

Gender and Dermatology

Ethel Tur
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Editors

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Preface

The nature of certain diseases is different between women and men. Genetic and hormonal differences affect skin structure and function, thus affecting disease processes. In addition, exogenous factors differ according to differences in lifestyle between the sexes. In the last two decades it has been recognized that women are more different medically than previously appreciated, and studies started being conducted accordingly. Methodologies used in dermatological research have improved substantially, providing means of objective evaluation of skin function and characteristics, leading to improvement in treatment and disease outcome.

Diseases differ between men and women in terms of prevention, clinical signs, therapeutic approach, prognosis, and psychological and social impacts.

This book outlines several aspects of differences between the skin of women and men in health and disease, based on available data. It is not designed to be exhaustive in its coverage of the subject, but rather to highlight certain aspects of it. We wish and hope that this book will ignite more interest in the topic of gender dermatology.

The editors are grateful to all our contributing authors for their efforts and cooperation in applying their knowledge and skill.

Special thanks to our team at Springer: Mr. Grant Weston, Responsible Editor, Mr. Andre Tournois, Project Coordinator, Mr. Karthik Periyasamy, Production editor, and Mr. Dinesh Vinayagam, Project Manager, for their meticulous work.

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Contents

| | | |
|-----------|--|------------|
| 1 | Effects of Gender on Skin Physiology and Biophysical Properties. | 1 |
| | Richard Randall Wickett and Greg G. Hillebrand | |
| 2 | Racial and Gender Influences on Skin Disease | 11 |
| | Daniel Callaghan and Neelam A. Vashi | |
| 3 | Aging of the Skin. | 25 |
| | Enzo Berardesca, Norma Cameli, and Maria Mariano | |
| 4 | Hair and Scalp Variation Related to Gender | 31 |
| | Ferial Fanian and Alexandre Guichard | |
| 5 | Nail Variations Related to Gender | 43 |
| | Robert Baran and Doug Schoon | |
| 6 | Cutaneous Autoimmune Connective Tissue Disorders | 53 |
| | Wohl Yonit | |
| 7 | Gender Differences in Psoriasis. | 63 |
| | Sivan Sheffer Levi and Yuval Ramot | |
| 8 | Gender Dermatology: Pigmentation Disorders | 83 |
| | Mor Pavlovsky | |
| 9 | Gender and Genodermatoses. | 89 |
| | Sivan Sheffer Levi and Vered Molho-Pessach | |
| 10 | Specific Dermatoses of Pregnancy. | 127 |
| | Arieh Ingber | |
| 11 | Nipples: A Sensitive Topic | 139 |
| | Eve Finkelstein, Deena Yael Meerkin, and Gina Weissman | |
| 12 | Acne Vulgaris. | 171 |
| | Gila Isman Nelkenbaum | |
| 13 | Melanocytic Nevi: Patterns and Gender Differences. | 181 |
| | Miryam Kerner | |
| 14 | Clinical and Therapeutic Considerations of Acquired Melanocytic Nevi. | 189 |
| | Baruch Kaplan | |

| | | |
|-----------|--|-----|
| 15 | Biology and Sex Disparities in Melanoma Outcomes | 193 |
| | Adi Nosrati and Maria L. Wei | |
| 16 | Infantile Hemangioma | 215 |
| | Shoshana Greenberger | |
| 17 | Cutaneous Leishmaniasis | 227 |
| | Michal Solomon and Eli Schwartz | |
| 18 | Fungal Infections (Onychomycosis, Tinea Pedis, Tinea Cruris, Tinea Capitis, Tinea Manuum, Tinea Corporis, different <i>Candida</i> Infections, and Pityriasis Versicolor) and Mycological Laboratory Analyses | 235 |
| | Avner Shemer and Meir Babaev | |
| 19 | Atopic Dermatitis | 243 |
| | Vered Atar-Snir | |
| 20 | Occupational Dermatitis in Nail Salon Workers | 249 |
| | Liran Horev | |
| 21 | Universal Concepts of Beauty and Their Implications on Clinical Approach to Female Cosmetic Patient | 255 |
| | Marina Landau | |
| 22 | Gender Differences in Mohs Micrographic Surgery | 267 |
| | Yoav C. Metzger | |
| 23 | Gender Differences in Facial Rejuvenation | 271 |
| | Benjamin C. Garden and Jerome M. Garden | |
| 24 | The Skin as a Metaphor: Psychoanalytic and Cultural Investigations | 281 |
| | Shlomit Yadlin-Gadot and Uri Hadar | |
| | Index | 299 |



