999;282:47-53), there was an inaccurate statement on page 48 that reads, “Texas requires that individuals claiming religious exemptions be a member of a recognized religious group that opposes all immunizations and submit a letter from a faith leader.” It should read, “Texas law requires that individuals claiming religious exemptions submit an affidavit signed by the parent or guardian stating that the immunization ‘conflicts with the tenets and practices of a recognized religious organization of which the applicant is an adherent or member.’” There is no requirement that the affidavit be signed by a faith leader or that exemption be for all vaccinations.

**Incorrect Wording:** In the Original Contribution entitled “Prognostic Value of 24-Hour Blood Pressure in Pregnancy” published in the October 20, 1999, issue of *The Journal* (1999;282:1447-1452), the footnotes to two of the tables were worded incorrectly. On page 1448, in Table 1, and on page 1449, in Table 2, the second footnote (1) should read, “\(P\) value is comparison between normotensive, white coat hypertensive, and true hypertensive groups for all characteristics.”