

Studies of Pulse Wave Velocity in Potential Diabetic Subjects

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SUMMARY

The arterial pulse wave velocity was studied in seventy-five potential diabetic subjects. A significant increase in the pulse wave velocity was found in the age group of 0 to 10 and 21 to 50 yrs. when compared to an age-related group of normal subjects. Such alterations of the pulse wave velocity have been interpreted as being an index of diffuse atherosclerosis and support the concept that early degenerative vascular disease occurs in patients genetically destined to develop diabetes mellitus. Its use as a diagnostic tool and a therapeutic index has also been postulated. *DIABETES* 14:489-92, July 1965.

Diabetes mellitus is the seventh-ranking cause of death in the United States, and arterial disease accounts for 70 per cent of the deaths in diabetic patients. It has been well documented that occlusive arterial disease occurs more commonly and tends to be more severe at an earlier age in diabetics than in the general population. Recently, Woolam, Schnur, Vallbona, and Hoff¹ showed that the pulse wave velocity (PWV) was significantly increased in diabetics who were otherwise free of clinical evidence of atherosclerosis and hypertension. The increase in the PWV was interpreted as indicating the presence of diffuse atherosclerosis, and the measurement of PWV in the diabetic population permitted early detection of atherosclerotic alterations.

Since a number of functional vascular abnormalities have been shown in the close relatives of known diabetics,²⁻⁴ it seemed pertinent to test further the hypothesis that arterial changes occur in patients with diabetes, irrespective of the status of the carbohydrate defect. This paper reports PWV changes observed in individuals judged to have potential for the eventual development of clinical diabetes mellitus.

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METHODS

Arterial pulse wave velocity was measured in a group of seventy-five persons free of clinical evidence of peripheral vascular disease but believed to be potential diabetics. These subjects were taken from clinic groups similar to those employed in the earlier study.¹

Standard glucose tolerance tests, performed after three days of a carbohydrate intake of 300 gm. per day, revealed no overt carbohydrate intolerance. A positive prednisone glucose tolerance test (prednisone GTT)⁵ was used as the prime criterion for selection of the potential diabetics. The test was performed as follows: A single dose of 30 mg. of prednisone was administered orally eight hours before the start of the glucose tolerance test. The test was judged abnormal if either the thirty-minute or one-hour blood sugar exceeded 159 mg./100 ml. and the two-hour value exceeded 139 mg./100 ml. Our experience indicates that in subjects with a positive family history of diabetes (one or more overt diabetics in the immediate family) the percentage of positive prednisone GTT increases with increasing age. It was not practical to obtain a sufficient number of children with a positive prednisone GTT; therefore, fourteen subjects in the younger age groups were selected on the basis of a history of diabetes in father, mother, or sib. Our studies indicate that the majority of subjects with this close family history will have a positive response to the prednisone GTT by forty-five years of age.

The stigmata suggesting the presence of diabetes are shown in table 1. Seventy of the subjects (93 per cent) presented two or more stigmata. There is considerable confusion concerning the terminology used to classify and describe the period prior to the onset of the characteristic carbohydrate defect in diabetes. To avoid this semantic difficulty the term *potential diabetic* is used in this paper to designate the entire group of seventy-five persons.

Pulse wave velocity was measured as previously de-

TABLE 1

Findings suggesting genetic diabetes in the seventy-five individuals

		Per cent
Family history of diabetes	35/68*	52
Glycosuria under stress	25/72	35
Fetal oversize (9 lb. or >)		
Offspring (women only)	6/28	21
Family	19/42	45
Obesity	32/75	43
Hyperlipemia or hypercholesterolemia	11/65	17
Cataracts or glaucoma	4/75	5
Unusual infection	3/75	4
Positive prednisone GTT	61/61	

*Number of positives/number with adequate history or data

scribed,¹ using a Sanborn Multi-Channel photographic instrument at a paper speed of 5 or 10 cm. per second. The pulse wave of the right carotid and right radial arteries were recorded simultaneously. Differences in the time of onset of these two pulses in the best five cycles of each record were read to nearest 0.002 second and averaged. The pulse wave velocity was calculated from this and the length of the arterial segment between the two electronic pickups. These procedures were reviewed to insure that they did not differ from those employed in the earlier study.¹

