

# Male Pattern Baldness and Coronary Heart Disease

## The Physicians' Health Study

Paulo A. Lotufo, MD, DrPH; Claudia U. Chae, MD; Umed A. Ajani, MBBS, MPH; Charles H. Hennekens, MD, DrPH; JoAnn E. Manson, MD, DrPH

**Objective:** To examine the association between male pattern baldness and the risk of coronary heart disease (CHD) events.

**Design, Setting, and Participants:** Retrospective cohort study among 22 071 US male physicians aged 40 to 84 years enrolled in the Physicians' Health Study. Of these, 19 112 were free of CHD at baseline and completed a questionnaire at the 11-year follow-up concerning their pattern of hair loss at age 45 years. Response options included no hair loss, frontal baldness only, or frontal baldness with mild, moderate, or severe vertex baldness.

**Main Outcome Measures:** Coronary heart disease events defined as nonfatal myocardial infarction (MI), angina pectoris, and/or coronary revascularization.

**Results:** During 11 years of follow-up, we documented 1446 CHD events in this cohort. Compared with men with no hair loss, those with frontal baldness had an age-adjusted relative risk (RR) of CHD of 1.09 (95% confidence interval [CI], 0.94-1.25), while those with mild,

moderate, or severe vertex baldness had RRs of 1.23 (95% CI, 1.05-1.43), 1.32 (95% CI, 1.10-1.59), and 1.36 (95% CI, 1.11-1.67), respectively (*P* for trend, <.001). Multivariate adjustment for age, parental history of MI, height, body mass index (weight in kilograms divided by the square of the height in meters as a continuous variable), smoking, history of hypertension, diabetes, high cholesterol level, physical activity, and alcohol intake did not materially alter these associations. Results were similar when nonfatal MI, angina, and coronary revascularization were examined separately, and when events were analyzed among men older and younger than 55 years at baseline. Vertex baldness was more strongly associated with CHD risk among men with hypertension (multivariate RR, 1.79; 95% CI, 1.31-2.44) or high cholesterol levels (multivariate RR, 2.78; 95% CI, 1.09-7.12).

**Conclusion:** Vertex pattern baldness appears to be a marker for increased risk of CHD events, especially among men with hypertension or high cholesterol levels.

*Arch Intern Med.* 2000;160:165-171

From the Division of Preventive Medicine, Department of Medicine, Harvard Medical School and Brigham and Women's Hospital (Drs Lotufo, Chae, Ajani, Hennekens, and Manson), the Cardiology Division, Massachusetts General Hospital (Dr Chae), and the Department of Epidemiology, Harvard School of Public Health (Drs Hennekens and Manson), Boston, Mass.

**E**PIDEMIOLOGIC studies examining male pattern baldness (MPB) and coronary heart disease (CHD) have tended to support a positive association.<sup>1-8</sup> In the Framingham Heart Study,<sup>5</sup> progression of hair loss during adulthood was associated with CHD in men, although there was no relationship with the extent of scalp baldness. In the First National Health and Nutrition Examination Survey (NHANES I),<sup>6</sup> an association was observed between severe baldness and CHD mortality in men younger than 55 years, but not among older men. In a case-control study, vertex baldness was associated with myocardial infarction (MI) among men younger than 55 years but frontal baldness was not.<sup>7</sup> The Copenhagen City Heart Study<sup>8</sup> showed a significant association between frontal baldness and MI independent of

age, while the observed association with vertex baldness was of borderline significance.

The Physicians' Health Study (PHS) of 22 071 apparently healthy men at baseline provided a unique opportunity to evaluate whether different patterns of male baldness at age 45 years were associated with future risk of coronary events, including nonfatal MI, angina, and coronary revascularization.

## RESULTS

As shown in the **Figure**, 57.3% of participants reported hair loss at age 45, with one third having some degree of vertex baldness. **Table 1** shows the distribution of baseline risk factors across hair-pattern categories. Participants with no hair loss were less likely to be never-smokers, to have high cholesterol levels, or to report a posi-

## PARTICIPANTS AND METHODS

The methods of the PHS have been described in detail elsewhere.<sup>9-11</sup> In brief, 22 071 US male physicians aged 40 to 84 years at entry in 1982 (92.1% white) with no history of MI, stroke, transient ischemic attack, or cancer (except nonmelanoma skin cancer) were assigned to aspirin or beta carotene in a randomized, double-blind, placebo-controlled, 2 × 2 factorial trial. At baseline, the physicians completed questionnaires that elicited information about height and weight, use of cigarettes and alcohol, and frequency of physical activity, as well as information about history of hypertension, high cholesterol levels, diabetes mellitus, and parental history of MI before age 60 years.

