Hypertension and Coronary Occlusion

By Arthur M. Master, M.D.

The problem of the relationship between hypertension and coronary occlusion has been re-examined. Using newly established limits of hypertension, 600 consecutive private patients with coronary occlusion—500 men and 100 women—all under 65 years of age, were studied. Hypertension did not appear to be a factor in producing coronary disease and occlusion among men, but was a definite factor in its causation among women. The possible relation of the serum cholesterol, the $S_1$ 12-20 lipoprotein fraction, and the sex hormones to atherosclerosis and hypertension is discussed.

Ever since coronary occlusion became a well recognized clinical entity, many writers have suggested that hypertension was a common antecedent of the condition in both men and women, and a significant factor in its etiology. My colleagues and I, also, have reported similar findings, and have concurred in these opinions.

Thus, in 1939, Master, Dack, and Jaffe studied 500 patients with coronary artery occlusion, 387 men and 113 women. Using a systolic pressure of 150 mm. Hg and/or a diastolic pressure of 90 mm. Hg as a definition of hypertension, they found that 219 of the men (56.5 per cent) and 90 of the women (80 per cent) were hypertensive; an average of 61.8 per cent. The number of patients who had had hypertension prior to the coronary occlusion was found to increase with advancing age. Thus, only 28 per cent of the men below 35 years of age were hypertensive, but the incidence rose rapidly to 80 per cent, at and above the age of 70 years. In the women with coronary occlusion, hypertension was found to be even more common than in the men, and to increase in frequency more rapidly; it was present in only 25 per cent of those below 35 years and in from 90 to 100 per cent of those who were 45 years of age or over.

In 1943, in a similar study, Master, Jaffe, Dack and Silver, employing a systolic blood pressure of 150 mm. Hg and/or a diastolic pressure of 96 mm. Hg as evidence of hypertension, found that 69 per cent of all the patients had suffered from hypertension before the coronary artery occlusion had occurred.

From the foregoing reports, it appeared that hypertension was an important predisposing factor in coronary occlusion, particularly in the older age groups and especially in women. Apparent confirmation of this opinion was found in the greater incidence of "hypertension" in patients with coronary occlusion than in the general population. Thus, for example, in the study to which reference was just made, "hypertension" was found to be four or five times more frequent in the 25 to 54 year age group of males and females with coronary occlusion, and two to three times more frequent in the 55 to 74 year group, than it was among the general population.

However, even in 1939, Master, Jaffe and Dack emphasized the fact that hypertension was not the only etiologic factor in coronary occlusion, since the majority of patients under 45 was not hypertensive. Durant and also Franklin questioned the relationship between hypertension and coronary occlusion. In retrospect, it seems obvious that the premise that "hypertension" caused coronary occlusion was untenable, since one definition of hypertension was applied to all ages and to both sexes. Furthermore, in the cited report of Master, Jaffe and Dack the prognosis was found to be the same, whether hypertension was or was not present. Conner and Holt, as well as many others, had also found that the occurrence of hypertension was of no significance in the prognosis of coronary thrombosis.

It is now our opinion that the conclusions formerly reached concerning the relationship of hypertension to coronary occlusion are not valid. "High" systolic and diastolic blood pres-
Six hundred consecutive patients with coronary occlusion, seen in private practice, were studied. Five hundred were men and 100 were women, all under the age of 65. Patients over 64 were not included in this study, solely because the newly established blood pressure limits had not been determined for individuals beyond that age. To this extent, therefore, the group studied was a selective one. This relative selectivity was not significant, however, since only 6 per cent of the male population of New York City and less than 7 per cent of the female population were more than 64 years old,