RESULTS

The mean pulse wave velocity, standard deviation and standard error of the mean for each decade of life were calculated for the potential diabetics and are shown in table 2. These were compared with the previously reported normals and diabetics,¹ figure 1. In the potential diabetics, the PWV was significantly faster than the normal in the 1 to 10- and 21 to 50-yr.-old groups. Over the age of fifty years, the PWV was more rapid, but not significantly so. The potential diabetics and overt diabetics were quite similar in their patterns: In both, the tendency toward increased PWV was most marked in the younger age groups.

In all groups, there was a faster PWV with increasing

PULSE WAVE VELOCITY IN NORMALS, POTENTIAL DIABETICS AND DIABETICS

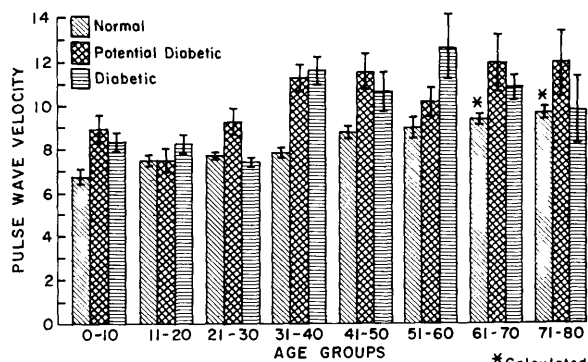


FIG. 1. The values for the normal and diabetic groups are taken from previous publications.¹ Pulse wave velocity (m/sec) \pm S.E.M.

age, which is consistent with the reports of others indicating there is loss of arterial elasticity with age.^{6,7}

Some authors⁸ have reported a relationship between elevated blood pressure and increased pulse wave velocity, while others⁹ found little correlation between the two. Abboud and Huston¹⁰ found no correlation between hypertension and arterial rigidity index, a test closely related to pulse wave velocity. In our series, there were fourteen cases with a systolic pressure above 160 mm. Hg and/or diastolic over 90 mm. In general the blood pressure elevation was minimal and often intermittent. There was no correlation between the increased BP and PWV; therefore, the results from the hypertensive patients were included in the series.

Fifty-one per cent of these potential diabetic subjects had individual PWV's which exceeded the normal range (normal mean \pm 2 S.D.) for their age groups.¹ The maximum deviation from normal occurred in the 31 to 40-yr. age group with eleven of fourteen subjects exceeding the normal range.

DISCUSSION

Defining the vascular defect (or defects) in diabetes mellitus is imperative if the present morbidity and death rate are to be favorably altered. There is good

TABLE 2
Pulse wave velocity (meters/second) in potential diabetics

Age	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Number	5	8	9	14	10	14	10	5
Mean	8.94	7.54	9.88	11.36	11.61	10.25	12.05	12.08
S.D.	1.59	1.58	1.79	2.34	2.69	2.61	4.42	3.40
S.E.	0.66	0.56	0.60	0.62	0.85	0.69	1.33	1.51
p*	<0.05	—	<0.001	<0.001	<0.01	<0.1	NS	NS

*Statistical comparison of the results from these potential diabetics with normal subjects.¹

evidence that the vascular lesions can be found microscopically prior to the manifestation of the characteristic carbohydrate defect.^{5,11,12} Moreover, the degree of atherosclerosis bears no direct relationship to the severity of the diabetes,¹³ and functional abnormalities can be detected before the carbohydrate defect and atherosclerosis are noted clinically. Huston and Abboud² found the arterial rigidity index to be increased in twenty-nine of fifty diabetics and in eleven of fifty persons with a normal intravenous standard glucose tolerance test and a positive family history of diabetes (steroid glucose tolerance tests were not performed). Lax and Feinberg³ observed an alteration in the contour of the arterial pulse wave in ninety-nine of 162 diabetics as compared to twenty-two of 275 healthy young people. They also noted that twelve of forty subjects with a family history of diabetes had similar alterations in their pulse wave contour. Glucose tolerance tests were not performed in this latter group.

