Common pattern baldness (androgenetic alopecia) is the most assessed scores ranging from III to VII (Ellis coxon matched pairs signed rank test), whereas no discrepancies score I in nine subjects was concurred by the trained observer in Ellis 1951; Norwood, 1975), which was printed in the respondent book-scheme shown to have good test^retest reliability) (Hamilton, wood Baldness scale (Norwood, 1975) (a standard classification to rate their degree of hair loss, if any , using the Hamilton^Nor- ational Twin Registry . All males (45% of the sample) were asked letting, designed to assess physical, psychologic, and social of common hair loss.

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Common pattern baldness (androgenetic alopecia) is the most common form of hair loss in humans. In Caucasians, normal male hair loss, commonly known as “male pattern baldness” (MPB; MIM 109200), is noticeable in about 20% of men aged 20, and increases steadily with age, so that a male in his 90s has a 90% chance of having some degree of MPB. In addition to being among the most common natural conditions that make men self-conscious, recent studies indicate associations of MPB with: (1) benign prostatic hyperplasia (MIM 600082; odds ratio (OR) = 3.23; 95% confidence interval (CI): 1.81–5.79) (Hawk et al, 2000); (2) coronary heart disease (relative risk = 1.36; 95% CI: 1.11–1.67) (Lotufo et al, 2000); (3) hyperinsulinemia (OR = 1.91; 95% CI: 1.02–3.56); and (4) insulin-resistance-assoc- iated disorders, such as obesity (MIM 601665; OR = 2.90; 95% CI: 1.76–4.79), hypertension (MIM 145000; OR = 2.09; 95% CI: 1.14–3.82), and dyslipidemia (OR = 4.45; 95% CI: 1.74–11.34) (Matilainen et al, 2000). MPB is also a risk factor for clinical nephrol- (threshold, indicated no test of the multiple threshold model, however (e.g., the Multiple threshold model tests performed on the 13 categories, assuming equal thresholds for twin 1 and twin 2, indicated no signiﬁcant departure from normality in either MZ (χ² = 117.94, p = 0.09) or DZ twins (χ² = 118.47, p = 0.09), supporting a single liability dimension model of hair loss. As contingency tables using all 13 categories may be too sparse to yield a meaningful test of the multiple threshold model, however (e.g., the χ² statistic may not be asymptotically distributed), the MZ and DZ data were combined and the 13 score categories were collapsed into the following eight groups: group 1 (0, I, II, IIIa; representing nonbaldness); group 2 (III); group 3 (IIla); group 4 (IIla, IV); group 5 (IVa); group 6 (V); group 7 (Va), and group 8 (VI, VII). Groups 2 to 8 represent significant cosmetic hair loss (Norwood, 1975), while maximizing counts for vertex and recessive hair loss. Multiple threshold model tests performed on both the full 8 × 8 table and after combining frequencies in the two off-diagonal quadrants, also indicated no signiﬁcant departure from normality (χ² = 55.47, p = 0.21 and χ² = 48.55, p = 0.36, respectively). These re- sults strongly support a single liability dimension model of hair loss, with frontal recession not etiologically distinct from vertex balding.

Subsequently, a single liability dimension–threshold model was applied to our hair loss data, using the full distribution of ordered hair loss scores (0–I–II–IIa–III–IIIa–IIIV–IV–IVa–V–Va–VI–VII) as an ordered sequence reflecting the severity of hair loss (see

Data collected from 476 MZ and 408 DZ male pairs, plus 143 MZ and 154 DZ male individual twins (mean ages for the MZ and DZ twins were 30.3 and 30.5 y, respectively) were analyzed using structural equation modeling, to estimate parameters of a model that include additive genetic effects (A), nonadditive ge- netic effects (i.e., dominance or epistasis) (D), shared or family environment (C), and random or unique environment (E) (Neale and Cardon, 1992). In addition to the 12 Hamilton–Norwood ca-t egories, scoring individuals who answered “no” to the question “have you experienced hair loss?”, as zero, resulted in a 13-point scale.