During the time of this study (1946-1948),

It is evident that the blood pressure which had been present before the coronary occlusion occurred is the criterion, since the arterial tension almost invariably falls after the coronary occlusion. The preocclusion pressure was, therefore, definitely ascertained in 478 of our 600 patients. In many of the 478 cases, the writer had himself recorded the blood pressure before the occlusion occurred. In the others the information was obtained directly from the referring physician, or from the patients, if they actually knew their previous blood pressure readings. In the remaining 122 patients, clinical judgment was used in estimating the previous blood pres-
sure. Cognizance was taken of the fact that the blood pressure usually falls rapidly and early in the attack of coronary occlusion, and that about one-third of the hypertensive patients thereafter permanently loses their hypertension.19 Hence, if, for example, on the second or third day of the coronary occlusion, the blood pressure was 160/100 mm. Hg, it was concluded that the pressure had probably been higher before the attack. If it was 180 to 240 mm. Hg systolic and 120 to 140 mm. Hg diastolic during the first and second days (a tension found in a recent case of coronary occlusion), hypertension was believed to have been present previously, in spite of the fact that the blood pressure prior to the attack was unknown, and in spite of the further fact that the blood pressure had continued to be normal—110 to 130 systolic and 80 to 90 mm. diastolic—for from 1 week to 14 months after the occlusion. If the blood pressure returned to a hypertensive level after a few months, or within a year after the attack of coronary occlusion, it was assumed that the patient had had hypertension before the attack. Finally, typical eye ground changes, an enlarged heart with characteristic contour of the left ventricle and aorta, and a typical electrocardiographic pattern of left ventricular strain were considered to be acceptable evidences of the presence of hypertension.

A few of the patients had “borderline” blood pressures, that is, blood pressure readings higher than the normal range, but not quite elevated to the limit definitely demarcating “hypertension.” 54 The borderline cases were not considered in this report, because they were so few, and because a clearer impression can be obtained by comparing patients who had definitely elevated blood pressure with those who had definitely normal blood pressure.

Of the 500 male patients who suffered a coronary occlusion (table 3) the largest number (25.6 per cent) was between 50 and 54 years of age; 23.0 per cent were between 55 and 59 years of age, 17.9 per cent were 45 to 49 years old, 15.4 per cent were 40 to 44 years old, 12.6 per cent were 60 to 64 years old. Thus, almost half of the male patients were between 50 and 60 years of age. These seem to be the dangerous years for coronary occlusion, at least when men under 65 are considered. Nevertheless, nearly two-fifths (38.7 per cent) of the patients were under 50 years of age.

The frequency of hypertension among the 500 male patients averaged 27.2 per cent. Beginning with the age of 40, when the number of cases was large enough to be statistically significant, the increase in the frequency of hypertension with age was barely perceptible. In the 40 to 49 year age group, the frequency of hypertension was 26 per cent; in the 55 to 59 year age group, it was nearly 29 per cent; and in the 60 to 64 year age group, it was 30 per cent. Thus, the frequency of hypertension, among men with coronary occlusion, increased only slightly, if at all, with the increasing years.

### Table 3.—Blood Pressure in Coronary Occlusion. 500 Males

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Hypertension</th>
<th>Borderline</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>(25-44)</td>
<td>500</td>
<td>136 (27.2)</td>
<td>32 (6.4)</td>
<td>332 (66.4)</td>
</tr>
<tr>
<td>25-39</td>
<td>27</td>
<td>6 (22.2)</td>
<td>1 (*)</td>
<td>20 (74.1)</td>
</tr>
<tr>
<td>40-44</td>
<td>77</td>
<td>20 (26.0)</td>
<td>3 (3.9)</td>
<td>54 (70.1)</td>
</tr>
<tr>
<td>45-49</td>
<td>90</td>
<td>23 (25.6)</td>
<td>5 (5.6)</td>
<td>62 (68.8)</td>
</tr>
<tr>
<td>50-54</td>
<td>128</td>
<td>35 (27.3)</td>
<td>6 (4.7)</td>
<td>87 (68.0)</td>
</tr>
<tr>
<td>55-59</td>
<td>115</td>
<td>33 (28.7)</td>
<td>10 (8.7)</td>
<td>72 (62.6)</td>
</tr>
<tr>
<td>60-64</td>
<td>63</td>
<td>19 (30.4)</td>
<td>7 (11.0)</td>
<td>37 (58.6)</td>
</tr>
</tbody>
</table>

* Less than 3 cases, per cent not calculated.

Only 27 per cent of the 500 men had had hypertension before the coronary occlusion occurred, whereas more than 70 per cent had had normal blood pressures previously. It would certainly appear, therefore, that hypertension, if it is a factor at all, is not the all important one in men who sustain coronary occlusion. This conclusion is at variance with that of any other reported study on the relationship of the blood pressure to the onset of coronary occlusion.

