The Pulse Wave Velocity as an Early Indicator of Atherosclerosis in Diabetic Subjects

By G. L. Woolam, P. L. Schnur, B.S., C. Vallbona, M.D., and H. E. Hoff, M.D., Ph.D.

Despite extensive studies of the velocity of the arterial pulse wave relatively little practical use has been made of this expression of the functional status of the cardiovascular system. It has long been recognized that the velocity of a pulse wave through a fluid-filled tube is, in part, a function of the distensibility of the wall of the tube. Investigations of the relationships between pulse-wave velocity, pressure, tension, distensibility, and tube volume have been made by Bramwell, Downing, and Hill on segments of excised carotid artery and by Hamilton, Remington, and Dow on mercury-filled Gooch tubing and on the aorta of cadavers. Factors that have been shown to affect the velocity of the pulse wave through the arterial tree are (a) degree of contraction of the smooth muscle of the vessel, (b) arterial wall elasticity, (c) intra-arterial diastolic pressure, (d) wall thickness, (e) vessel tortuosity, (f) diastolic diameter of the vessel, (g) blood density, and (h) blood flow velocity. In normotensive subjects, variations in the velocity of the propagation of the pulse wave are due almost entirely to elasticity alterations.

The theoretic implication that the transmission of the pulse wave is altered in diffuse atherosclerosis has been corroborated in studies carried out in human subjects. In a recent study, Simonson and Nakagawa observed that individuals with clinically evident coronary artery disease had higher values of pulse wave velocity than healthy subjects, and they also stressed the value of measurements of the pulse wave velocity as indicators of diffuse atherosclerosis.

The large incidence of premature vascular degeneration in diabetes has been well documented. Atherosclerosis has been reported as the cause of death in more than 50 per cent of the fatalities in diabetic subjects. Furthermore, the reported incidence of vascular complications in diabetes appears to be progressively increasing. It would seem pertinent, therefore, to study whether the propagation of the pulse wave is altered in individuals with diabetes mellitus and, if so, to determine whether this alteration is due to atherosclerotic changes in the structure of the arterial wall.

Materials and Methods

The pulse wave velocity was measured in 52 diabetic persons and the results were compared to those obtained in a group of 87 healthy individuals. The method of study was identical for all the subjects.

The pulse wave velocity was measured from simultaneous tracings of the arterial pulse detected in two points of the cardiovascular system. The transducer used to record the pressure pulse was a piezoelectric crystal microphone of high efficiency and high frequency response. The value of the piezoelectric crystal microphone for recording the pressure pulse was recognized in 1941 by Miller and White, but they used a pneumatic coupling between the cup applied to the pulsating area and the microphone. This coupling was the cause of a small time lag between the occurrence of the pulse wave and its registration. The crystal pick-up that we used for this study was applied directly to the skin over the vessel, thereby eliminating any time lag and the low efficiency of a pneumatic coupling. One pressure pulse pick-up was applied to the wrist and held in position with an elastic bracelet. The second pick-up was held by the operator over the carotid vessel near the site of the bifurcation. Thus, simultaneous tracings of the pressure

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pulse at the right radial and at the right carotid arteries could be obtained. All recordings were made with a Sanborn Twin-Viso direct-writing instrument. The speed of the recording paper was 10 cm. per second.

In all the subjects the measurements were made between 2 and 5 p.m., at least 2 hours after meals, with the subject at a resting state (but not basal), in the supine position, and at the resting expiratory level. Alterations in pulse wave velocity due to extraneous factors were minimized by observance of the above conditions. The arterial blood pressure was obtained by the auscultatory method in the right arm with the subject in the supine position before and after the recording of the pressure pulses.

In order to calculate the velocity of the propagation of the pressure pulse wave, it was necessary to make an accurate measurement of the length of the segment of the arterial tree where the pulse wave was recorded. This distance could not be measured directly, but it was computed as the difference between two separate measurements. The first measurement was the distance from the proximal tip of the right clavicle (the usual point of bifurcation of the innominate artery) to the point where the transducer was applied over the right carotid artery. This distance was measured along the right side of the neck which was slightly extended. The second measurement was that of the distance from the proximal tip of the right clavicle to the place where the transducer was applied at the styloid process of the radius. This distance was measured along the course of the brachial and radial arteries with the arm extended and the shoulder abducted 90 degrees. Bazett and Dreyer correlated measurements calculated in this fashion in the intact cadaver with actual measurements of the distance between two points of the arterial tree after dissection. The error between the two measurements was of the order of 1 cm. or less.

The time of arrival of the pulse wave at the point of recording was taken as the intercept of the diastolic portion of the pressure pulse wave and the ascending limb produced by the rapid ejection of blood from the ventricle. The intercept could always be clearly defined, and errors introduced in attempting to determine the transition of the presystolic ejection phase to the phase of rapid ejection were thus avoided. Differences in time of onset of the carotid and radial pulses in the best five cycles of each record were read to the nearest 0.002 second and averaged.

