Effects of Age on the Carotid Pulse in Two Greek Populations

By A. S. DONTAS, M.D., A. KEYS, PH.D., L. ANTHOPOULOS, M.D., and N. SCHULZ

SUMMARY

Right carotid pulses were recorded from 795 men in Crete in 1960 and 593 men in Corfu in 1961, representing 95% and 86% of the males, aged 25 to 74 years, in selected areas of the two islands, both areas having remarkably low prevalence of atherosclerotic disease. Five years later carotid pulses were recorded from 677 (from Crete) and 410 (from Corfu) of the same subjects.

Peak times became longer with age, reaching stable values in Corfu men in their thirties and in Crete men in their forties. Beyond this age, medians of peak times were 0.22 sec, and medians of relative peak times 24% in both areas. The relative height of the anacrotic break decreased linearly from a median value of 80 to 85% to 50 to 55% between the ages of 25 and 60 years in both areas. In general, the observed median 5-year (1960-1961 vs. 1965-1966) changes in pulse contours were similar to the differentiated groups at an earlier age than did the anacrotic break but the latter continued to be of differential value to a later age.

Elevated blood pressure had an effect on the carotid pulse similar to that of aging but less intense. However, the rate of change with aging was slower in Crete, an area with relatively higher prevalence of hypertensive disease, than in Corfu, an area with a higher incidence of coronary heart disease.

Additional Indexing Words: Blood pressure Longitudinal pulse study in populations

THE PURPOSE of this study was to determine whether carotid pulses can be recorded externally with standardized technic during epidemiologic surveys under field conditions and whether these pulses can characterize populations and individuals. Furthermore, it was of interest to see whether repeated determinations of pulses in a given population (longitudinal study) could provide data on the changes with aging, similar to data obtained by studying different age groups within the same population (cross-sectional study). Finally, an inquiry was made into the possibility that aging trends might be correlated with other indices of disease in the cardiovascular system.

A previous study reported by this group concerning two areas of Finland, a country with high prevalence of coronary heart disease, was limited to two out of every three individuals aged 40-49 years, and a large number of these subjects were not even restudied 5 years later.1 The purpose of the present study was to examine the carotid pulse in a different region, one that is relatively free of atherosclerotic disease, and to study the highest possible percentage of the population twice, 5 years apart. As such, we chose two parts of Greece, namely Crete and Corfu, that
were studied by the International Cooperative Study on Cardiovascular Epidemiology. The prevalence of "all coronary" heart disease is much lower in these islands (59 and 54 respectively per 10,000 males, aged 40-59 years) than in the United States or Finland, but interesting regional differences are present. For example, Crete has shown significantly higher prevalence of hypertensive disease, that is, definite hypertension with significant fundus changes (170 per 10,000 vs. 0 in Corfu), whereas Corfu has evidenced significantly higher 5-year incidence of "all coronary" disease (267 per 10,000 vs. 76 per 10,000 in Crete). Whether the pulse changes with aging in a population are influenced more by hypertensive or by atherosclerotic disease, therefore, deserves an answer.

Methods

The subjects studied were all males aged 40-59 years in the early fall of 1960 or 1961, registered respectively in selected villages of Crete and Corfu and composing the cohort studied by the International Cooperative Study. To obtain broader age coverage, tracings were also recorded from all males aged 25-29 and 70-74, living in the same villages. The size of the initial cohorts was 795 in Crete and 593 in Corfu. The subjects were classified into age quinquennia, and the resulting groups were numbered as follows: group 6 (aged 25-29), group 9 (aged 40-44), group 10 (aged 45-49), group 11 (aged 50-54), group 12 (aged 55-59), and group 15 (aged 70-74). As many as possible of the initial subjects were studied again 60 mo later: 677 men in Crete and 410 in Corfu.