### FOLLOW-UP

Every 6 months for the first year and annually thereafter, follow-up questionnaires were mailed to the study participants to obtain information about the occurrence of new medical diagnoses. Medical records were obtained and reviewed by the Endpoints Committee to confirm the self-reported diagnosis of MI (using World Health Organization criteria<sup>12</sup>), angina, and coronary revascularization procedures (coronary artery bypass graft or percutaneous coronary angioplasty). A validation study confirmed the self-report for 97.8% of the cases of angina, as described elsewhere.<sup>9</sup> In 11 years of follow-up, there were 1305 cases of angina, 550 cases of nonfatal MI, and 1089 coronary revascularization procedures. For our primary analyses, we used a combined end point of the first reported CHD event ( $n = 1446$ ). We also examined types of CHD events separately. Vital status was known for more than 99% of participants.

### ASSESSMENT OF HAIR LOSS

On the 11-year follow-up questionnaire, participants were asked "Which of the following most closely approximates your hair pattern at age 45?" and were given 5 possible choices<sup>13</sup> for their answers, as shown in the **Figure**. These 5 sketches were based on the Hamilton scale

for baldness, as modified by Norwood.<sup>13</sup> They represent no hair loss, frontal baldness only, or frontal baldness with mild, moderate, or severe vertex baldness. We chose to assess hair loss at age 45 years to differentiate those men with early, androgen-dependent balding from those with senescent baldness, which is more common after age 50.<sup>14</sup>

### STUDY POPULATION

Of the 22 071 randomized subjects in the PHS, 20 294 were alive at the 11-year follow-up. Of these, 19 112 answered the questionnaire and did not report angina or other cardiovascular events at baseline.

### DATA ANALYSIS






After adjusting for age and treatment assignment, we calculated relative risks (RRs) and 95% confidence intervals (CIs) for the occurrence of CHD events associated with categories of MPB using conditional logistic regression models. Multivariate logistic regression models were used to control for age (1-year categories), aspirin and beta carotene assignment, body mass index (weight in kilograms divided by the square of the height in meters as a continuous variable), height (as a continuous variable), cigarette smoking (never, past, <20 cigarettes per day, ≥20 cigarettes per day), alcohol consumption (daily, weekly, monthly, rarely/never), hypertension (self-reported systolic blood pressure ≥160 mm Hg, diastolic blood pressure ≤95 mm Hg, or taking antihypertensive medication), high serum cholesterol level (self-reported cholesterol level ≥6.47 mmol/L [250 mg/dL] or taking cholesterol-lowering medication), parental history of MI before age 60 years, and frequency of vigorous exercise (0, 1, 2-4, ≥5 times per week). Effect modification by cardiovascular risk factors was assessed by examining the relationship of hair-loss pattern and CHD risk within subgroups stratified by the presence or absence of the specific risk factor. For each RR, we calculated the 95% CI and performed a test for linear trend according to hair-pattern category. All statistical analyses were performed using SAS software, with 2-tailed  $P$  values of <.05 considered significant.

tive parental history of myocardial infarction. Participants with severe vertex baldness reported a higher prevalence of diabetes than men classified in other hair-pattern categories.

During 11 years of follow-up, the study participants experienced 1446 CHD events. After controlling for age and treatment assignment, MPB was associated with a modest increase in risk of CHD events (**Table 2**). Compared with men with no hair loss, those with frontal baldness had a relative risk of CHD of 1.09 (95% CI, 0.94-1.25), while those with mild, moderate, or severe vertex baldness had relative risks of CHD of 1.23 (95% CI, 1.05-1.43), 1.32 (95% CI, 1.10-1.59), and 1.36 (95% CI, 1.11-1.67), respectively ( $P$  for linear trend <.001). The strength of the association was not materially altered in multivariate analyses after controlling for mul-

iple potential confounders. We detected no effect modification when we performed analyses stratified by age (older and younger than 55 years at baseline).

