The predictive value of catecholamines in assessing outcome in traumatic brain injury

PAUL D. WOOLF, M.D., ROBERT W. HAMILL, M.D., LOUYSE A. LEE, B.S., CHRISTOPHER COX, PH.D., AND JOSEPH V. MCDONALD, M.D.

Departments of Medicine, Neurology, and Neurosurgery, and Division of Biostatistics, University of Rochester Medical Center, Rochester, New York

Because of the central role of the sympathetic nervous system in mediating the stress response, plasma norepinephrine (NE), epinephrine (E), and dopamine (DA) levels were measured in 61 traumatically brain-injured patients to determine whether catecholamine (CA) levels obtained within 48 hours after injury provide reliable prognostic markers of outcome. Patient outcome was determined at 1 week using the Glasgow Coma Scale (GCS) and at the time of discharge using the Glasgow Outcome Scale (GOS). Levels of NE, E, and DA correlated highly with the admission GCS score (NE: \( \text{r} = 0.58, \ p < 0.0001 \); E: \( \text{r} = 0.46, \ p < 0.0025 \); DA: \( \text{r} = 0.27, \ p < 0.04 \)). Moreover, in the 21 patients with GCS scores of 3 or 4 on admission, NE levels predicted outcome at 1 week. All six patients with NE levels less than 900 pg/ml (normal level less than 447 pg/ml) improved to GCS scores of greater than 11, while 12 of 15 with NE values greater than 900 pg/ml remained with GCS scores of 3 to 6 or died. Levels of E and DA were not as useful. Catecholamine levels also increased significantly as the GOS score worsened. Levels of NE and E were significantly higher in patients who died or remained persistently vegetative than in those with better outcomes. In the 54 patients who survived beyond 1 week, significant correlations were present between the length of hospitalization and NE (\( \text{r} = 0.71, \ p < 0.0001 \)) and E (\( \text{r} = 0.61, \ p < 0.0001 \)) levels. Concentrations of NE (\( \text{r} = 0.61, \ p < 0.0004 \)) and E (\( \text{r} = 0.48, \ p < 0.01 \)) were also highly correlated with the duration of ventilatory assistance. Analysis of the interactions of CA levels and GCS scores, duration of ventilatory assistance, and length of hospitalization revealed that the CA's either enhanced the reliability of the GCS score or were independent predictors of outcome.

Thus, these findings indicate that alterations in circulating CA levels reflect the severity of the neurological insult and provide support for the use of CA measurements as a physiological marker of patient outcome in both the acute and chronic phases of traumatic brain injury.

Key Words • head injury • catecholamine • prognosis • Glasgow Coma Scale • Glasgow Outcome Scale

One of the consequences of traumatic brain injury is the initiation of a cascade of deleterious events that result in worsening neurological impairment and severe metabolic and/or systemic derangements, which appear to be secondary, at least in part, to activation of the sympathetic nervous system. Such disturbances include increased cerebrospinal fluid pressure, enhanced brain oxygen requirements, cardiac arrhythmias and necrosis, pulmonary compromise, altered nutritional requirements, and hypogonadism. Our preliminary nutritional report demonstrated that catecholamine levels reflect the severity of neurological impairment as determined by the Glasgow Coma Scale (GCS) scores and appear to be reliable predictors of outcome. Heretofore, clinical assessment has provided the prognostic indices. While easy to use, the GCS is less reliable in patients with the lowest scores. Addition of age, duration of coma, and type of injury improves the predictive accuracy of the GCS, but problems remain in predicting outcome in individual patients with the worst GCS scores. Because sympathetic nervous system activation in stress is well recognized and because it responds in a graded fashion, we investigated the use of plasma catecholamine determinations as an endogenous marker for the prediction of patient morbidity and mortality.