Records were obtained at rest in bed during a 2-hour period when physical examination, electrocardiograms, and urine and blood samples were obtained from every subject. The period of rest preceding the test was not longer than 5 min, but only very rarely did the heart rate exceed 100 beats/min. The right carotid pulse was obtained on the recumbent subject with the head supported by a firm pillow, during short expiratory apnea. A circular tambour, 4.5 cm in diameter, covered with a thin rubber cuff, was applied over the point of maximal carotid pulsation and was connected by rigid tubing (PE-280) 15 cm long to a Statham P23AA transducer. The system cuff- tube-transducer had a capacity of 3.5 ml and was subjected to an inner pressure of 50 mm Hg.

The output of the transducer was fed to a transistorized two-stage push-pull d-c amplifier with a-c coupling at its exit circuit, with a time constant of 2 sec. The amplifier's output was fed into a Sanborn Visette electrocardiograph in the studies on Crete in 1960 and on Corfu in 1961 and 1966. In the studies on Crete in 1965, the output was fed into an ink-jet two-channel Elema Mingograph, along with a standard ECG lead. The frequency response of the Sanborn recorder was flat ±10% up to 15 Hz and down to 80% at 40 Hz. The Elema recorder had a higher frequency response, flat to 40 Hz. In every survey the tracings were obtained by a different person, following detailed instructions by one of us (A.S.D.). Technical difficulties and the language barrier of the person recording in Corfu in 1966, resulted in a significantly lower number of tracings on that occasion.

Determinations were made (by A.S.D. and L.A. separately on all pulses) during an average of 3 to 5 cycles for all subjects, except for two with atrial fibrillation in Corfu, and one with supraventricular tachycardia in each area. The following factors were determined: (1) peak time (P), that is the interval from foot to summit of the pulse wave, whether this was relatively early or late in systole; (2) relative peak time, that is peak time over pulse cycle (C) time; and (3) relative height of the anacrotic break, that is the ratio of amplitudes of the first anacrotic slowing (a) to that of the maximal pulse height (b). The types of tracings obtained with the two recorders, the measured pulse items, and the effects of aging are illustrated in the three examples of figure 1. The beat-to-beat variation and the possible distortion by jugular pulse admixture are apparent. Tracings in which the jugular pulse's a wave exceeded 30% of the carotid pulse's amplitude were rejected. The data in figure 1 indicate that changes in sensitivity or paper speed do not alter ratios of amplitudes or intervals, but the "personal" character of the pulse is expressed only partially by the measured items. Repeat variability of pulse items by this method, reported elsewhere, lies within the range of most electrocardiographic items. The pulse data were punched into appropriate cards, along with anthropometric, blood pressure, and electrocardiographic information on each subject; correlations, when appropriate, were carried out on a digital PDP-8/S computer.

Results

Peak Times

This is a bimodally distributed pulse characteristic with values centering around modes of 0.11 and 0.22 sec.* Thus, the cumulative

*A variety of names is to be found in the literature in identifying the two summits: early vs. late peak,
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Carotid pulses of three men in 1960 (Sanborn heated-stylus tracings) and in 1965 (Elema ink tracings). The Sanborn tracings were obtained with uniform amplitude and paper speed of 25 mm/sec. In the Elema tracings the amplitude was increased at the middle of the top and bottom tracings, and the paper speed was doubled from 25 to 50 mm/sec in the center tracing. Measured items* are indicated on one pulse of each Sanborn tracing and are indicated and labeled on two pulses of each Elema tracing. The decrease in a/b ratios and mild increase in P values in the repeat study is obvious. The marked increase in dicrotic incisura level is not analyzed herein. The small initial wave prior to the main carotid pulse deflection in the two upper Sanborn tracings and the center Elema tracing is due to the a wave of the jugular pulse. Despite this common artifact the peak time and the point of anacrotic slowing are evident and have been used in the calculation of the data.