To determine the relation of hypertension to coronary occlusion in women, we studied the histories of 100 women, examined consecutively, with coronary occlusion (table 4). Among the 100 women, coronary occlusion occurred at a later age than among the men. The largest number (32 per cent) of the female
patients was between 60 and 64 years of age; 28 per cent were between 55 and 59 years of age; 18 per cent were between 50 and 54 years of age. Thus, three-fifths of the female patients were 55 years of age or older, whereas barely 22 per cent were less than 50 years old.

A tabulation of the blood pressure incidence of hypertension in the 100 women who sustained coronary occlusion is shown in table 4. Seventy-one per cent of the women had had hypertension preceding the attack, according to the new limits established by Master, Dublin and Marks.34 The actual number of female patients in each decade is too small, so that no conclusion can be drawn concerning the increasing incidence of hypertension with increasing age among women. We can say definitely, however, that hypertension was a very significant factor in women who sustained coronary occlusion. This is quite different from the conclusion drawn from the observations among the men.

Even when the newer, more liberal definition of hypertension is employed, hypertension is, apparently, just as common among women as it was when the much lower limits of high blood pressure were accepted as criteria. The probable explanation for this seeming contradiction lies in the fact that women over the age of 55 more often suffer from coronary occlusion; in this age group, relatively "high" blood pressures are as frequent, whether the new definitions of hypertension, or whether the old limits (150 mm. Hg systolic and/or 90 mm. Hg diastolic) are used.

The results of a recent postmortem study by Zeman and Schwartz37 are in keeping with the findings reported in this clinical study, namely, that hypertension does not appear to be a factor in producing coronary disease and occlusion among men, but is a definite factor in its production among women. Zeman and Schwartz37 reported on a postmortem study of 154 unselected patients, from the Home for Aged and Infirm Hebrews of New York City. All had been over 60 years of age; 66 were males and 88 were females. The subjects were divided into three groups: those who had had a normal blood pressure, those who had had a systolic hypertension, and those who had had both a systolic and a diastolic hypertension. Among the males, in these three groups, no significant difference was found in the incidence of coronary occlusion. About one-third of all the males had had a coronary occlusion. None of the females, who had had a normal blood pressure, suffered from a coronary occlusion; those who did suffer from an occlusion had either a systolic hypertension or both a systolic and a diastolic hypertension.

**Discussion**

The average age of the men who sustained a coronary occlusion (51.1 years) was lower than that of the women (54.8 years), a difference of almost 4 years. In another recently reported series the difference was even greater, that is, the women were 6.4 years older at the time of the attack.35

Men developed coronary occlusion much more frequently than did women; furthermore, it occurred at an earlier age in men, and only one-fourth of the men had had hypertension prior to the attack. On the other hand, the majority of women who sustained a coronary occlusion did have hypertension, and they were, on the average, four or five years older than the men. What accounts for these differences between the sexes, and how significant are they? The following brief explanations seem plausible, but it should be remembered that they are theoretic, and are based merely on some suggestive data.39

The normal serum cholesterol, the Gofman lipoprotein fraction $S_f$ 12–20, and the beta-lipoprotein fraction of the blood have been found to vary with sex and age.40–42 In men,
the serum cholesterol reaches its peak at the age of 55, and in women between the sixtieth and seventieth years. This may account, in part, for the later occurrence of coronary occlusion in women. In men, the Svedberg flotation fraction of the blood, that is, the S₁₂₋₂₀ lipoproteins, rises from 25 mg. per 100 cc. at the age of 25 to 39 mg. per 100 cc. at the age of 30, and remains at that high level until the sixtieth year. In women, on the contrary, the rise is slow between the age of 25 and 60. Only at the age of 60, do women attain the high figure which men have at the age of 30. This, too, may account for the greater incidence and earlier occurrence of coronary artery disease and coronary occlusion in males. In men, between the ages of 18 and 35, there is more beta-lipoprotein in the plasma than in women of the same age. This is another possible cause for the earlier development of coronary sclerosis in males. Dock's finding that the intima of the coronary arteries in the newborn male is thicker than in the newborn female may also account for the greater frequency of coronary disease in men.

We have shown that three-fourths of the women with coronary occlusion and only one-quarter of the men had had previous hypertension, according to the new criteria. The serum cholesterol and the S₁₂₋₂₀ lipoprotein ratio are higher in patients with hypertension than in those with normal blood pressure, and may be the factors through which hypertension accelerates atherosclerosis. Why hypertension is a prerequisite for the development of coronary disease and occlusion among the majority of women, and only among a minority of men, is not clear.