Clinical Material and Methods

Sixty-one patients (50 male), aged 17 to 95 years (median 25 years), who had suffered traumatic brain
injury within the preceding 48 hours (median 20.5 hours) were studied. Motor-vehicle accidents accounted for 54% of the injuries, while the remainder were caused by pedestrian accidents (18%), falls (16%), assaults (7%), skiing (3%), and farm accidents (2%). Brain injury was the sole medical problem in 32 patients, while associated bone injuries were present in 24. Four subjects had abdominal injuries, two had pulmonary contusions, and facial lacerations were present in one. No patient was in shock or had septic loci at the time of study. None were treated with dopamine (DA) or other pressors; 45 patients received opiates including codeine, morphine, and/or meperidine. Sixteen patients had intracranial pressure determined by direct measurement and it was elevated in eight. Patient outcome was determined using the Glasgow Outcome Scale (GOS) either at the time of discharge from the acute-care hospital or when the attending physician indicated that the patient was ready for placement at a chronic-disease facility.

Blood samples for catecholamine measurement were obtained at 7 a.m. and 8 p.m. in tubes containing 9 mg ethyleneglycol tetra-acetic acid (EGTA) and 6 mg glutathione. The mean of all of the values for the initial 48 hours was then used to establish the baseline for all subsequent analyses. Although this approach may not accurately reflect initial sympathetic nervous system activation, plasma levels remained relatively stable during the 48-hour interval after the accident in the 42 patients from whom multiple samples were obtained, with mean values of 15.9% ± 1.6% (standard error of the mean) for norepinephrine (NE), 24.4% ± 2.9% for epinephrine (E), and 24.2% ± 3.5% for DA. Plasma samples were stored at −80°C until assayed by a modification of the radioenzymatic technique of Peuler and Johnson. The corresponding intra-assay and inter-assay coefficients of variation are, respectively, 7.7% and 16.8% for NE, 6.9% and 14.4% for E, and 6.8% and 13.0% for DA (normal values for NE: <447 pg/ml, E: <71 pg/ml, and DA: <91 pg/ml).

Biostatistical methods included one-way analysis of variance (ANOVA) for determination of the significance of the catecholamine differences among groups with a posteriori analysis of least-significant differences to distinguish between any two groups. Regression analysis was performed by the method of least squares. When appropriate, log transformation of the data was performed to normally distribute the data and to equalize the variances about the mean. In determining the effects of the catecholamines on the outcome variables (GOS scores, duration of respirator therapy, and length of acute hospitalization), it was necessary to adjust for the effect of GCS scores, which has been shown to affect outcome and which we have demonstrated to correlate with catecholamine levels. This was achieved by performing either a weighted regression analysis for GOS scores (because of the discrete nature of the outcome scale) or an ordinary bivariate regression analysis using the predictor variables, GCS scores, and each of the catecholamines in turn.

**Results**

Mean catecholamine levels obtained within 48 hours of brain injury were highly correlated with the GCS scores (Fig. 1). Analysis of patients with severe (GCS score 3 or 4, 21 patients), marked (GCS score 5 to 7, 14 patients), moderate (GCS score 8 to 11, 14 patients), and mild (GCS score > 11, 12 patients) neurological abnormalities revealed significant differences among the four catecholamines.
Catecholamines in assessing head-injury outcome

**TABLE 1**

*Mean catecholamine levels (pg/ml) obtained within 48 hours after traumatic brain injury correlated with GCS score*

<table>
<thead>
<tr>
<th>Catecholamine</th>
<th>Glasgow Coma Scale (GCS) Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-4</td>
</tr>
<tr>
<td></td>
<td>5-7</td>
</tr>
<tr>
<td></td>
<td>8-11</td>
</tr>
<tr>
<td></td>
<td>&gt; 11</td>
</tr>
<tr>
<td>no. of cases</td>
<td>21</td>
</tr>
<tr>
<td>norepinephrine*</td>
<td>1502.6 ± 265.2$d$</td>
</tr>
<tr>
<td>epinephrine†</td>
<td>400.2 ± 108.1</td>
</tr>
<tr>
<td>dopamine</td>
<td>190.2 ± 68.7</td>
</tr>
<tr>
<td></td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>601.6 ± 140.2§</td>
</tr>
<tr>
<td></td>
<td>187.6 ± 45.6</td>
</tr>
<tr>
<td></td>
<td>62.2 ± 11.1</td>
</tr>
<tr>
<td></td>
<td>630.8 ± 115.1</td>
</tr>
<tr>
<td></td>
<td>108.6 ± 14.9</td>
</tr>
<tr>
<td></td>
<td>59.8 ± 21.3</td>
</tr>
<tr>
<td></td>
<td>413.3 ± 47.1</td>
</tr>
<tr>
<td></td>
<td>101.8 ± 13.6</td>
</tr>
</tbody>
</table>

* Groups were significantly different by p < 0.0004.
† Groups were significantly different by p < 0.0001.
§ Significantly (p < 0.05) greater than remaining groups.