*Peak times (in sec) are as follows in the three examples: Upper panel: (Sanborn) 0.32, 0.33, 0.29, 0.28, and 0.28, (Elema) 0.27, 0.28, 0.26, 0.40, 0.25, and 0.26. Middle panel: (Sanborn) 0.24, 0.24, 0.24, and 0.24, (Elema, slow) 0.25, 0.27, 0.26, and 0.24, (fast) 0.25, 0.24, 0.27, 0.27. Bottom panel: (Sanborn) 0.11, 0.11, 0.12, 0.12, 0.11, and 0.10; (Elema) 0.14, 0.15, 0.14, 0.16, and 0.17. Relative height of the anacrotic break (in % of max. amplitude) is as follows: Upper panel: (Sanborn) 66, 60, 44, and 65; (Elema, low gain) 30, 46, and 31, (high gain) 24, 34, and 38. Middle panel: (Sanborn) 74, 73, 83, and 86; (Elema, slow) 48, 43, 41, and 45, (fast) 37, 48, 39, and 41. Bottom panel: (Sanborn) 81, 84, 89, 76, 90, 93, and 91; (Elema, low gain) 66 and 65, (high gain) 59, 60, and 65.

percussion vs. tidal wave, anacrotic vs. systolic shoulder, first and second systolic maximum among others. No attempt has been made at systematic selection of either summit herein, because frequently only a single peak on a convex plateau was obvious and because in a digital transformation the highest deflection would be automatically selected by the computer as the peak.

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frequency distribution of peak times plotted on probability paper resulted in both examined cohorts into nonlinear relations (fig. 2). The peak time increases strikingly and early with age; this was also documented by Freis and Kyle; thus differences occur mainly between the ages of 25 and 35 with minimal changes thereafter. When peak time values accumulate around 0.22 sec, the distributions appear to approach normality, as evidenced by the progressive linearity of the cumulative distribution on probability ordinates.

Figure 2
Cumulative frequency distribution of carotid peak times in three age groups in Crete, 1960, and four age groups in Corfu, 1961, plotted on probability ordinates. Abscissa indicates absolute peak time values. Each value on the ordinate indicates the percentage of subjects with the particular value of peak time or shorter. Age group numbers refer to the following age groups: 6: 25-29 years; 9: 40-44; 11: 50-54; and 12: 55-59 years.

Figure 3
Distribution of median carotid peak times according to age in the two areas. Open circles = initial survey; full circles = 5-year follow-up study of the same subjects.
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In general, the cohort of Corfu, 1961, presents the age changes earlier, since the upper half of the distribution of group 6 (age 25-29) has already approached the cluster of lines of the more aged groups (fig. 2, right). On the other hand, the cohort from Crete, 1960, contains more subjects with long peak times, so that 20% of pulses in groups 9 through 12 have peak times longer than 0.26 sec.

The 5-year follow-up changes of the medians of peak times in the two regions are indicated in figure 3. It is evident that in Crete, these changes follow closely the cross-sectional trends with the probable exception of the older groups, which appear to have 0.01 to 0.02 sec shorter values. In the Corfu cohort, which in 1961 contained almost entirely mature-type pulses with peak times around 0.22 sec, all times were shorter by about 0.02 sec in 1966. This is probably due to minor differences in paper speed because factoring peak time by cycle time eliminates these differences (see next section). The power supply for both areas was a generator in 1960 and 1961 and the a-c state current in 1965 and 1966.

Relative Peak Times

The distribution of relative peak times (P/C values) is also bimodal in the younger age groups 6 and 9, but thereafter it approaches normality, indicated by the linearity in the distributions on probability paper of the older age groups (fig. 4). Age groups 9 through 12 have nearly identical distributions in both areas. The age differences within each area are significant by the t-test (P ≤ 0.04) between groups 6 and 9, and between 10 and 11 of Crete in 1960, and of Corfu in 1961.

The 5-year changes of the medians of relative peak times for each age quinquennium are indicated in figure 5. These longitudinal changes follow closely the cross-sectional trends obtained in the initial surveys, except in the two oldest groups, which have somewhat shorter median values in both resurveys. Here also the Corfu material shows more influence of age, because the stable value of P/C (24%) is reached at about the age of 30 in this material, and a full decade later in the material from Crete.