In the present study, the pulse wave velocity as measured between the carotid and radial arteries was significantly increased in the years from early childhood through middle adult life (except for the second decade of life) in subjects with great potential for development of clinical diabetes. In addition, the abnormality in the PWV appears to be as marked in these potential diabetics as in the overt diabetics.

If a given individual is born with the genetic potentiality of developing diabetes, it is often forty to sixty

years before the diagnosis can be made on the basis of overt hyperglycemia. During this latent period carbohydrate tolerance apparently varies considerably, and intolerance slowly progresses to the point that it is sustained and is clinically recognizable. The carbohydrate abnormality may be detected earlier by stressing the metabolic processes with steroids or with an acute illness.

Similarly, the vascular abnormality is demonstrable subclinically early in life,^{5,11,12} and the rate of progression is highly variable, being rapid in some instances and quite slow in others (figure 2). If progression is rapid, the patient may die in the fourth or fifth decade of arterial disease before the carbohydrate defect is clinically recognized. If the vascular defect progresses slowly, the patient may have a prolonged survival in spite of brittle or poorly controlled carbohydrate abnormalities.¹⁴⁻¹⁶ It would appear from these results that rapid progression of the arterial vascular defect may occur more often than realized.

The results of this and other studies suggest that PWV might be used as a clinical and diagnostic tool in the diagnosis of diabetes mellitus and premature atherosclerosis. Serial determinations might also be used as an index of the efficacy of a therapeutic program designed to reduce the rate of progression of the atherosclerotic changes. The availability of data which are expressed in exact values and may be subjected to statistical analysis is a major advantage.

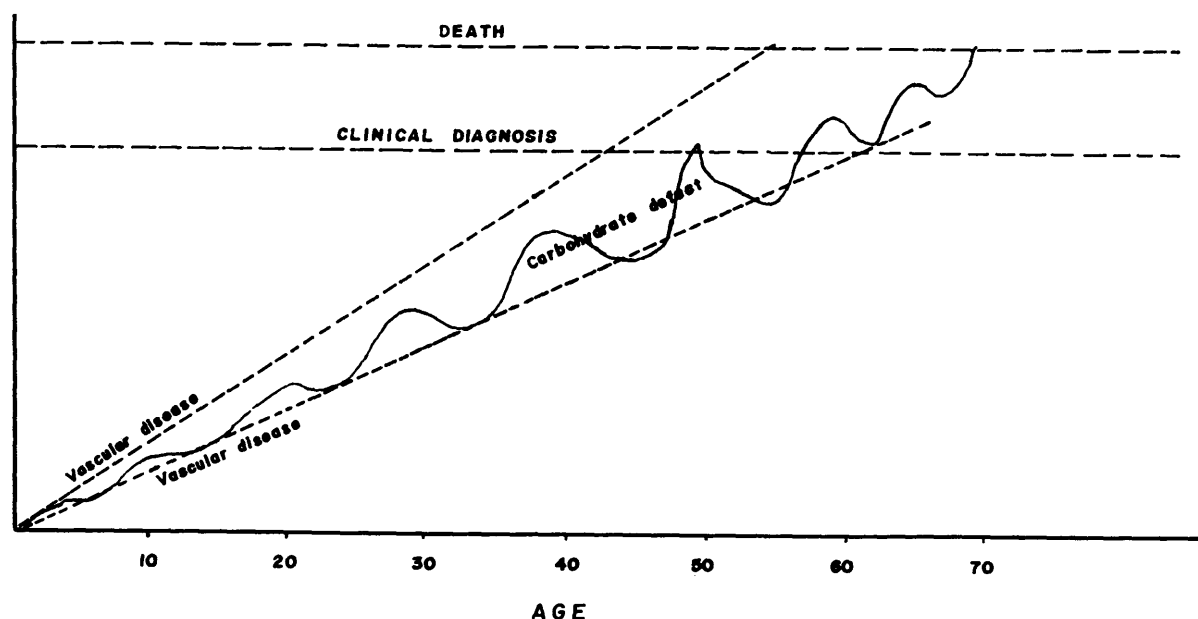


FIG. 2. Postulated relation of progression of vascular disease to carbohydrate defect.

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