The four groups (Table 1). In the group with GCS scores of 3 or 4, NE and E were elevated four- to fivefold and DA twofold, significantly (p < 0.05) higher than in patients less severely injured. Patients with the worst impairment were younger (28.3 years) than those with less severe dysfunction (GCS scores 5 to 7, age 33.8 years; scores 8 to 11, age 40.6 years; GCS scores > 11, age 36.5 years). Catecholamine concentrations were significantly higher in patients without pupillary responses than in those with them (NE: 2016.5 ± 423.6 vs. 662.3 ± 67.0 pg/ml, p < 0.0001; E: 556.6 ± 192.4 vs. 155.7 ± 19.1 pg/ml, p < 0.0001; DA: 299.6 ± 122.7 vs. 60.1 ± 8.5 pg/ml, p < 0.0001). There were no associations between the intracranial pressure measurements or the presence of intracranial hypertension and any of the catecholamines.

Catecholamine levels in the 21 patients with GCS scores of 3 or 4 on admission were correlated with patient outcome 1 week after injury (Fig. 2). Of patients with NE levels above 1300 pg/ml, 89% either died (four patients) or remained unchanged neurologically (four patients), compared to those with NE levels below 1300 pg/ml, of whom 67% improved to GCS scores greater than 11 ($\chi^2 = 6.48$, p < 0.02). Indeed, all patients with NE values below 900 pg/ml demonstrated this degree of improvement, whereas only three of 13 with NE above 900 pg/ml had a GCS score over 11 at 1 week. The NE level was not as useful in predicting outcome in patients with less severe neurological dysfunction on admission, as four of eight patients with GCS scores of 5 to 10 improved to GCS scores over 11 despite NE levels above 900 pg/ml. The E and DA levels were less helpful in indicating improvement in function at 1 week.

Patients with the worst prognoses displayed the greatest degree of sympathetic nervous system activation. In those patients surviving beyond 1 week, patient outcomes were highly associated with catecholamine levels obtained within 48 hours after injury (Fig. 3). One-way ANOVA revealed that NE (F: 13.00, p < 0.0001, $r^2 = 0.48$), E (F: 8.28, p < 0.0001, $r^2 = 0.37$), and DA (F: 9.09, p < 0.0001, $r^2 = 0.40$) concentrations were significantly different among patient outcome groups (dead, persistent vegetative state, severe disability, moderate disability, and good recovery). In patients with the two worst prognoses, plasma NE and E levels were higher than in those with better outcomes (p < 0.05); patients who were left with a severe disability had higher NE levels (p < 0.05) than did those with a good recovery. In patients who ultimately died, DA levels were higher than in patients who lived. There were no significant age differences within the GOS groupings, although...
patients who died tended to be older (good recovery, age 23.6 years; moderate disability, age 34.4 years; severe disability, age 31.2 years; persistent vegetative state, age 32.1 years; and dead, age 52.0 years).

Analysis of the interactions between the catecholamines and GCS scores determined within 48 hours following brain injury and the GOS scores revealed that levels of NE, but not E or DA, significantly enhanced the accuracy of the GCS score in predicting outcome over the entire range of GCS values (Fig. 4 and Table 2); NE levels, independent of their relationship with GCS scores, contributed to the prediction of patient prognosis. Calculating from the equation for the derived linear predictor (linear predictor = 1.19 - 0.0565 GCS + 0.000168 NE), very high NE levels had a very great impact on the predicted GOS results, while both GCS scores and NE levels were of equivalent importance at

![FIG. 3. Glasgow Outcome Scale scores on discharge versus admission catecholamine levels (in pg/ml). Note the log transformation of the horizontal axes. Black column = norepinephrine; cross-hatched column = epinephrine; open column = dopamine. GR = good recovery; MD = moderate disability; SD = severe disability; PV = persistent vegetative state; D = dead.](image)