When the end points of nonfatal MI, angina, and coronary revascularization were considered separately, similar results were obtained for each outcome (**Table 3**). In a subgroup analysis, we examined possible modifiers of the association between baldness pattern and CHD risk by cardiovascular risk factor status (**Table 4**). Vertex baldness was more strongly associated with CHD risk in the subgroup of men with hypertension (RR, 1.79; 95% CI, 1.31-2.44) or high cholesterol levels (RR, 2.78; 95% CI, 1.09-7.12) than in men without these risk factors. Frontal baldness was a significant indicator of risk only among the subgroup of hypertensive participants (RR, 1.75; 95% CI, 1.24-2.48).

Hamilton Baldness Scale Modified by Norwood <sup>13</sup>	I	II-IIIA	III-Vertex-V	VI	VII
Physicians' Health Study Classification	No Baldness	Baldness			
		Frontal	Mild Vertex	Moderate Vertex	Severe Vertex
Illustration on the 11-y Questionnaire					
No. of Respondents (%)	8159 (42.7)	4408 (23.1)	3423 (17.9)	1771 (9.3)	1351 (7.1)

Hair pattern classification and frequency among participants in the Physicians' Health Study. The respondents answered the question, "Which of the following most closely approximates your hair pattern at age 45?" with reference to the 5 diagrams pictured above.

**Table 1. Baseline Distribution of Clinical Characteristics by Classification of Hair Pattern\***

Characteristic	Hair Pattern				
	No Baldness	Baldness			
		Frontal	Vertex		
			Mild	Moderate	Severe
No. of respondents, %	8159 (42.7)	4408 (23.1)	3423 (17.9)	1771 (9.3)	1351 (7.1)
Mean ( $\pm$ SD) age, y†	52.0 $\pm$ 8.7	52.7 $\pm$ 8.9	51.8 $\pm$ 8.8	53.0 $\pm$ 9.0	52.8 $\pm$ 9.2
Risk factors (age-adjusted)					
Body mass index, kg/m <sup>2</sup>	24.9	24.8	25.0	24.9	25.1
Height, cm	178.4	178.5	177.7	177.5	177.6
Hypertension, ‡ %	10.5	10.0	11.8	11.5	10.9
High cholesterol, § %	8.4	8.8	9.1	8.6	8.8
Diabetes mellitus,    %	1.8	1.9	1.5	1.6	2.4
Parental history of MI, ¶ %	12.5	13.9	13.5	15.1	13.3
Frequency of vigorous exercise, %					
0/wk	27.0	26.0	26.5	27.6	28.5
1/wk	18.8	18.3	19.6	17.7	17.5
2-4/wk	37.9	38.9	37.9	37.9	38.8
5+/wk	16.3	16.6	15.9	16.8	15.1
Smoking, %					
Never smoked	49.6	49.9	51.3	53.4	56.3
Past smoker	39.8	39.6	37.9	37.5	35.1
Current smoker					
<20 cigarettes per day	3.5	3.9	4.2	4.1	3.6
$\geq$ 20 cigarettes per day	7.1	6.5	6.6	5.0	4.9
Alcohol use, %					
Rarely/never	14.9	13.9	14.4	13.0	14.8
Monthly	11.2	10.7	11.7	10.3	11.4
Weekly	49.1	50.8	51.3	53.0	50.7
Daily	24.8	24.6	22.6	23.7	22.9
Treatment group, %					
Aspirin	50.1	50.3	50.4	50.0	48.4
Beta-carotene	50.0	49.3	50.9	50.5	51.1

\*Ascertained on the 11-year questionnaire.

†Crude value.

‡Self-reported systolic blood pressure of 160 mm Hg or higher, diastolic blood pressure of 95 mm Hg or higher or antihypertensive treatment.

§Self-reported blood cholesterol level of 6.47  $\mu$ mol/L ( $\geq$ 250 mg/dL) or higher or treatment with cholesterol-lowering medication.

||Self-reported diabetes.

¶MI indicates myocardial infarction occurring in either parent before age 60 years.