The mean velocity of the pulse wave in this portion of the arterial tree was then calculated by the formula, \( V = \frac{L}{T} \) (\( V \) = velocity in meters per second; \( L \) = length of the vessels in meters; and \( T \) = time of transmission of the pulse wave in seconds). The standard error of the measurement, calculated from two consecutive determinations in 10 healthy subjects was 0.068 meter per second.

The pulse wave velocity was determined by this method in 44 male and in eight female diabetic subjects ranging in age from 5 to 75 years. The adult patients were hospitalized at the Houston Veterans Administration Hospital. The children were staying in a summer camp of the Houston Area Diabetes Association. All these patients were taking either oral hypoglycemic agents or insulin, but they did not receive other drugs known to affect the cardiovascular system. None exhibited any evidence of arteriosclerosis or hypertension by clinical history and physical examination. The duration of diabetes in these subjects as determined from the clinical history varied from 1 month to 42 years.

Eighty-seven healthy individuals, 73 males and 14 females, ranging in age from 4 to 56 years were examined by the same technic as a control group. The majority of these subjects were staff physicians or employees of the Texas Institute for Rehabilitation and Research and medical students of Baylor University College of Medicine. There was no evidence of hypertension or diabetes in these subjects on the basis of history or recent physical examinations.

Results

The statistical data pertaining to the pulse wave velocity and the blood pressure of the 87 healthy subjects are presented in table 1.*

Table 2 indicates the data on pulse wave velocity and blood pressure obtained in the 52 diabetic subjects. The duration of the illness in each age group is also listed. In each patient a calculation was made of the ratio between the observed pulse wave velocity and the mean value obtained in the healthy subjects of the same age group (\( Q = \frac{V_p}{V_h} \)). The mean of the ratios between observed and predicted values in the different age groups of the diabetic patients are also presented in table 2. The probability

*The individual values for each healthy subject and patient of this study have been deposited as Document number 6913 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D.C. A copy may be secured by citing the Document number and by remitting $1.25 for photoprints, or $1.25 for 35 mm. microfilm. Make checks payable to: Chief, Photoduplication Service, Library of Congress.
Healthy Subjects

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of subjects</th>
<th>1-10</th>
<th>11-20</th>
<th>21-39</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse wave</td>
<td>Range</td>
<td>5.51-8.46</td>
<td>6.40-8.62</td>
<td>6.00-9.00</td>
<td>6.22-10.19</td>
<td>7.38-11.00</td>
<td>7.25-10.91</td>
</tr>
<tr>
<td>velocity (Vp)</td>
<td>Vp</td>
<td>6.75</td>
<td>7.51</td>
<td>7.78</td>
<td>7.86</td>
<td>8.80</td>
<td>9.04</td>
</tr>
<tr>
<td>(m/sec.)</td>
<td>σ</td>
<td>0.97</td>
<td>0.92</td>
<td>0.89</td>
<td>1.00</td>
<td>1.00</td>
<td>1.17</td>
</tr>
<tr>
<td>Systolic</td>
<td>Range</td>
<td>90-100</td>
<td>106-137</td>
<td>110-140</td>
<td>106-140</td>
<td>105-140</td>
<td>116-142</td>
</tr>
<tr>
<td>blood pressure</td>
<td>X</td>
<td>98</td>
<td>121</td>
<td>123</td>
<td>126</td>
<td>128</td>
<td>132</td>
</tr>
<tr>
<td>(mm. Hg)</td>
<td>σ</td>
<td>8.14</td>
<td>8.66</td>
<td>7.06</td>
<td>9.86</td>
<td>9.99</td>
<td>9.52</td>
</tr>
<tr>
<td>Diastolic</td>
<td>Range</td>
<td>58-72</td>
<td>70-82</td>
<td>72-88</td>
<td>64-95</td>
<td>48-90</td>
<td>80-92</td>
</tr>
<tr>
<td>blood pressure</td>
<td>X</td>
<td>64</td>
<td>76</td>
<td>77</td>
<td>77</td>
<td>79</td>
<td>83</td>
</tr>
<tr>
<td>(mm. Hg)</td>
<td>σ</td>
<td>6.31</td>
<td>3.67</td>
<td>5.50</td>
<td>8.28</td>
<td>11.10</td>
<td>4.50</td>
</tr>
</tbody>
</table>

Table 1

values for the differences between the mean pulse wave velocities of the diabetic patients and the healthy subjects are indicated in the table. There was no significant correlation (r = 0.07) between the duration of diabetes and the degree of increase in pulse wave velocity (as determined by Q). When the individual values of pulse wave velocity were correlated with the duration of illness a higher, but not significant negative correlation was obtained (r = -0.41).

The coefficient of correlation between pulse wave velocity and the systolic blood pressure was 0.45 for the healthy subjects and 0.28 for the diabetic persons. The correlation coefficients for diastolic blood pressure and pulse wave velocity in the healthy and diabetic groups were 0.46 and 0.40, respectively.