Anacrotic Break

Figure 6 indicates the cumulative frequency distribution of this item in the Crete, 1960, and Corfu, 1961, material. As previously documented in a U. S. sample, values of a/b are normally distributed, with the exception of the younger age groups 6 and 9 from Crete. The lines of successive age groups are transposed to the left, and this occurs more markedly in Corfu. Thus, differences between identical age groups of Corfu vs. Crete are

Figure 4

Cumulative frequency distribution of relative peak times in three age groups in Crete, 1960, and four age groups in Corfu, 1961. Abscissa indicates percentage of cycle time occupied by peak time. Age group numbers indicate ages as in figure 2.
significant \((P \leq 0.01)\) by the Kolmogorov-Smirnov two-tailed test between all but the oldest groups of the two areas. Differences between successive age groups within each area are significant \((P \leq 0.02)\) by the \(t\)-test between groups 6 and 9, 9 and 10, 10 and 11, 12 and 15 of Crete in 1960, and groups 6 and 9, 9 and 10, 10 and 11 of Corfu in 1961.

The longitudinal changes of the medians of the distributions are indicated in figure 7. In both areas, the median values decrease linearly with age, but this is arrested at levels of 50 to 55% in both populations, the Corfu pulses reaching this level at an earlier age. The Crete, 1965, data (full circles) confirm the observation from peak times that longitudinal and cross-sectional data of this cohort yield the same age trends. By contrast, the Corfu, 1966, data present a greatly reduced age trend so that all medians are concentrated between 75 and 65%. The significantly fewer subjects examined in 1966 and difficulties in this survey, resulting in several poor quality records, suggested that the different results were related to inadequacies of observer-subject interaction; so no further analysis of these data was carried out.

The question of whether a "true" uniform carotid aging effect does exist in Crete and whether this is a consistent individual change is answered in table 1, where the mean values and individual changes of a/b in men examined in 1960 and 1965 are indicated and tested with regard to consistency and significance. The mean levels are significantly lower in the second round in all age groups except the two oldest ones, and the sign change (decrease of value) is also consistent in the same groups. Further, a \(t\)-test was carried out between a/b values of Cretan men who were originally in the age groups of 45-49, 50-54, and 55-59, against those reaching these ages 5 years later, since these were the only available data on two "related" populations of the same ages.* The differences in mean a/b values are not significant for the age groups 45-49 and 55-59, and just reach the 5% level \((t, 2.08;\)

*This test was not carried out for values of \(P\) or \(P/C\) as these items are grossly identical beyond the age of 45.

\(\text{Figure 5}\)

Distribution of medians of relative peak times according to age and area. Open circles, initial survey; full circles, 5-year repeat study of the same subjects.
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Cumulative frequency distribution of relative heights of the anacrotic break in all groups of subjects in the initial surveys of the two areas. Values on the abscissa indicate the pulse upstroke level at which the first slowing occurs. Age group numbers are as indicated in the section on "Methods."

Median values of the distribution of relative heights of the anacrotic break according to age and area. Open circles: initial survey. Full circles: 5-year resurvey, Crete, left, and Corfu, right.
Table 1

<table>
<thead>
<tr>
<th>Age in 1960 (yr)</th>
<th>1st survey</th>
<th>2nd survey</th>
<th>Differences, 1st-2nd surveys</th>
<th>Frequency of *</th>
<th>Sign test †</th>
<th>Significance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean ± sd</td>
<td>Mean ± sd</td>
<td>Mean ± sd</td>
<td>t</td>
<td>Frequency of *</td>
<td>Sign test †</td>
</tr>
<tr>
<td>25-29</td>
<td>62</td>
<td>81.50 ± 12.10</td>
<td>75.48 ± 11.61</td>
<td>6.02 ± 14.26</td>
<td>1.81</td>
<td>3.322</td>
</tr>
<tr>
<td>40-44</td>
<td>136</td>
<td>74.14 ± 15.16</td>
<td>65.58 ± 13.67</td>
<td>8.56 ± 19.62</td>
<td>1.68</td>
<td>5.088</td>
</tr>
<tr>
<td>45-49</td>
<td>165</td>
<td>67.55 ± 13.94</td>
<td>61.12 ± 13.55</td>
<td>6.43 ± 19.41</td>
<td>1.51</td>
<td>4.255</td>
</tr>
<tr>
<td>50-54</td>
<td>146</td>
<td>64.47 ± 14.79</td>
<td>59.79 ± 14.84</td>
<td>4.67 ± 19.42</td>
<td>1.61</td>
<td>2.907</td>
</tr>
<tr>
<td>55-59</td>
<td>119</td>
<td>63.14 ± 13.74</td>
<td>59.81 ± 15.40</td>
<td>3.34 ± 18.00</td>
<td>1.65</td>
<td>2.022</td>
</tr>
<tr>
<td>70-74</td>
<td>40</td>
<td>54.61 ± 14.62</td>
<td>60.19 ± 15.08</td>
<td>-5.37 ± 15.85</td>
<td>2.27</td>
<td>2.460</td>
</tr>
</tbody>
</table>