## COMMENT

These data from a large retrospective cohort study of US male physicians indicate that MPB is a marker for risk

of CHD, with increasing risk associated with hair loss. While early studies of baldness and CHD were limited by small sample size,<sup>1-4</sup> our findings agree with results from recent large epidemiologic studies.<sup>5,6,8</sup> In the case-

**Table 2. Risk of Coronary Heart Disease\* by Hair Pattern**

Characteristic	Hair Pattern					P Trend†
	No Baldness	Baldness				
		Frontal	Vertex			
			Mild	Moderate	Severe	
<b>Total Cohort</b>						
Cases (n = 1446)	548	333	275	163	127	
Age- and treatment-adjusted RR	1.00	1.09	1.23	1.32	1.36	<.001
95% CI	Referent	0.94-1.25	1.05-1.43	1.10-1.59	1.11-1.67	
Multivariate RR‡	1.00	1.09	1.24	1.33	1.30	<.001
95% CI	Referent	0.93-1.27	1.05-1.46	1.08-1.62	1.03-1.63	
Age <55 y at baseline						
Cases (n = 568)	224	119	119	58	48	
Age- and treatment-adjusted RR	1.00	1.00	1.32	1.26	1.38	.005
95% CI	Referent	0.79-1.25	1.05-1.66	0.94-1.70	1.00-1.91	
Multivariate RR‡	1.00	1.02	1.23	1.23	1.26	.06
95% CI	Referent	0.80-1.31	0.95-1.59	0.88-1.71	0.87-1.81	
Age ≥55 y at baseline						
Cases (n = 878)	324	214	156	105	79	
Age- and treatment-adjusted RR	1.00	1.15	1.18	1.36	1.37	.002
95% CI	Referent	0.95-1.38	0.96-1.44	1.07-1.72	1.05-1.79	
Multivariate RR‡	1.00	1.13	1.25	1.39	1.36	.002
95% CI	Referent	0.92-1.38	1.00-1.55	1.08-1.80	1.02-1.82	

\*First event of confirmed angina, nonfatal myocardial infarction, coronary artery bypass grafting, or percutaneous transluminal coronary angioplasty; n indicates number of cases in model adjusted for age and treatment assignment; RR, relative risk; and CI, confidence interval.

†Test for linear trend.

‡Controlled for age (year), aspirin assignment, beta carotene assignment, body mass index, height (in centimeters), hypertension (yes/no), high cholesterol level (yes/no), diabetes (yes/no), parental history of myocardial infarction (yes/no), physical activity (0, 1, 2-4, ≥5 times per week), smoking (never, past, current <20, ≥20 cigarettes per day), and alcohol use (never, monthly, weekly, daily).

control study of 1432 men aged 21 to 54 years (665 cases of first MI and 772 controls), men with severe vertex baldness had a 3-fold higher risk of MI when compared with those with no hair loss.<sup>7</sup> A subgroup of men with severe vertex baldness and hypertension, high cholesterol levels, or parental history of MI had an even higher risk of MI before age 60 years. Our data are compatible with these findings for hypertension and high cholesterol levels, but we detected no modifying effect by parental history of MI. Our findings also extend the age range in which MPB serves as a marker for CHD and expand the range of outcomes to include angina and coronary revascularization as well as MI.

Three cohort studies have found an association of MPB and CHD risk. In the Framingham Heart Study,<sup>5</sup> the extent (defined as the number of bald areas) and progression of hair loss were analyzed in relation to risk of CHD. Baldness was assessed in 1956 and 1962 in a cohort of 2017 men observed for 24 years for new CHD events, cardiovascular events, CHD, and all-cause mortality. Men with rapid hair loss (n = 34) during the 5-year interval had a relative risk of CHD of 2.4 (95% CI, 1.3-4.4) when compared with those who had no or slight progression of baldness (n = 224). However, the absolute number of bald areas was not associated with risk of CHD. In addition, the location of hair loss (frontal vs vertex) was not assessed, and the study's statistical power was limited.

In NHANES I,<sup>6</sup> a subgroup of participants (n = 3932) was examined according to the presence and degree of baldness measured by dermatologic examination. Se-

vere baldness was positively associated with CHD mortality (RR, 2.51; 95% CI, 1.01-6.24); it was less strongly associated with CHD incidence in men younger than 55 years (RR, 1.72; 95% CI, 0.96-3.08) but not in older men. In contrast, our data indicate an association between vertex baldness and CHD in young and older men, as well as an association between severity of hair loss and increasing risk of CHD. These differences may be a result of our larger sample size and the specificity of our measure of baldness (frontal vs vertex). The Copenhagen Heart Study<sup>8</sup> observed 5837 men over 12 years and assessed 2 types of baldness, frontoparietal and crown-top, both of which were associated with CHD.