![FIG. 4. Prediction of Glasgow Outcome Scale (GOS) score using the Glasgow Coma Scale (GCS) and norepinephrine (NE) determinations derived by generalized bivariate regression analysis. The estimated linear predictor is given by the linear predictor equation: 1.19 - 0.0565 GCS + 0.000168 NE. The predicted value is GOS = exp(linear predictor). The GOS scores are: 1 = good recovery; 2 = moderate disability; 3 = severe disability; 4 = persistent vegetative state; 5 = dead. Each data point represents an actual patient.](image)

**TABLE 2**

<table>
<thead>
<tr>
<th>Catecholamine</th>
<th>Chi-Square</th>
<th>p Value</th>
<th>Catecholamine Coefficients</th>
<th>GCS Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>generalized regression analysis of GOS score†</td>
<td>dopamine</td>
<td>2.27</td>
<td>0.10</td>
<td>0.000490</td>
</tr>
<tr>
<td></td>
<td>epinephrine</td>
<td>1.99</td>
<td>0.10</td>
<td>0.000282</td>
</tr>
<tr>
<td></td>
<td>norepinephrine</td>
<td>4.17</td>
<td>0.05</td>
<td>0.000168</td>
</tr>
<tr>
<td>logistic regression analysis of poor outcome‡</td>
<td>dopamine</td>
<td>7.26</td>
<td>0.01</td>
<td>0.0109</td>
</tr>
<tr>
<td></td>
<td>epinephrine</td>
<td>9.24</td>
<td>0.01</td>
<td>0.00618</td>
</tr>
<tr>
<td></td>
<td>norepinephrine</td>
<td>13.75</td>
<td>0.001</td>
<td>0.00237</td>
</tr>
<tr>
<td>logistic regression analysis of poor outcome§</td>
<td>dopamine</td>
<td>3.32</td>
<td>0.10</td>
<td>0.0086</td>
</tr>
<tr>
<td></td>
<td>epinephrine</td>
<td>3.90</td>
<td>0.05</td>
<td>0.00471</td>
</tr>
<tr>
<td></td>
<td>norepinephrine</td>
<td>6.15</td>
<td>0.02</td>
<td>0.00172</td>
</tr>
</tbody>
</table>

* GCS = Glasgow Coma Scale. Chi-square: single degree of freedom likelihood ratio statistic.
† GOS = Glasgow Outcome Scale. Analysis involved using GCS score and catecholamines as predictors.
‡ Poor outcome: severe disability, persistent vegetative state and dead.
§ Poor outcome: moderate disability, persistent vegetative state, and dead.
Catecholamines in assessing head-injury outcome

TABLE 3
Mean catecholamine levels (pg/ml) according to outcome and pupil reactivity

<table>
<thead>
<tr>
<th>Catecholamine</th>
<th>Good Outcome, Reactive Pupils</th>
<th>Good Outcome, Nonreactive Pupils</th>
<th>Bad Outcome, Reactive Pupils</th>
<th>Bad Outcome, Nonreactive Pupils</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of cases</td>
<td>F</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>norepinephrine</td>
<td>41   ± 55.5</td>
<td>1</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>epinephrine</td>
<td>1722 ± 128.4</td>
<td>1.56</td>
<td>1.15</td>
<td>1.20</td>
</tr>
<tr>
<td>dopamine</td>
<td>214  ± 63.9</td>
<td>204.6 ± 467.2</td>
<td>570.6 ± 212.7</td>
<td>307.1 ± 135.4</td>
</tr>
</tbody>
</table>
* Patients in the Glasgow Outcome Scale categories “dead” and “persistent vegetative state” were considered “bad outcomes;” while patients in the categories “severe and moderate disability” and “good recovery” were placed in the “good outcome” group. Pupil data on two patients are missing. Values are means ± standard errors of the mean. Groups significantly different at p < 0.0002.
† Significantly greater than good outcome, reactive pupils (p < 0.05).
‡ Significantly greater than bad outcome, reactive pupils (p < 0.05).

intermediate values. For example, a patient with an admission GCS score of 3 and NE level of 3215 pg/ml would have a linear predictor of 1.56, while another patient with the same GCS score and an NE value of 783 pg/ml would have a linear predictor of 1.15. A comparable linear predictor of 1.20 is obtained from a patient with a GCS score of 6 and an NE level of 2089 pg/ml. The linear predictor values (Fig. 4) indicated an outcome score of 5 (dead) for the first patient and 3 (severe disability) for the last two, outcomes that were actually observed.