A major goal of the genetic analysis was to test the multiple threshold model (Reich et al, 1972; Kendler, 1993), which posits that different types of hair loss reflect different levels of severity on a single dimension, rather than distinct etiologies. These thresholds can be regarded as the x-value of the normal distribution that divides the area under the curve in such a way that it gives the right proportion of individuals in each (hair loss) group, thus reflecting the prevalence of each group (Neale and Cardon, 1992). For each of the two zygosity groups, the fit of a mul- tiple threshold model was tested by calculating the poly- choric correlation for the Hamilton–Norwood hair loss gradings, using POLYCORR (http://ourworld.compuserve.com/homes/ jsubersax/xpc.htm) or PRELIS 2.30 (J˛reskog and S˛rbom, 1999). The polychoric correlation, also termed the “correlation of liability”, assumes that underlying the observed polychotomous distribution of hair loss status there exists a continuous, normally distributed latent liability (Kendler, 1993). A χ² goodness-of-fit test is used to test whether the multiple threshold model provides a good fit to the observed data. Calculation of 95% CI for the polychoric correlations, the comparison of threshold values within twin pairs and across zygosity groups, and genetic model fitting by maximum likelihood univariate analysis of raw data were performed using the Mx program (Neale et al, 1999).

Multiple threshold model tests performed on the 13 categories, assuming equal thresholds for twin 1 and twin 2, indicated no significant departure from normality in either MZ (χ² = 117.94, p = 0.09) or DZ twins (χ² = 118.47, p = 0.09), supporting a single liability dimension model of hair loss. As contingency tables using all 13 categories may be too sparse to yield a meaningful test of the multiple threshold model, however (e.g., the χ² statistic may not be asymptotically distributed), the MZ and DZ data were combined and the 13 score categories were collapsed into the following eight groups: group 1 (0, I, II, IIIa; representing nonbaldness); group 2 (III); group 3 (IIla); group 4 (IIla, IV); group 5 (IVa); group 6 (V); group 7 (Va), and group 8 (VI, VII). Groups 2 to 8 represent significant cosmetic hair loss (Norwood, 1975), while maximizing counts for vertex and recessive hair loss. Multiple threshold model tests performed on both the full 8 × 8 table and after combining frequencies in the two off-diagonal quadrants, also indicated no significant departure from normality (χ² = 55.47, p = 0.21 and χ² = 48.55, p = 0.36, respectively). These re- sults strongly support a single liability dimension model of hair loss, with frontal recession not etiologically distinct from vertex balding.

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Electro nic Database Information: accession number and URL for data in this article are as follows: Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omni1 (for MPB; MIM 109200), benign prostatic hyperplasia (MIM 600082), obesity (MIM 601665), hypertension (MIM 145000), and prostate cancer (MIM 176807)).
No significant differences in threshold liability distributions were observed within twin pairs and across zygosity groups. The age corrected maximum likelihood (ML) twin pair polythetic correlation for hair loss gradings in MZ twin pairs ($r = 0.81; 95\% \text{ CI: } 0.77-0.85$) was over twice as large as the DZ correlation ($r = 0.39; 95\% \text{ CI: } 0.28-0.49$), indicating a strong genetic effect. Furthermore, genetic model fitting by ML univariate analysis of raw data using Mx (Neale et al, 1999) (Table I), indicated that an additive genetic and nonshared environmental (AE) model best explained individual differences in MPB, and that 81\% of the total variance could be attributed to additive genetic effects (i.e., 81\% heritability, 95\% CI: 77-85\%).

Given the differences between some of the Hamilton–Norwood gradings are quite subtle, we re-analyzed our data using more clear-cut (dichotomous) categories of hair loss. For these analyses, males with gradings of III, IIIa, IIIv , IV , IVa, V , Va, VI, or VII were classified as bald, whereas males with gradings of 0, I, II, or IIa were classified as nonbald. Analogous to the previous genetic analyses, an AE model best explained individual differences in MPB, with 80\% of the total variance attributed to additive genetic effects (95\% CI: 70-87\%). Furthermore, the AE model best explained individual differences in MPB for dichotomized clear-cut vertex balding (0, I, or II vs. IIIv, IV, V, VI, or VII) and recessive balding (0, I, or II vs. IIIa, IVa, or Va) producing heritability estimates of 89\% (95\% CI: 75-95\%) and 96\% (95\% CI: 87-99\%), respectively. As predicted under the multiple threshold model, and reflected in their overlapping confidence intervals, the use of different grouping thresholds/schemes does not produce significantly different heritabilities.