In a subgroup analysis, we found that the association between MPB and CHD risk was even stronger among men with hypertension or high cholesterol. Although the baseline prevalence of these risk factors was only slightly higher in men with hair loss, a possible link between baldness and these risk factors was suggested in the Olivetti Heart Study in Naples, Italy,<sup>15</sup> in which 872 men underwent measurements of blood pressure levels, serum cholesterol levels, and direct examinations of the scalp, with hair pattern coded as no hair loss, frontal hair loss, and frontal-occipital hair loss. A positive association was found between the frontal-occipital baldness pattern and both diastolic blood pressure and high cholesterol level.

A plausible explanation for an association between baldness and CHD may be elevated androgen levels. Men with severe baldness seem to have a greater number of androgen receptors in the scalp<sup>16</sup> and higher levels of both

**Table 3. Risk of Nonfatal Myocardial Infarction, Angina, and Coronary Revascularization by Type of Hair Pattern**

Characteristic*	Hair Pattern					P Trend†
	No Baldness	Baldness				
		Frontal	Vertex			
			Mild	Moderate	Severe	
<b>Nonfatal myocardial infarction</b>						
Events (n = 550)	197	135	112	58	48	
Age- and treatment-adjusted RR	1.00	1.22	1.38	1.28	1.39	<.001
95% CI	Referent	0.98-1.53	1.09-1.75	0.95-1.73	1.01-1.92	
Multivariate RR‡	1.00	1.26	1.46	1.32	1.30	<.02
95% CI	Referent	0.99-1.61	1.13-1.88	0.95-1.84	0.90-1.86	
<b>Angina</b>						
Events (n = 1305)	502	300	237	150	116	
Age- and treatment-adjusted RR	1.00	1.07	1.14	1.33	1.35	
95% CI	Referent	0.92-1.24	0.97-1.35	1.09-1.61	1.09-1.68	
Multivariate RR‡	1.00	1.07	1.16	1.35	1.27	.002
95% CI	Referent	0.91-1.26	0.98-1.38	1.09-1.66	1.00-1.60	
<b>Coronary revascularization</b>						
Events (n = 1089)	411	257	196	129	96	
Age- and treatment-adjusted RR	1.00	1.12	1.15	1.40	1.37	<.001
95% CI	Referent	0.95-1.32	0.97-1.38	1.14-1.72	1.09-1.73	
Multivariate RR‡	1.00	1.13	1.15	1.39	1.27	.004
95% CI	Referent	0.95-1.35	0.95-1.39	1.10-1.74	0.98-1.65	

\*n indicates number of cases in model adjusted for age and treatment assignment.

†Test for linear trend.

‡Controlled for age (year), aspirin assignment, beta carotene assignment, body mass index, height (in centimeters), hypertension (yes/no), diabetes (yes/no), high cholesterol (yes/no), parental history of myocardial infarction (yes/no), physical activity (0, 1, 2-4, ≥5 times per week), smoking (never, past, current <20, ≥20 cigarettes per day), and alcohol use (never, monthly, weekly, daily).

serum total and free testosterone.<sup>17</sup> In a recent trial with finasteride,<sup>18</sup> a drug that inhibits the conversion of testosterone to dihydrotestosterone in scalp and other tissue by blocking the 5 $\alpha$  reductase enzyme, arrest of hair loss and substantial hair regrowth were noted among men receiving the agent. High levels of androgens may directly contribute to both atherosclerosis and thrombosis, and may adversely influence risk factors such as hypertension and high cholesterol. Receptors for dihydrotestosterone have been found in mouse and baboon heart muscle and endothelial cells.<sup>19,20</sup> In rats, dihydrotestosterone may directly accelerate atherosclerosis by stimulating the proliferation of vascular smooth muscle cells.<sup>21</sup> Administration of testosterone was associated with a significant increase in platelet thromboxane A<sub>2</sub> receptor density in rodents.<sup>22</sup>

A similar effect—an increase in platelet aggregation—was observed in young men receiving clinical replacement doses of testosterone following orchiectomy.<sup>23</sup> Complete androgen deprivation for 6 months or more after orchiectomy has been associated with improved endothelial function compared with men having normal androgen levels.<sup>24</sup> Testosterone exacerbates hypertension in spontaneously hypertensive rats by reducing pressure-natriuresis<sup>25</sup> and by increasing levels of 11-deoxycorticosterone through inhibition of 11 $\beta$ -hydroxylase activity.<sup>26,27</sup>