If patient outcome is simplified into two categories, either good or bad, then by logistic regression analysis each of the three catecholamines contributed to the prediction of a good (good recovery and moderate disability) or bad (persistent vegetative state and death) outcome over and above that expected from the worsening GCS scores (Table 2). This prediction is best if severe disability is not included with dead and persistent vegetative state in the poor-outcome group (Table 2). The level of NE is clearly the best predictor, followed by E, while DA has marginal utility.

The impact of pupillary responses on plasma catecholamine levels in the setting of good or bad patient outcomes (severe disability was included in the good-outcome classification) is shown in Table 3. Significant differences in the levels 48 hours after injury of NE (F: 24.25, p < 0.0001, r^2 = 0.49), E (F: 20.72, p < 0.0001, r^2 = 0.43), and DA (F: 10.00, p < 0.0002, r^2 = 0.27) were present among patients with nonreactive pupils and a bad outcome, reactive pupils and a bad outcome, and reactive pupils and a good outcome (there was one patient with a good outcome and nonreactive pupils).

In the 54 patients surviving at 1 week, there were highly significant correlations between the requirements for hospitalization in an acute-care facility and the plasma levels of NE (Fig. 5) and E, but not DA (NE, F: 52.24, p < 0.0001, r^2 = 0.50; E, F: 30.13, p < 0.0001, r^2 = 0.37; DA, F: 1.87, p not significant, r^2 = 0.04).

Results of bivariate analysis of log-transformed length of stay are shown in Table 4. Of the three catecholamines, NE yielded the best correlation and DA the worst. The positive regression coefficients for the catecholamines and the negative regression coefficients of GCS scores indicate that as catecholamine levels increase or as the GCS scores worsen, length of hospitalization increases. In the case of NE, the GCS score did not contribute to the prediction of duration of hospitalization since only the NE coefficient was significant;

![Fig. 5. Correlation of plasma norepinephrine levels and length of hospitalization.](image-url)
there was no correlation between the logarithm of the length of stay and the admission GCS score.

Twenty-nine of the patients required ventilatory assistance. Concentrations of NE (Fig. 6) and E were highly correlated with duration of ventilation (NE, F: 15.99, p < 0.0004, r² = 0.37; E, F: 7.94, p < 0.01, r² = 0.23). Bivariate analysis indicated that the GCS variable did not contribute significantly to any of the three regressions (Table 4). The positive regression coefficients for the CA reinforce the positive correlation between catecholamine levels and duration of ventilatory assistance.

Discussion

In the present study, we expanded our hypothesis that activation of the sympathetic nervous system, as indicated by circulating catecholamine concentrations, accurately reflects the severity of brain injury as determined by GCS scores. We used the GCS because it would permit correlation with the large existing body of head trauma data. In this study, we confirmed our preliminary observations and extended those of other investigators, that, within 48 hours after brain injury, NE and E levels are highly correlated with the GCS scores obtained concurrently. Based on these data, we then determined whether catecholamine levels would be useful indicators of patient outcome. Similar conclusions have been reached using the NE concentration as a prognostic marker for patients with chronic congestive heart failure.

Our data clearly demonstrated that a catecholamine gradient was present in patients surviving more than 1 week, since patients with the worst outcome had the highest levels. Independent of its correlation with the concurrent GCS score, NE made a significant contribution to the prediction of patient outcome over the entire range of GCS scores. Moreover, all catecholamines contributed to the prediction of a poor prognosis (that is, death or a persistently vegetative state, with or without inclusion of patients with severe disabilities) over and above that expected from the impact of a worsening GCS score on sympathetic nervous system activation. The relative magnitudes of the bivariate regression coefficients for the prediction of GOS scores demonstrated that large NE values greatly affected the predicted outcome. This is particularly relevant because the corresponding regression using GCS scores alone demonstrated that the GCS was not a good predictor of poor outcomes. As can be seen in Fig. 4, this is not the case for the bivariate regression. Moreover, the catecholamines reflected the need for healthcare resources, since they were highly correlated with both the duration of respirator therapy and the duration of acute-care hospitalization independent of the contribution from worsening neurological function.