Effects of Gender on Skin Physiology and Biophysical Properties

Richard Randall Wickett and Greg G. Hillebrand

Abbreviations

| | |
|------|---------------------------|
| N.S. | No significant difference |
| SC | Stratum corneum |
| TEWL | Transepidermal water loss |

1.1 Introduction

This chapter will review the literature on gender differences in skin physiology focusing on non-invasive biophysical measures of skin function. While there are countless studies on the biophysical properties of human skin, there are fewer that examine gender differences. Many studies are sponsored by the cosmetic industry and not surprisingly focus on women and often compare effects of aging or photoaging. Unfortunately, the literature that explores gender differences does not always present a clear picture as will be seen. This contribution will review sebum production, skin pH, barrier function as assessed by transepidermal water loss (TEWL), stratum

corneum (SC) hydration measured by electrical properties, skin viscoelasticity and facial skin wrinkling.

1.2 Sebum Production

On average sebum production is approximately the same between men and women up to about age 50. However, there is extreme variability between individuals. Pochi et al. measured sebum production rates in men and women between the ages of 40 and 79 over a three-hour period using absorbent paper on the forehead [1]. Results are presented in Table 1.1.

Sebum production clearly drops off in women after age 50 probably because of menopause. In all age groups, even 70–79, there was considerable overlap between the ranges measured with higher sebum producing women producing more sebum in 3 h than lower producing men.

A more comprehensive study of gender differences in skin sebum production is that by Luebberding et al. [2]. The authors investigated 300 women and men between the ages of 20 and 74. Sebum production was measured on the cheeks and foreheads using the Sebumeter [3]. Mean values and standard deviations and statistical significance levels (p values) for each age range and over the entire age range are given in Table 1.2. There were 30 subjects of each sex in each age range.

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Table 1.1 Sebum production rates and ranges in female and male subjects

| Age range | Number F/M | Female ^a | Range ^a | Male ^a | Range ^a |
|-----------|------------|---------------------|--------------------|-------------------|--------------------|
| 40–49 | 31/50 | 1.86 | 0.12–4.80 | 2.39 | 0.54–5.14 |
| 50–59 | 21/14 | 1.08 | 0.07–2.38 | 2.43 | 1.05–4.36 |
| 60–69 | 18/14 | 0.88 | 0.22–1.62 | 2.42 | 0.83–4.95 |
| 70–79 | 12/13 | 0.85 | 0.33–2.19 | 1.69 | 0.63–3.23 |

^aSebum production in mg/10 cm² of skin in 3 h data from Pochi et al. [1]

Table 1.2 Sebum levels on the forehead for females and males

| Age range | Female ^a | SD | Male ^a | SD | p |
|-----------|---------------------|-------|-------------------|-------|--------|
| 20–29 | 115.50 | 57.13 | 120.77 | 50.24 | NS |
| 30–39 | 114.82 | 63.60 | 127.53 | 53.87 | NS |
| 40–49 | 130.77 | 63.74 | 125.93 | 50.27 | NS |
| 50–59 | 96.73 | 61.25 | 125.93 | 59.66 | <0.05 |
| 60–74 | 66.89 | 43.68 | 139.10 | 66.84 | <0.001 |
| 20–74 | 105.45 | 61.66 | 105.45 | 61.66 | <0.001 |

^aSebum measurement in µg/cm² data from Luebberding et al. [2]

While the overall mean was smaller for women than men, significant differences were not seen before the 50–59 age group in agreement with the results of Pochi et al. above. Note the large standard deviations indicating the large variation in sebum production across the sample populations. Sebum production on the cheek was lower than on the forehead but age and sex differences showed very similar trends. Firooz et al. [4] also reported lower sebum production in females compared to males in pooled data from several age groups and body sites. Among all the skin parameters reviewed in this work, lower sebum production in females compared to males above the age of 50 was observed most consistently.