Androgens also alter lipid profiles. In a systematic review of observational studies of anabolic steroid use, androgen administration was associated with lower levels of high-density lipoprotein (HDL) cholesterol and higher total-HDL cholesterol ratios.<sup>28</sup> Induction of ex-

perimental hypogonadism with a gonadotropin-releasing hormone antagonist (Nal-Glu) for 6 weeks increased HDL levels by 26% and total cholesterol levels by 12% among healthy young men. These lipid alterations are most likely due to decreased androgen levels because they are reversed by administration of the gonadotropin-releasing hormone antagonist together with testosterone.<sup>29</sup>

One alternative possible link between MPB and CHD could be a similar pattern of inheritance, as others have speculated.<sup>30</sup> Unfortunately, little is known about the genetics of hair loss and baldness. Male pattern baldness was first defined as an autosomal dominant trait 80 years ago,<sup>31</sup> although recent studies suggest a polygenic mode of inheritance.<sup>32</sup> Recent findings suggest genetic similarities between MPB and polycystic ovary syndrome,<sup>33,34</sup> a common familial condition in women characterized by elevated levels of androgens. Women with this disorder are likely to have an increased risk of subclinical atherosclerosis,<sup>35</sup> low levels of HDL cholesterol, high levels of triglycerides,<sup>36</sup> and an increased prevalence of MPB among their brothers.<sup>33</sup> Other genetic factors may play a role in explaining the association between MPB and CHD risk. However, controlling for parental history of premature coronary disease did not materially alter the association between MPB and CHD risk in our data.

Several potential limitations of our study warrant discussion. We did not have data about hair pattern in those participants who died before the 11-year follow-up (n = 1777), of whom approximately one third died from cardiovascular disease.<sup>11</sup> The data

**Table 4. Association Between Hair Loss Pattern and CHD Risk Within Subgroups\***

Risk Factor	Hair Pattern	RR (95% CI)
Parental history of myocardial infarction	No (n = 956)	Yes (n = 215)
	No loss	1.00 (referent)
	Frontal	1.15 (0.96-1.37)
Diabetes	No (n = 1111)	Yes (n = 60)
	No loss	1.00 (referent)
	Frontal	1.11 (0.94-1.31)
Hypertension	No (n = 901)	Yes (n = 270)
	No loss	1.00 (referent)
	Frontal	0.98 (0.82-1.18)
High cholesterol	No (n = 1139)	Yes (n = 32)
	No loss	1.00 (referent)
	Frontal	1.10 (0.93-1.29)
Smoking habit	Never smoked (n = 506)	Ever smoked (n = 665)
	No loss	1.00 (referent)
	Frontal	1.19 (0.93-1.53)
Alcohol intake	<1 time/wk (n = 508)	≥1 time/wk (n = 663)
	No loss	1.00 (referent)
	Frontal	1.14 (0.89-1.45)
BMI	<27.8 (n = 959)	≥27.8 (n = 212)
	No loss	1.00 (referent)
	Frontal	1.05 (0.87-1.25)
Physical activity	>1 time/wk (n = 561)	≤1 time/wk (n = 610)
	No loss	1.00 (referent)
	Frontal	1.13 (0.89-1.42)

\*Data are given as relative risk (RR) (95% confidence interval [CI]) after multivariate adjustment for covariates—age (year), aspirin assignment, beta carotene assignment, body mass index (BMI) (<27.8 kg/m<sup>2</sup>, ≥27.8 kg/m<sup>2</sup>), height (in centimeters), hypertension (yes/no), high cholesterol level (yes/no), diabetes (yes/no), physical activity (≤1 time per week, 1 time per week), smoking (never smoked, ever smoked), and alcohol use (<1 time per week, ≥1 time per week)—other than the subgroup itself.

about hair pattern at age 45 years were obtained on the 11-year questionnaire, at which time the physicians were aged 51 to 95 years. Recall bias is unlikely but cannot be excluded, as physicians may be aware of a possible association between MPB and CHD risk. In addition, the self-report of baldness pattern by questionnaire (Figure) was not internally validated and may have been a source of misclassification. However, the proportion of men with no hair loss in our population (42.7%) was close to that obtained in the NHANES I study<sup>6</sup> (47.5%), which was validated by dermatologic examinations. Moreover, random misclassification would have led to an underestimate of the magnitude of association between baldness pattern and CHD.