*Where: - = decrease in 1965 from 1960; 0 = no change in 1965 from 1960; + = increase in 1965.
† Necessary tally of less frequent sign for significant probability of 1%.
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Table 2

Regression Coefficients (a, b) of Equation Y = a + bx,* Standard Errors of Estimate (SEE) and Product-Moment Correlation Coefficients (r)

<table>
<thead>
<tr>
<th>Comparison</th>
<th>a (intercept)</th>
<th>b (slope)</th>
<th>SEE</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crete, 1960</td>
<td>98.16</td>
<td>-0.6245</td>
<td>14.04</td>
<td>-0.373†</td>
</tr>
<tr>
<td>Crete, 1965</td>
<td>89.89</td>
<td>-0.5186</td>
<td>14.08</td>
<td>-0.302‡</td>
</tr>
<tr>
<td>Corfu, 1961</td>
<td>96.43</td>
<td>-0.7982</td>
<td>14.31</td>
<td>-0.432‡</td>
</tr>
</tbody>
</table>

*Y = relative height of anacrotic break in percentage of maximal amplitude; x = age in years (data from ages 25 to 59; for Crete, 1965, 30 to 64).
†, ‡, § P values: †P < 0.01, ‡P < 0.005, §P < 0.001.
Abbreviation: NS = not significant.

items in the initial survey differed significantly between the two cohorts in all but the eldest groups and since the 5-year resurveys in each population yielded longitudinal age-trends not different from the cross-sectional age-trends, with the exception of the measurement of anacrotic break in Corfu, 1966. These data have further shown that the pulse changes proceed up to a certain age, beyond which the pattern remains stable. This pattern is reached at an earlier age in the Corfu material (table 2). Finally, the data indicate that the carotid pulse can characterize individuals, since the 5-year changes per individual are consistent and the magnitude of change constant up to the late fifties (table 1).

Of the pulse items studied, the absolute and relative peak times are the earliest to show the effects of age: They increase from an early age and reach stable, median values of 0.22 to 0.23 sec and 23 to 25% respectively, at the age of 35 in Corfu, and 45 in Crete. In the cross-sectional studies by Freis and Kyle3 and by our own group,4 increase of amplitude of the "second systolic maximum," or appearance of "long" peak times, was the most prominent difference in the carotid pulse between subjects less than 30 and those from 30 to 45. Our previous longitudinal study on Finns1 indicated median peak times of 0.17 and 0.14 sec, respectively in age groups 40-44 and 45-49 in the East, and 0.13 and 0.14 sec in the same ages in West Finland. Although peak times increased in the 5-year resurvey, particularly in the East Finnish sample, they remained in general shorter than those of the same age groups of the two Greek areas. This should be

Table 3

Crete, 1960, and Corfu, 1961, Combined Data: Significant Chi-Square Values (> 3.84)