Discussion

The Pulse Wave Velocity in Healthy Subjects

The values of pulse wave velocity in healthy subjects have been established by several workers who utilized technics similar to the one we used in this study. Hallock in 1934 studied the pulse wave velocity in the radial artery and in the aorta in 591 subjects. The values that he reported for the radial pulse wave velocity are similar to those of this study, but the mean values of all our groups are consistently higher than those of Hallock's study. This is most manifest in the younger age groups. A test of significance of this discrepancy is precluded because of the unavailability of the individual values for each one of the subjects in Hallock's study.

A significant increase of the pulse wave velocity with age was found in the studies of Hallock and Bramwell. Bramwell reported, however, that the rate of increase in pulse wave velocity was smaller in the higher age groups. This is in contradiction with the values reported by Hallock and it is probably an invalid conclusion, since the size of the sample of Bramwell's study in the older individuals is smaller than that of Hallock. Our sample beyond the age of 50 is also very small and for this reason we could not obtain statistical values beyond this age. However, from the linear regression equation obtained with the values on healthy subjects below 50 we were able to predict the values for subjects beyond 50 years of age (fig. 1). Our predicted values are in complete agreement with those observed by Hallock in subjects of comparable ages. The slope of the regression equation reflects the increase in pulse wave velocity that is expected when the arteries become less distensible due to structural changes that take place with age.

The Pulse Wave Velocity in Diabetic Subjects

The pulse wave velocity of the diabetic subjects was higher than that of the healthy subjects in all but one age group. This is reflected in the value of the ratio between the observed pulse wave velocity in diabetic subjects and that predicted for the corresponding decade of age (Q). The mean value
Table 2

Diabetic Subjects

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number of subjects</th>
<th>1-10</th>
<th>11-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
<th>61-70</th>
<th>71-80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of diabetes (months)</td>
<td>Range</td>
<td>12-48</td>
<td>6-90</td>
<td>84-144</td>
<td>1-132</td>
<td>2-252</td>
<td>1-60</td>
<td>1-168</td>
<td>1-120</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>Range</td>
<td>90-122</td>
<td>98-114</td>
<td>116-130</td>
<td>106-130</td>
<td>106-148</td>
<td>112-142</td>
<td>110-144</td>
<td>118-136</td>
</tr>
</tbody>
</table>

*Q = \( \frac{V_b}{V_h} \) for each age group except for subjects between 61-70 and 71-80 years where \( V_h \) was extrapolated from the regression equation.
PULSES WAVE VELOCITY

Graphic presentation of the pulse wave velocity in diabetic subjects. The solid line expresses the regression equation of the values for the healthy subjects of this study. The dotted line represents the regression equation of the values obtained in healthy subjects in Hallock's study.20

Influence of the Duration of the Disease

The results of this study failed to indicate any positive correlation between the duration of the disease and the increase of the pulse wave velocity. Indeed, we have observed high pulse wave velocities in very young diabetic persons. It should be recognized, however, that the duration of the illness, as it was expressed in this study, may not be a precise measurement of the time at which the altered metabolic forces began to exert their influence. Furthermore, information was not available to us as to the degree of control that was obtained in these subjects under the variety of therapeutic regimens to which they had been subjected.

Students of diabetes have long debated the exact role that the control of carbohydrate metabolism in diabetes may have on the eventual development of degenerative vascular complications.25 This remains an unsettled question because of the problems involved in the evaluation of the intervening factors. A clarification of this point awaits the collection and analysis of data of longitudinal studies carried out in a sufficient number of diabetic patients. If such longitudinal studies are indeed warranted, it is the conclusion of
A radial pulse tracing of a healthy person (A) is presented with that of a diabetic patient (B) in order to illustrate the significant decrease in amplitude of the dicrotic wave (d) observed in the diabetic patient.

this study that periodic evaluations of the pulse wave velocity should help the clinicians to detect early atherosclerotic changes. Correlation of the information thus gathered with measurements of other physiological and biochemical variables may permit a better understanding of the pathogenesis of cardiovascular complications of diabetes.

Summary
The arterial pulse wave velocity was measured in 87 healthy individuals and in 52 diabetic patients who did not have clinical evidence of atherosclerosis or hypertension. A significant increase in the pulse wave velocity was found in the diabetic subjects. This increase was not correlated with the duration of their illness as judged from clinical history. It is very likely that the high values of pulse wave velocity were indicative of an incipient process of diffuse atherosclerosis and that the measurement of the pulse wave velocity brought this into evidence earlier than the classic signs and symptoms. Serial measurements of the pulse wave velocity in diabetic subjects may permit early detection of atherosclerosis in these patients.

References
17. Beyerhol, O.: Studies on the velocity of

I have three personal ideals. One, to do the day's work well and not to bother about tomorrow . . . The second ideal has been to act the Golden Rule, as far as in me lay, toward my professional brethren and toward the patients committed to my care. And the third has been to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with the courage befitting a man.—SIR WILLIAM OSLER. Aphorisms From His Bedside Teachings and Writings. Edited by William Bennett Bean, M.D. New York, Henry Schuman, Inc., 1950, p. 84.
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