The normal arterial tension is slightly higher in women than in men, beginning at the age of 45 to 50. Whether this is sufficient to initiate or accelerate the process of atherosclerosis in women, at the age of 55 to 60, is questionable. Our study of 74,000 gainfully employed people indicates that, until the age of 45, women have a definitely lower blood pressure than men, but that thereafter their pressure is slightly higher than that found in men. The difference is small but distinct. If one agrees with Moschowitz, who believes that heightened arterial tension eventually produces arteriosclerosis, this difference in normal blood pressure in the sexes may serve as a possible explanation of the earlier occurrence of coronary disease and occlusion among men than among women.

The continued investigation of the blood lipoproteins seems to be a promising avenue of approach to the problem of coronary disease. The discovery of means to keep this blood fraction low may help to prevent coronary disease, and lead even to the prevention of hypertension.

For many years, the relationship of both arteriosclerosis and hypertension to the sex hormones has been a subject of intriguing speculation. The predominance of coronary artery atherosclerosis in men has suggested that female sex factors protect women. Many investigators have described the beneficial effect of androgens and estrogens in angina pectoris among men and in hypertension among women. A review of the literature on this subject may be found in Hueper's monograph on "Arteriosclerosis." However, estrogens have usually been found to be ineffective clinically in coronary disease of men. Furthermore, the observations that the estrogens reduce the serum lipids in those with coronary atherosclerosis have not gone unchallenged. Glass, Engelberg, Marcus, and Gofman have administered estrogens in men and women but found no significant change in the cholesterol-lipid ratio or in the S₁₂₋₂₀ lipoprotein fraction. Altogether, the field of sex hormonal treatment has not been investigated adequately.

**Summary and Conclusion**

Hitherto, hypertension was believed to be a common antecedent of coronary occlusion in both men and women, and a significant factor in its etiology. This belief was invalid, since the same definition of hypertension was employed in patients of all ages and in both sexes.

New definitions of hypertension, varying with the age and sex of the patients, were, therefore, necessary. These were established by Master, Dublin and Marks, who adequately sampled and statistically analyzed the blood pressure readings of 74,000 working men and women, between the ages of 16 and 65.
The problem of the relationship between hypertension and coronary occlusion was then re-examined. Using these newly established limits of hypertension, we studied 600 consecutive private patients with coronary occlusion—500 men and 100 women—all under the age of 65 years.

The blood pressure which had been present before the coronary occlusion occurred was the criterion. (The borderline cases were not considered in this report.)

Men sustain coronary occlusion much more frequently than women, and at an earlier age.

The frequency of hypertension in the men averaged 27.2 per cent, and increased only slightly, if at all, with age. More than 70 per cent had had a normal blood pressure before the onset of the coronary occlusion! Hypertension, therefore, is not the all important factor in the causation of coronary occlusion in men. This conclusion differs from that of any reported studies on the relationship of increased blood pressure to the onset of coronary occlusion.

Seventy-one per cent of the women had had hypertension preceding the attack. In women who sustain coronary occlusion, therefore, hypertension is a very significant etiologic factor.

The results of a recent postmortem study confirmed our clinical findings: hypertension did not appear to be a factor in producing coronary disease and occlusion among men, but was a definite factor in its causation among women.

The possible effects of the serum cholesterol, the S1 12–20 lipoprotein fraction, and the sex hormones on atherosclerosis and hypertension have been briefly discussed. These fields of investigation hold particular promise for the treatment and prevention of coronary disease in men and of hypertension in women.

**SUMARIO ESPAÑOL**

El problema de la relación entre la hipertensión y la oclusión coronaria ha sido re-examinado. Usando los nuevos establecidos límites para la hipertensión, se estudiaron 600 casos privados consecutivos (500 hombres y 100 mujeres) todos bajo la edad de 65 años. La hipertensión no aparentó ser un factor en la producción de enfermedad coronaria u oclusión en los hombres, pero sí fue un factor definitivo en las mujeres. La posible relación del colesterol del suero, la fracción de lipoproteínas S1 12–20, y las hormonas sexuales a la ateroesclerosis y la hipertensión se discute.

**REFERENCES**

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