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Cutaneous Blood Flow in Aging Skin

This is the first of three reviews of technical literature examining the facts and misconceptions of aging skin. The three topics are cutaneous blood flow, cutaneous biochemistry and skin thickness.

Changes in cutaneous blood perfusion with age, if present, could have profound effects on skin physiology, including alterations in concentration gradients for percutaneous penetration of compounds, alterations in diffusion of glucose and other nutrients to the epidermis, and implications for wound healing. While a decrease in blood flow to the skin is often an assumed effect of aging, little direct evidence-based knowledge exists.

This article reviews the research and attempts to provide a foundation for future study. Distinctions are not always easily made between intrinsic physiologic aging and extrinsic aging due to photo-exposure, wind, relative humidity and other environmental factors. Distinctions that can be made will be reported here.

Methods

This review results from a literature search on age-related changes in cutaneous blood perfusion conducted in *PubMed*, *Em-Base*, *Science Citation Index* and the UCSF dermatological library's collection of books on the topic of aging skin. The review includes brief descriptions of commonly used quantitative methods and a discussion of research data.

Techniques

Cutaneous blood perfusion has been quantitatively studied in vitro as well as in vivo. In vitro histologic methods include the study of frozen sections stained with alkaline phosphatase for microscopic analysis. However, this technique is older and gives only a two-dimensional view, tending to yield overestimates of actual cutaneous perfusion.[1] A more recent immunohistochemical method studies specimens of skin stained for the CD31 antigen, the platelet endothelial cell adhesion molecule.[2]

In vivo methods include the use of intravital capillaroscopy, including native microscopy and fluorescin angiography, for noninvasive three-dimensional visualization of cutaneous blood flow.[1] Native microscopy uses an epi-illuminated microscope for in vivo viewing of superficial vasculature in immobilized, paraffin-treated skin.[1] Fluorescin angiography visualizes capillaries after intravenous administration of a bolus of sodium fluorescin solution.[1]

> Results of studies using LDV or LDF are somewhat mixed.

Laser Doppler flowmetry (LDF) and laser Doppler velocimetry (LDV) are commonly used in vivo methods that involve a helium-neon laser light being transmitted to the skin via an optical fiber. The laser Doppler signal penetrates to an estimated depth of more than 1 mm, giving information about deeper vessels and arteriovenous anastemoses, not seen by capillaroscopy methods.[1] Light reflected from nonmoving tissue contains radiation at the same frequency as the incident source. Light reflected off of moving red blood cells, however, is Doppler-shifted.

The instrument extracts the frequency-shifted signal and derives a numerical reading proportional to blood flow.[3,4] LDF and LDV involve essentially the same principles, but the instruments process the information slightly differently such that LDF results in an improved signal-to-noise ratio compared to LDV.[4] Estimates of cutaneous blood flow obtained using LDF and LDV are reported in arbitrary units and are not absolute; they are instrument- and laboratory-specific.[5]

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Photoplethysmography, another optical method, provides a measurement of arterial pulsations of the dermal plexus. Infrared radiation is directed into the skin, scattered, absorbed and reflected, primarily by hemoglobin in the tissue. Backscattered radiation is measured and the change of blood volume in the illuminated tissue is correlated to the amount of light absorbed by the blood. Greater blood flow results in greater absorption and less backscattered radiation.[4]

Data and Discussion

Results of studies using LDV or LDF are somewhat mixed; this often appears to be the result of varying age ranges and smaller sample sizes. Fluhr et al. found no significant difference in children vs. adults, but this did not allow for an assessment of changes in elderly skin because the average age of the older group was only 44.[6] Likewise, Kelly et al. found little difference in blood flow between young (age 18-26) and elderly (age 65-88) subjects; however, the presence of only 10 subjects in each age group makes the study less than conclusive.[1] Another LDV study found that skin's vasodilation response to heat stress and vasoconstriction in response to cold challenge appears delayed in elderly (age 70–83) subjects compared to younger (age 20–30) subjects, indicating a possibly reduced vessel density in aged skin.[7] Again, this study included only 10 elderly subjects and nine younger subjects, so it may not provide the most conclusive answer to questions about the effect of age on cutaneous perfusion.

Intravital capillaroscopy measurements of 26 subjects using fluorescin angiography and native microscopy suggest a decrease in dermal papillary loops and little change in horizontal vessels (post-capillary venules, ascending arterioles, and part of subpapillary plexus) with increasing age.[1] An immunohistochemical study of 19 individuals aged 20–84 revealed little effect of intrinsic aging of buttock skin on blood perfusion, but progressive and marked decrease in cutaneous perfusion in the photoaged eye corners.[2] A photoplethysmographic study including 69 individuals, aged 3–99, revealed significantly decreased capillary circulation in forehead skin with advancing age. Specific numbers, however, were not given.[8]

Conclusion

A review of this data makes a clear conclusion difficult because so much variation exists between studies. It appears possible that increased age may be associated with decreased cutaneous perfusion, especially in photo-exposed areas. However, this certainly is not an obvious or universal effect of aging. Future studies with more subjects and greater standardization of technique and body site studied may be helpful in further clarifying our understanding of the effects of age on cutaneous perfusion.

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MEASURING CUTANEOUS BLOOD FLOW

Setting standards for product claims and efficacy is an important task under the EU Cosmetics Directive. The European Group on Efficacy Measurement of Cosmetics and Other Topical Products (EEMCO) was formed in 1994 to develop industry-wide test methodologies and universal standards for cosmetic product claims substantiation.

The EEMCO guidance for the measurement of skin microcirculation was written by Berardesca et al. and published in *Skin Pharmacology and Applied Skin Physiology* in 2002. According to these authors, skin microcirculation can be measured by means of different techniques, based mainly on the quantification of the skin's optical and thermal properties, which are modified by the amount of blood perfusion.[9] The advantages and disadvantages of the main techniques in use are discussed, and optimization of measurements for laser Doppler techniques is described.

The assessment of skin microcirculation is useful in cosmetology for the quantification of the sun protection factor, skin irritation, and efficacy of anti-redness treatments.