1.3 Skin Surface pH

pH is defined as ‘the negative logarithm of the hydrogen ion concentration’. The most common method for measuring the skin’s surface pH is to apply a flat surface membrane electrode hydrated with distilled water to the skin surface and measure the apparent pH. This leads to the definition of skin surface pH in bioengineering terms as: ‘apparent pH as measured by a flat glass elec-

trode at the skin surface with a hydrated skin-electrode interface [5]. In healthy skin, surface pH is lower than physiological pH ranging from about 4.5–5.5 on most body sites under most conditions. There has been increasing interest in the role of skin surface pH in maintaining a healthy stratum corneum barrier [5].

Measurements of gender differences in skin pH have not produced completely consistent results though there is a trend for females to have slightly higher pH than males. Table 1.3 shows a summary of results from several labs comparing the skin surface pH in men vs. women at various body sites and age groups. Table 1.3 doesn’t present specific pH values because in some cases the authors only provide graphical data so exact numerical values are not available. Luebberding et al. present numerical pH data and found that males have significantly lower pH on every body site for every age group [2]. The overall averages were 5.12 for females and 4.58 for males. This was among the largest differences seen in any of the papers reviewed. Zlotogorski [6] found 5.1 on the cheek for males and 5.2 on the cheek for females and the difference was not statistically significant. In contrast Ehlers and Ivens [7] reported higher skin pH in males (5.8) compared to females (5.5) on the forearm.

In a large cross-sectional study of skin condition, Hillebrand and colleagues measured cheek and forearm skin surface pH in 450 subjects (191 males, 259 females) ranging in age for 9–78. The subjects were art festival goers (ArtPrize 2015, Grand Rapids Michigan) who happened to walk by the study venue and volunteered to be participants. Thus, subjects were literally recruited *off the street* and represent a *real world* sampling of the local population. Furthermore, the skin was not washed or prepared in any manner prior to making the measurement in order to measure an

Table 1.3 Skin pH results from various authors

| Age range | Number F/M | Body site | Result | Reference |
|--------------|------------|-----------|--------|-------------------------|
| 20–60 | 292/282 | Forehead | M = F | Zlotogorski [6] |
| 20–60 | 292/282 | Cheek | M = F | Zlotogorski [6] |
| 21–37 | 37/46 | Face | M < F | Kim [8] |
| 13–70 | 354/304 | Forehead | M < F | Man [9] |
| 0–12 | 142/128 | Forearm | M < F | Man [9] |
| 36–50 | 82/60 | Forearm | M < F | Man [9] |
| 51–70 | 28/31 | Forearm | M < F | Man [9] |
| 70+ | 31/24 | Forearm | M = F | Man [9] |
| 70+ | 31/24 | Forehead | M = F | Man [9] |
| 20–74 | 150/150 | Forehead | M < F | Luebberding [2] |
| 20–74 | 150/150 | Cheek | M < F | Luebberding [2] |
| 20–74 | 150/150 | Neck | M < F | Luebberding [2] |
| 20–74 | 150/150 | Forearm | M < F | Luebberding [2] |
| 20–74 | 150/150 | Hand | M < F | Luebberding [2] |
| Not reported | 6/6 | Forearm | M > F | Ehlers [7] |
| 9–78 | 259/191 | Forearm | M < F | Hillebrand ^a |
| 9–78 | 259/191 | Cheek | M = F | Hillebrand ^a |

^aG. G. Hillebrand unpublished data

unadulterated apparent pH. Skin pH ranged as low as pH 3.1 to as high as pH 6.8 or nearly 4 orders of magnitude in hydronium ion concentration! While there was no significant gender-dependent difference in cheek skin pH (mean \pm SD: 5.28 ± 0.43 for males and 5.23 ± 0.47 for females), males showed significantly ($p < 0.001$) lower forearm skin pH compared to females (mean \pm SD: 4.59 ± 0.61 for males vs. 4.78 ± 0.65 for females). Figure 1.1 shows the percentage of males and females in specific pH ranges from pH 3 to pH 7. Females tend to skew to higher pH in accord with the difference in the population means. What is noteworthy is the large overlap in the wide bell curves for skin pH frequencies between males and females. Thus, the difference in mean pH between genders is small compared to the variance for the entire population (Hillebrand, unpublished data).