Finally, because 92.1% of the PHS participants were white, our results may not be generalizable to men of other racial groups in whom baldness pattern frequency<sup>37</sup> and risk of CHD may differ.<sup>38</sup> In summary, however, our study provides support for the hypothesis

that vertex pattern baldness is a marker for increased risk of CHD events. The observed association was independent of age and was stronger in a subgroup of men with hypertension or high cholesterol. Further research is needed to corroborate these findings and to clarify the biological mechanisms that may explain this relationship. Although early vertex baldness may be a non-modifiable risk factor for CHD, it may serve as a useful clinical marker to identify men at increased risk who may benefit from aggressive screening and primary prevention efforts directed toward other known modifiable risk factors for CHD.

Accepted for publication April 13, 1999.

This study was supported by grants HL26490, HL34595, CA34944, and CA40360 from the National Institutes of Health, Bethesda, Md.

Paulo A. Lotufo, MD, is recipient of fellowship 97-02424-8 from the Fundação de Amparo a Pesquisa de Estado de São Paulo, São Paulo, Brazil.

We are grateful to the 22 071 dedicated and conscientious physicians who participated in this trial. We also thank Anna Klevak, PhD, for her expert assistance.

Reprints: JoAnn E. Manson, MD, DrPH, Division of Preventive Medicine—Brigham and Women's Hospital, 900 Commonwealth Ave E, Boston, MA 02215-1204.

## REFERENCES

- Cotton SG, Nixon JM, Carpenter RG, Evans DW. Factors discriminating men with coronary heart disease from healthy controls. *Br Heart J*. 1972;34:458-464.
- Ben-Halim MM, Meyrick G, Jeans WD, Murphy D, Burton JL. Myocardial infarction, androgen and the skin. *Br J Dermatol*. 1978;98:63-68.
- Cooke NT. Male pattern alopecia and coronary artery disease in men. *Br J Dermatol*. 1979;101:455-458.
- Persson B, Johansson BW. The Kockum Study: twenty-two year follow-up—coronary heart disease in a population in the south of Sweden. *Acta Med Scand*. 1984;216:485-493.
- Herrera CR, D'Agostino RB, Gerstman BB, Bosco LA, Belanger AJ. Baldness and coronary heart disease rates in men from the Framingham Study. *Am J Epidemiol*. 1995;142:828-833.
- Ford ES, Freedman DS, Byers T. Baldness and ischemic heart disease in a national sample of men. *Am J Epidemiol*. 1996;143:651-657.
- Lesko SM, Rosenberg L, Shapiro S. A case-control study of baldness in relation to myocardial infarction in men. *JAMA*. 1993;269:998-1003.
- Schnohr P, Lange P, Nyboe J, Appleyard M, Jensen G. Gray hair, baldness, and wrinkles in relation to myocardial infarction: the Copenhagen City Heart Study. *Am Heart J*. 1995;130:1003-1010.
- Manson JE, Grobbee DE, Stampfer MJ, et al. Aspirin in the primary prevention of angina pectoris in a randomized trial of United States physicians. *Am J Med*. 1990;89:772-776.
- Manson JE, Buring JE, Satterfield S, Hennekens CH. Baseline characteristics of participants in the Physicians' Health Study: a randomized trial of aspirin and beta-carotene in U.S. physicians. *Am J Prev Med*. 1991;7:150-154.
- Hennekens CH, Buring JE, Manson JE, et al. Lack of effect of long-term supplementation with beta-carotene on the incidence of malignant neoplasms and cardiovascular disease. *N Engl J Med*. 1996;334:1145-1149.
- World Health Organization. *Ischaemic Heart Disease Registers: Report of the Fifth Working Group, Including a Second Revision of the Operating Protocol*. Copenhagen, Denmark: Regional Office for Europe, World Health Organization; April 26-29, 1971.
- Norwood OT. Male pattern baldness: classification and incidence. *South Med J*. 1975;68:1359-1365.
- Kligman AM. The comparative histopathology of male pattern baldness and senescent baldness. *Clin Dermatol*. 1988;6:108-118.
- Trevisan M, Farinara E, Krogh V. Baldness and coronary heart disease risk factors. *J Clin Epidemiol*. 1993;46:1213-1218.
- Hibberts NA, Howell AE, Randal VA. Balding hair follicle dermal papilla cells con-