<table>
<thead>
<tr>
<th>Age groups</th>
<th>High BP and high P/C</th>
<th>Low BP and low P/C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic BP vs. relative peak time (P/C)</td>
<td></td>
</tr>
<tr>
<td>9 (40-44 yr)</td>
<td>11.8</td>
<td>NS</td>
</tr>
<tr>
<td>15 (70-74 yr)</td>
<td>NS</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Diastolic BP vs. relative peak time (P/C)</td>
<td></td>
</tr>
<tr>
<td>9 (40-44 yr)</td>
<td>8.6</td>
<td>5.5</td>
</tr>
<tr>
<td>10 (45-49 yr)</td>
<td>4.9</td>
<td>NS</td>
</tr>
<tr>
<td>12 (55-59 yr)</td>
<td>NS</td>
<td>11.2</td>
</tr>
<tr>
<td></td>
<td>Systolic BP vs. anacrotic break</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High BP and low a/b</td>
<td>Low BP and high a/b</td>
</tr>
<tr>
<td>11 (50-54 yr)</td>
<td>4.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

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interpreted as expressing population differences, since the technic was the same in all areas and the relative peak times of the West Finns were also generally shorter than those of the East Finns, and both were shorter than those of U. S. railroad men, and men of Crete and Corfu, at ages 45-49. Thus, a long peak time in early age is not necessarily an indication of excessive burden of coronary disease, particularly in comparisons between national groups.

The large 5-year increase in peak times in East Finland differentiated the two Finnish samples more clearly than did the 5-year changes in anacrotic break. Differentiation between the two Greek populations on the basis of peak times is effective only in the youngest age groups (group 6), because the subjects in all other groups have reached the long values, identical in both areas. Unlike the arteries of the lower extremities, the common carotid is not a usual site of occlusion. Therefore, peak times significantly longer than 0.24 sec, as recorded distally from extremital arterial occlusions, are observed in the carotid pulse primarily in aortic valve stenosis, rather than in the common local arteriosclerosis, which may occur during aging in any population. Furthermore, in heart disease of various etiology the left ventricular ejection time, calculated from the foot to the incisura of the carotid pulse, becomes shorter. Since the peak time is a large fraction of the ejection time, it should not be expected to increase under those circumstances; in fact, Crete and Corfu men aged 70-74 evidenced a minimal decrease in P and P/C values in the 5-year resurveys.

In contrast to changes in duration of systolic fractions, the changes in relative contour amplitudes, resulting in lower relative levels of anacrotic break, differed in two respects: (1) They progressed up to a more advanced age. (2) They were significantly different between the two Greek populations up to age 70, Crete having consistently more "juvenile" pulses. These data indicate that peak times are an early indicator of aging changes of the carotid pulse, whereas the anacrotic break can differentiate subjects and groups up to a more advanced age. They further indicate that within Greece the changes in carotid pulse upstroke between 25 and 60 are influenced more by abnormalities related to coronary heart disease levels than by differences in prevalence of hypertension.

The prevalence of hypertension in the two islands studied is rarer than in the 18 population samples covered by the Cooperative Study, particularly at ages 50-59. In this age group, 6% of the Cretans and 7% of men of Corfu had diastolic blood pressure ≥ 100 mm Hg, whereas figures for U. S. railroad men, West Finns, East Finns, and all 18 samples combined, were 19, 9, 24, and 13.7%, respectively. The low rates of hypertension and the finding that, within the two Greek areas, high deciles of blood pressure have an effect on the pulse in only certain age groups, indicate that the effect of elevated blood pressure cannot be further evaluated in a relatively hypertension-free population, such as the present one. The carotid pulse reflects altered myocardial contraction as well as local arterial changes, and the factors prolonging the cardiac ejection rate and those increasing the vessel stiffness have opposite effects on the arterial pulse upstroke.

A short comment about the Corfu data of 1966: The present technic involves careful positioning of a small tambour over the area of maximal carotid pulsation. Thus improper application, insufficient cuff pressure, or respiratory difficulties will result in large venous pulse admixture or other anomalies distorting relations of heights without grossly influencing the arrival of the arterial pulse wave and the main upstroke. Therefore, time elements have been used in the present analysis, but amplitude measurements appeared to be much less reliable and have been rejected for analysis. In conclusion, it should be stressed that in the execution of analogous skilled nontraumatic technics in epidemiologic surveys with limited time available, the operator must be thoroughly familiar with the method and develop a close observer-subject cooperation, otherwise the results might become useless by operational defects.
Acknowledgment

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