1.4 Transepidermal Water Loss

Measurement of TEWL [10] has been shown to be a valid method to evaluate skin barrier function in-vivo [11]. Several researchers

have investigated possible gender differences in TEWL with varying results. Some of the results are presented in Table 1.4. Luebberding et al. [2] reported higher TEWL in males than in females with significant differences on the forehead, cheek, neck and forearm. Chilcott and Farrar [12] reported higher TEWL in males compared to females on the forearm and Firooz et al. [4] also reported higher TEWL in males in pooled data from eight body sites. Wilhelm et al. [13] and Hadi et al. [14] did not observe any significant effect of gender on TEWL.

Chilcott and Farrar [12] used the ServoMed EP-2 Evaporimeter (ServoMed, Kinna, Sweden) to measure TEWL while Luebberding et al. [2] used the TEWAmeter[®] TM300 (Courage & Khazaka, Cologne, Germany). This may in part explain the higher forearm results seen by Luebberding. While results from the two instruments correlate very well, TEWAmeter data tend to be up to two times higher than ServoMed data [11, 15]. Li et al. [16] also reported lower TEWL in female subjects compared to males in Chinese subjects from two age groups, 18–25 and 40–50 on various body sites.

Fig. 1.1 Percent of subjects (frequency %) having forearm pH values in a specific pH range

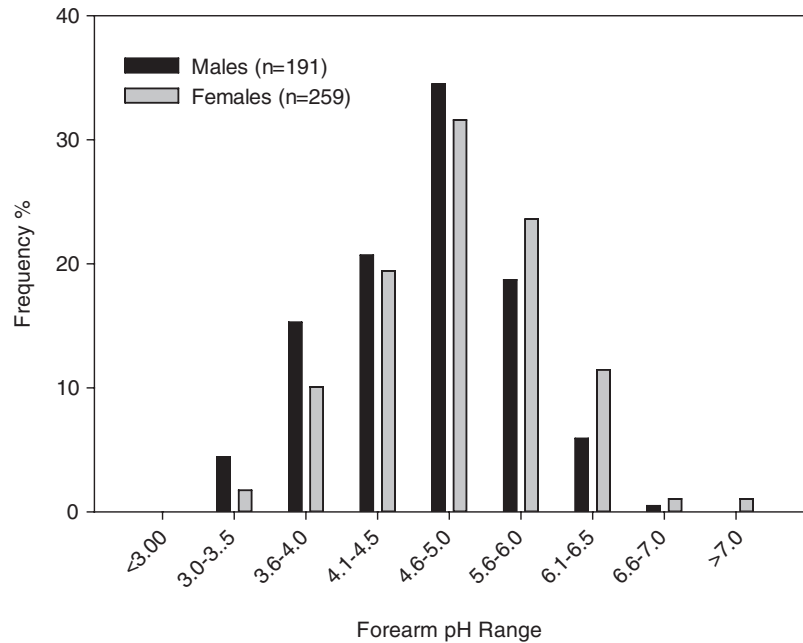


Table 1.4 TEWL females and males

| Ages | No. (F/M) | Body site | Female | Male | P | Reference |
|-------|-----------|-----------|--------|-------|-----------|-----------------|
| 20–74 | 150/150 | Forehead | 10.51 | 9.29 | P < 0.01 | Luebberding [2] |
| 20–74 | 150/150 | Cheek | 11.15 | 10.34 | P < 0.05 | Luebberding [2] |
| 20–74 | 150/150 | Neck | 9.25 | 6.96 | P < 0.001 | Luebberding [2] |
| 20–74 | 150/150 | Forearm | 9.10 | 5.50 | P < 0.001 | Luebberding [2] |
| 20–74 | 150/150 | Hand | 11.52 | 10.92 | N.S. | Luebberding [2] |
| 18–28 | 10/8 | Forearm | 4.68 | 4.98 | P < 0.05 | Chilcott [12] |
| 10–60 | 25/25 | 8 sites | 9.52 | 15.49 | P < 0.05 | Firoz [4] |

N.S. no significant difference

1.5 Stratum Corneum Hydration

The stratum corneum needs to maintain proper hydration in order to function properly and lack of adequate moisture in the SC can lead to dry skin. Instrumental methods to measure SC hydration in-vivo rely on measuring either surface conductance or capacitance [17–20]. Luebberding et al. [2] measured skin hydration with the CM 825® (Courage & Khazaka, Cologne Germany) on five body sites on 150 subjects of each gender broken into five age groups. Results from each body site, pooled by age are presented in Table 1.5.