Catecholamine responses were independent of age and intracranial pressure. Older patients have a poorer prognosis following brain injury and our patients who died were older than those in the remaining four GOS groups, but the differences were not significant. While experimentally induced increases in intracranial pressure have been shown to stimulate catecholamine release, levels of NE, E, and DA were comparable in the patients with normal or with measured elevations in ICP. As expected, patients with nonreactive pupils had a worse outcome and we were able to show that the levels of each of the catecholamines are higher in such patients. Moreover, there is a four- to fivefold gradient for each of the catecholamines in patients with nonreactive pupils and poor outcomes compared to those for patients with good outcomes and reactive pupils.

Finally, our data indicate that plasma NE levels in patients with GCS scores of 3 or 4 on admission, who were otherwise indistinguishable, segregated patients with regard to prognosis. Thus, all patients with NE levels below 900 pg/ml had improved neurological function at 1 week (GCS score > 11), while only one improved when the NE level was above 1300 pg/ml. Intermediate values gave mixed results. The predictive power of NE thus seems to be superior to that of GCS scores, since the latter only predict outcome with 97% accuracy in 60% of patients with acute brain injury. While the predictive capabilities of the GCS are improved by the addition of duration of coma, age, pathological process, pupil reactivity, and reflex eye movements, the data are less useful in predicting individual patient outcome than in describing population statistics.

The mechanism(s) underlying the association of the sympathetic nervous system response and the magnitude of neurological dysfunction, morbidity, and mortality is unclear. We have no data on the source of the circulating catecholamines, although adrenal demedulation (but not sympathectomy) has been shown to abolish their responses to hemorrhage. Levels of NE,
Catecholamines in assessing head-injury outcome

E, and DA all rose after traumatic brain injury. However, in every case correlation with the severity of neurological dysfunction, patient outcome, and duration of ventilatory assistance and of hospital stay correlated best with NE levels and worst with DA.

The elevations in catecholamine levels may simply be epi-phenomena, quantitating the degree of "stress," however, in brain-injured patients catecholamine levels reflect a variety of complications. They correlate with hypertension, 6,7 tachycardia, 4 increased cardiac output work, 9 and enhanced oxygen delivery and utilization. 6 Treatment with beta adrenergic blockade not only lowers blood pressure but also corrects the underlying hemodynamic abnormalities. 28 The electrocardiographic changes and cardiac arrhythmias associated with head trauma are believed to be due to autonomic imbalance or over-reactivity, 17 and both myocardial lesions 11,30 and cardiac arrhythmias are prevented by alpha and beta adrenergic blockade. 24 The well-recognized correlation between increased NE excretion and hypermetabolism in a variety of serious medical problems 12,27,32 is present in brain-injured patients as well. 5 Finally, the correlation of the cerebral metabolic rate with the GCS 1 is adrenergically mediated. Thus, there are a great deal of data to suggest that sympathetic nervous system activation may, in fact, contribute to the poor outcome in patients with the most marked brain injury.

In conclusion, we have established that activation of the sympathetic nervous system, one of the principal integrators of bodily function in stress, 12 is an indicator of the severity of traumatic brain injury and a prognostic variable for the prediction of patient morbidity and mortality. Because the catecholamines themselves may be maladaptive, particularly in the most severely affected patients, their measurement might provide a guide for determining which patients might benefit from therapy with adrenergic blockade.

Acknowledgments

The authors wish to thank the nurses of the Emergency Department and the Surgical Intensive Care Unit for their enthusiastic support, Ms. Cynthia Bean and Mrs. Patricia D'Angelo for their technical assistance, and Mrs. Elizabeth Skelton for her secretarial help.

References

25. Passon PG, Pueler JD: A simplified radiometric assay for


Manuscript received July 28, 1986. Accepted in final form November 4, 1986. Address reprint requests to: Paul D. Woolf, M.D., Department of Medicine, Endocrine-Metabolism Unit, P.O. Box 693, University of Rochester Medical Center, Rochester, New York 14642.