Surprisingly, there is only one known extensive family study on androgenetic alopecia published (Osborn, 1916). This study of hair growth patterns in 22 families concluded that common baldness is an autosomal dominant phenotype in men and an autosomal recessive phenotype in women. Owing to a lack of details regarding examination methods and the practice of omitting symptom-free women in some pedigrees, however, the validity of these results remain controversial. Additionally, although the results from the two other known twin studies produced concordance rates of 100\% and 92.3\% for MZ, and 50\% and 68.7\% for DZ twins, they are far too small—including only three MZ and

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**Figure 1.** Hamilton–Norwood standards for classification of the most common types of MBP. Adapted from Norwood (1975). Types I, II, III, IV, V, VI, and VII represent the most common forms of MPB. Type IIIv has no more front temporal hair loss than type III, but has considerable hair loss at the vertex. Type A variants (IIa, IIIa, Iva, and Va) have hair loss restricted to the anterior region, which eventually recedes to equivalence with type VI (Norwood, 1975). Frequencies in our sample (2029 males aged 25–36 y) are: zero hair loss (61.2%), I (6.5%), II (4.2%), IIa (29%), III (4.3%), IIIa (1.5%), IIIv (38%), IV (1.6%), IVa (1.0%), V (0.8%), Va (1.1%), VI (0.4%), and VII (0.5%).

**Figure 2.** The multiple threshold model for the level of severity of hair loss for the best fitting AE model.
eight DZ male pairs (Niermann, 1964; Kuster and Happle, 1984), and 65 MZ (42 male, 23 female) and 16 DZ (14 male, two female) pairs (Hayakawa et al, 1992), respectively—to permit reliable conclusions.

Therefore, our results represent one of the first large-scale studies on the heritability of MPB and indicate that additive genetic effects play a major part in the progression of common hair loss. Moreover, a recent study by Ellis et al (2001), which tested polymorphisms in the androgen receptor (AR) gene, found a Stul restriction site in 98.1% of 54 young (18–30 y) bald men (p = 0.0005) and in 92.3% of 392 older (&gt;50 y) bald men (p = 0.000004) compared with 76.6% of 107 nonbald ( &gt; 50 y) men, suggesting that a polymorphism in or near AR may influence male pattern baldness. However, this finding has not been replicated in other studies.

Hair loss similarities between father and son have also been observed in a study on the frequency of MPB in brothers of men having prematurely bald fathers (66%) compared with brothers of men with unaffected fathers (46%); Harris, 1946; Kuster and Happle, 1984). Further evidence against a single and/or X-linked gene of major effect comes from a study by Smith and Wells (1964), which observed hair loss in only 33% of the fathers of 18 women suffering from severe pattern baldness (Kuster and Happle, 1984). Additionally, a study examining 410 men with premature baldness found evidence of a genetic influence from the father's side in 236 cases (Galewsky, 1932; Jackson, 1932; Kuster and Happle, 1984). Hence, other (autosomal) genes, possibly of large effect, remain to be found.

It is worth noting that these heritabilities are based on a relatively young population—ranging in age from 25 to 36 with a mean of 30 y. As some of the nonbald subjects will inevitably develop balding—with the rate of baldness known to increase steadily with age—it is possible that heritability (A) will differ with age. For example, through the age-dependent expression of genes, and/or a change in the body's resilience to the major effects of a genetic influence in early phases of life. Also, the accumulation of environmental influences (E) may play a larger part in older ages. Twin studies in older cohorts are required to investigate these possibilities.

The negative psychosocial effects associated with male hair loss include decreased self-esteem, dissatisfaction with body image or appearance, self-consciousness, perception of aging, and often emotional stress. Furthermore, these effects tend to be more pronounced in younger men (Girman et al, 1998). Certainly, MPB in itself has a considerable effect on the quality of life for many men. Because it is a clearly observable trait, however, which generally precedes the diagnosis of benign prostatic hyperplasia and clinical prostate cancer by decades (Hawk et al, 2000), genes influencing MPB may prove valuable in determining susceptibility to life-threatening prostatic disorders. Moreover, genes influencing MPB may lead to the identification of novel mechanisms, which may influence cardiovascular disease and/or insulin resistance.


Niermann H: *Zwillingsdermatologie*. Berlin: Springer-Verlag, 1964