Females showed higher hydration on the cheek and hand while males had higher values on the neck. Differences on the forehead and forearm

Table 1.5 Capacitance by body site and gender^a

| Body site | Female | Male | P value |
|-----------|--------|-------|-----------|
| Forehead | 52.94 | 50.94 | N.S. |
| Cheek | 60.81 | 57.62 | P < 0.05 |
| Neck | 54.34 | 59.62 | P < 0.001 |
| Forearm | 44.07 | 43.10 | N.S. |
| Hand | 38.62 | 32.49 | P < 0.001 |

^aData from Luebberding et al. [2]. 150 subjects of each sex in each age group. Age range = 20–74. N.S. no significant difference

were not statistically significant. Li et al. [16] found females to have significantly higher hydration on the décolletage area but no other body sites. Neither Firooz et al. [4] nor Wilhelm et al. [13] reported significant gender differences in hydration.

1.6 Elasticity

Skin is a viscoelastic material. It has the unique ability to rebound after being stretched allowing itself to return to its initial size and maintain a tight covering over the body surface. Unfortunately, skin elasticity declines after the third decade in both men and women, especially on chronically sun-exposed skin sites [21–23]. This loss in elasticity is likely the major driver for visible facial skin wrinkling and sagging [24]. Skin elasticity is commonly measured using the non-invasive suction method [25–27]. The Cutometer® is one of the more widely used suction-based skin elasticity instruments because of its portability, speed and simplicity (Courage + Khazaka Electronic, Koln, Germany). The stress/strain curve can be divided into different regions such as maximum deformation (Uf) and immediate retraction (Ur). Ratios of these absolute parameters yield relative parameters of skin elasticity (e.g. Ur/Uf or R7) that are independent of skin thickness. Nedelec et al. [28] used the Cutometer MPA 580 with a 6-mm probe to measure skin elasticity at 16 body sites on 121 males and 120 females who were mostly Asian or Caucasian and aged between 20 and 85 years old. They found no consistent trend for gender differences in skin elasticity (R7) across age groups. Cua et al. [29] also did not observe a significant difference in skin elasticity between males and females though their sample size was very small. Ishikawa et al. [30] compared skin elasticity on men vs. women in a large subject sample on multiple skin sites. Specifically, they used the Cutometer SEM 474 to measure skin elasticity on the forearm, hand, finger and chest of 96 males and 95 females ages 9–87. Again, there was no significant difference in skin elasticity between males and females. Lueberding et al. [31] used the Cutometer MPA 580 to measure skin elasticity on the cheek, neck and dorsum of the hand in 150 males and 150 females ages 20–74. Skin elasticity (Ur/Uf) declined with age in both genders, but was only slightly higher in women than in men. The authors noted that there was a more rapid decline in elasticity in women after 40 years of age. Firooz et al. [4] also used the Cutometer

MPA 580 to measure skin elasticity in 25 females and 25 males ages 10–60. While women had slightly higher elasticity than men, the difference was not statistically significant. More recently, Hadi et al. [14] used the DermaLab® Combo to measure the skin elasticity on the forearm of 50 males and 50 females, ages 18–27. Females showed slightly higher skin elasticity than males but the difference was not statistically significant. Finally, Ma et al. [32] used the Cutometer MPA 580 to measure skin elasticity on the forehead and cheek of 240 healthy male and female volunteers living in Shanghai, aged 20–70 years. There was no significant difference in forehead skin elasticity between the genders. However, the researchers did observe lower cheek skin elasticity (both R5 and R7) in older (age 50–70) males than females. In summary, while skin elasticity declines with age in both males and females, gender-associated differences in skin elasticity at any given age are small and likely not clinically meaningful.