- tain higher levels of androgen receptors than those from non-balding scalps. *J Endocrinol*. 1998;156:59-65.
17. Demark-Wahnefried W, Lesko SM, Conaway MR, et al. Serum androgens: associations with prostate cancer risk and hair patterning. *J Androl*. 1997;18:495-500.
  18. Kaufman KD, Olsen EA, Whiting D, et al. Finasteride in the treatment of men with androgenetic alopecia: Finasteride Male Pattern Hair Loss Study Group. *J Am Acad Dermatol*. 1998;39(4 pt 1):578-589.
  19. Sheridan PJ, McGill HC Jr, Aufdemorte TB, Triplett RG, Holt RG. Heart contains receptors for dihydrotestosterone but not testosterone: possible role in the sex differential in coronary heart disease. *Anat Rec*. 1989;223:414-419.
  20. McGill HC Jr, Sheridan PJ. Nuclear uptake of sex steroid hormones in the cardiovascular system of the baboon. *Circ Res*. 1981;48:238-244.
  21. Fujimoto R, Morimoto I, Morita E, Sugimoto H, Ito Y, Eto S. Androgen receptors, 5 alpha-reductase activity and androgen-dependent proliferation of vascular smooth muscle cells. *J Steroid Biochem Mol Biol*. 1994;50:169-174.
  22. Matsuda K, Ruff A, Morinelli TA, Mathur RS, Halushka PV. Testosterone increases thromboxane A2 receptor density and responsiveness in rat aortas and platelets. *Am J Physiol*. 1994;267(3 pt 2):H887-H893.
  23. Ajayi AA, Mathur R, Halushka PV. Testosterone increases human platelet thromboxane A2 receptor density and aggregation responses. *Circulation*. 1995;91:2742-2747.
  24. Herman SM, Robinson JT, McCredie RJ, Adams MR, Boyer MJ, Celermajer DS. Androgen deprivation is associated with enhanced endothelium-dependent dilatation in adult men. *Arterioscler Thromb Vasc Biol*. 1997;17:2004-2009.
  25. Reckelhoff JF, Zhang H, Granger JP. Testosterone exacerbates hypertension and reduces pressure-natriuresis in male spontaneously hypertensive rats. *Hypertension*. 1998;31:435-439.
  26. Gallant S, Alfano J, Charpin M, Brownie A. Expression of adrenal cytochromes P-450 in testosterone-induced hypertension. *Hypertension*. 1991;18:523-528.
  27. Crofton JT, Share L. Gonadal hormones modulate deoxycorticosterone-salt hypertension in male and female rats. *Hypertension*. 1997;29(1 pt 2):494-499.
  28. Glazer G. Atherogenic effects of anabolic steroids on serum lipid levels: a literature review. *Arch Intern Med*. 1991;151:1925-1933.
  29. Bagatell CJ, Knopp RH, Vale WW, Rivier JE, Bremner WJ. Physiologic testosterone levels in normal men suppress high-density lipoprotein cholesterol levels. *Ann Intern Med*. 1992;116:967-973.
  30. Sheikh K. Re: "Baldness and ischemic heart disease in a national sample of men" [letter]. *Am J Epidemiol*. 1997;145:670-671.
  31. Osborn D. Inheritance of baldness. *J Hered*. 1916;7:347-355.
  32. Küster W, Happle R. The inheritance of common baldness: two B or not two B? *J Am Acad Dermatol*. 1984;11:921-926.
  33. Carey AH, Chan KL, Short F, White D, Williamson R, Franks S. Evidence for a single gene effect causing polycystic ovaries and male pattern baldness. *Clin Endocrinol (Oxf)*. 1993;38:653-658.
  34. Govind A, Obhrai MS, Clayton RN. Polycystic ovaries are inherited as an autosomal dominant trait: analysis of 29 polycystic ovary syndrome and 10 control families. *J Clin Endocrinol Metab*. 1999;84:38-43.
  35. Guzick DS, Talbott EO, Sutton-Tyrrell K, Herzog HC, Kuller LH, Wolfson SK Jr. Carotid atherosclerosis in women with polycystic ovary syndrome: initial results from a case-control study. *Am J Obstet Gynecol*. 1996;174:1224-1229.
  36. Talbott E, Guzick D, Clerici A, et al. Coronary heart disease risk factors in women with polycystic ovary syndrome. *Arterioscler Thromb Vasc Biol*. 1995;15:821-826.
  37. Setty LR. Hair pattern of the scalp of white and Negro males. *Am J Phys Anthropol*. 1970;33:49-56.
  38. Karter AJ, Gazzaniga JM, Cohen RD, Casper ML, Davis BD, Kaplan GA. Ischemic heart disease and stroke mortality in African-American, Hispanic, and non-Hispanic white men and women, 1985 to 1991. *West J Med*. 1998;169:139-145.