1.7 Facial Wrinkling

When it comes to facial wrinkling, which sex ages faster, men or women? Chung et al. [33] assessed facial wrinkling on 236 men and 171 women using standardized visual grading scales. The results suggest that while the pattern of facial wrinkling is similar between the sexes, women showed more severe wrinkles after adjusting for age, sun exposure and smoking. Gender-dependent differences in facial wrinkling should also consider facial location. In the perioral region (upper lip), women exhibit more and deeper wrinkles than men [34]. However, on the forehead, men show an earlier onset and more severe wrinkling at every age than women [32]. Hamer et al. [35] measured facial wrinkling using digital imaging in 3831 Europeans (58% female) aged 51–98. Men had higher wrinkle area than women in the younger age groups (<75) but women showed more wrinkles in the older age group (>75). Chien et al. [36] developed photographic scales for perioral and crow's feet wrinkles that were gender specific meaning that there

was a scale for men and a scale for women. They used the grading scales to assess facial wrinkling on 71 men and 72 women, aged 21–91 years. All subjects were graded using both scales. Interestingly, a participant’s score on the female-specific scale differed significantly from the male-specific scale score showing that it is important to use gender-specific scales for the visual grading of facial wrinkling. The researchers found that perioral wrinkling was more severe in women than men. For participants older than 45 years, there was even greater gender disparity. Tsukahara et al. measured facial wrinkling in 173 Japanese men and women [37]. Men showed increased forehead wrinkles compared with women at all ages. However, the difference in facial wrinkle severity tended to disappear in the older age groups and there were no gender-related differences at any age for upper eyelid wrinkles. In related work, 3D analysis of skin replicas found that the depth of eye wrinkles in men showed an annual variation with more wrinkles at the corner of the eye in the fall compared to the spring; no such annual variation was observed in women [38]. The varying density of sebaceous glands on the face may partly explain the variation in facial wrinkling at different facial sites. Tamatsu et al. [39] looked at cadaver skin specimens from females and males ranging in age from the 20s to 90s at age of death. The found a negative correlation between wrinkle depth and

sebaceous gland density. Sebaceous gland density was found to be significantly lower in the lateral canthus than in the forehead on both males and females. However, while the sebaceous gland density was significantly lower in females than in males in both facial regions, there was no significant gender-dependent difference in wrinkle depth.

In a cross-sectional study of skin condition, Hillebrand and colleagues measured facial wrinkling in the periorbital area (under eye and crow’s feet wrinkles) on 147 Caucasian males and 183 Caucasian females, aged 10–78. Regression analysis showed that both *gender* and *age* to be significant ($p < 0.05$) factors in describing the variance in wrinkle severity (Fig. 1.2a). However, when other factors are considered in the regression analysis, like the subject’s body mass index, smoking history in pack years and years working outside, gender drops out as a significant factor suggesting that some of the variance initially explained by gender can be explained by other gender-associated confounding factors. We will discuss confounding factors more later in the chapter. Figure 1.2b shows the data in Fig. 1.2a replotted as age group means for males and females. While females had higher wrinkles than men in all age groups, none of the pairwise comparisons between males and females in any given age group were significantly different (one-way ANOVA, Tukey Test).

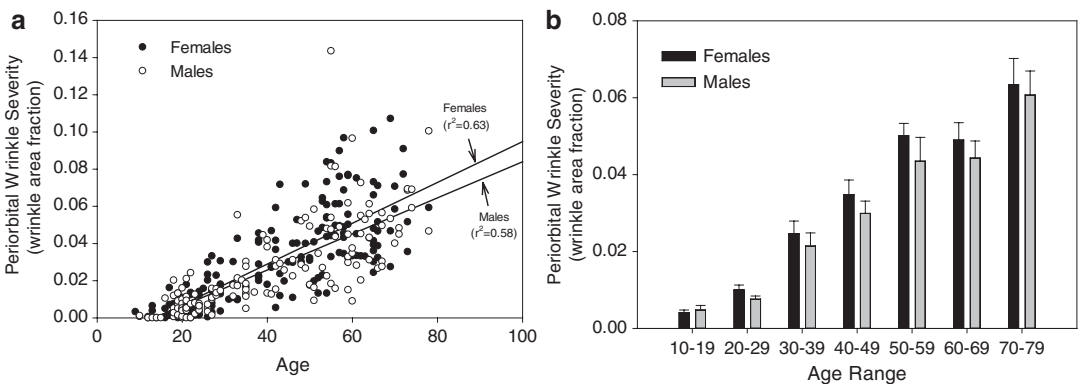


Fig. 1.2 Wrinkle severity in the periorbital region for Caucasian females and males. (a) Scatter plot where each point represents a subject’s wrinkle severity. Lines repre-

sent best fit linear regression curves. (b) Age group means \pm standard error

1.8 Confounding Factors

The differences observed between male and female skin may be ascribed to intrinsic factors like hormones [40] and other genetically determined variables or extrinsic factors like differences in smoking, diet, sun protection and skin care routines. Even differences in facial expression patterns may differ between the sexes and influence skin condition, especially facial wrinkling [41]. Below we discuss confounding factors that should be considered when designing and interpreting clinical data for men and women.

1.8.1 Smoking History

Smoking has been shown to increase facial wrinkling [34]. A report by Okada et al. involving identical twins underscores the risk of smoking on appearance and health. They compared facial wrinkling in identical twins and showed that a 5-year difference in smoking history can have a noticeable effect on skin aging [42]. Similar observations were reported by Doshi et al. [43]. The exact mechanism for how smoking affects skin wrinkling is not understood but may involve changes in skin barrier function and associated changes in chronic skin dryness caused both by smoking and exposure to *second-hand* smoke [44] which is associated with having more wrinkles [41, 43, 44]. Since men are more likely to smoke than women (Centers for Disease Control and Prevention [45]), smoking needs to be considered as a confounding variable when comparing the skin condition of males to females.

1.8.2 Diet and Nutrition

Consuming an adequate amount of fruit and vegetables has been shown to reduce the risk of excess weight gain, type 2 diabetes, cardiovascular disease, and specific cancers [46, 47]. Pezdiric et al. [47] has recently reviewed the summation of evidence linking diet and skin health. The majority of studies conducted in this space focus on the effect of dietary supplements on skin con-

dition and most enroll only females. In a cross-sectional study of 4025 women ages 40–74, Cosgrove et al. found that higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates are associated with better skin-aging appearance [48]. Higher intakes of vegetables, fruit, olive oil, and legumes may cause less skin wrinkling and are protective against actinic damage [49]. Iizaka et al. measured nutritional status and habitual dietary intake, stratum corneum hydration and xerosis in 118 older (>65) Japanese subjects, mostly females [50]. They concluded that a dietary pattern characterized by higher vegetable and fruit intake was associated with a better skin condition. Since men's daily intake of fruits and vegetables is less than that of women [51], dietary differences in the sample population should be considered in interpretation and analysis of clinical results as well as in clinical design.

1.8.3 Skin Care Habits and Practices

A person's daily skin care routine will undoubtedly affect their skin condition. Regular use of moisturizers will improve skin barrier function, skin hydration, and lessen the advancement of wrinkling [14, 41]. Those who regularly protect their skin from acute and chronic sun exposure will slow the advancement of skin aging. Male facial skin is largely influenced by beard grooming routines [52, 53]. In this regard, many of the differences observed between male and female skin may be attributable to differences in skin care habits and practices, especially differences on the face [54].

1.8.4 Sun Exposure

Sun exposure is well known to be a major cause of wrinkling, especially in facial skin [23, 55–57]. When discussing gender differences in facial wrinkles the relative tendency for sun exposure and the frequency of sunscreen application should be considered as regular sunscreen use may provide some protection against the signs of

photoaging [58, 59]. Haluza et al. reported that Australian men are more likely to suffer sun exposure and less likely to use sunscreen compared to their female counterparts [60]. This may explain the earlier onset [35] and more severe wrinkling seen in men on the forehead [37] but is not consistent with the higher levels of perioral wrinkles seen in women [36].

1.9 Summary

One of most important and difficult questions whenever comparing measured properties between two groups is whether statistically significant differences are clinically relevant. We have reviewed and summarized many of the studies aimed at improving our understanding of the similarities and differences between male and female skin with particular attention to differences in biophysical skin properties. We noted that results depended on the method used, the body site being measured, the age of the subjects, and their prior history of smoking, sun exposure, and use of skin care products. The most consistent difference between the genders reported in this review is lower sebum production in women, especially over the age of 50. However, because of the high individual variability in sebum output there is overlap between the high sebum producing females and low sebum producing males (Table 1.1). Thus care must be taken when drawing conclusions from the differences reported in the studies summarized here.

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