

repeated every two minutes until the temperature reaches 44°C. Blood flow is recorded at the end of each two-minute interval (12).

For the axon reflex vasodilator response, vasoactive substances such as substance P, capsaicin, or histamine are administered topically or intradermally (30–32). Alternatively, acetylcholine is administered with the aid of electrophoresis (27). The extent of the response is measured at several distances from the site of administration. The same procedure is followed for measuring the response to direct stimulation with a firm mechanical stroke with a dermatograph (Lewis triple response) (27).

With the isotonic test, the subject squeezes a partially inflated blood pressure cuff with maximum effort, at which the pressure is recorded, and one-third of it is calculated. The subject is then instructed to grip the cuff at this value of one-third of the maximum pressure. This isotonic exercise causes vasodilatation, and an increase in skin blood flow results (16).

54.3.2 CHOOSING SUBJECTS

When comparing subjects or various groups of subjects, variations in population regarding sex (33, 34), age (20), and race (35) should be taken into account. Assuring that subjects match for these variables will decrease the variance within the results.

54.4 APPLICATIONS

LDF may be used to study the time course of circulatory changes caused by physiological or pathological processes, including changes caused by pharmacological substances. Internal and external factors, skin conditions, and general conditions that affect the skin are all candidates for LDF investigations.

54.4.1 SKIN PHYSIOLOGY, PHARMACOLOGY, AND PATHOLOGY

54.4.1.1 Percutaneous Penetration

LDF was applied for tracing the percutaneous penetration of vasoactive agents such as methyl nicotinate (6), prostacyclin (36), or methadone (37) and for studying variations in normal skin (6, 19). For instance, LDF assisted in evaluating the enhancement effect of ultrasound on skin penetration (38). Thus, spatial variations (19), percutaneous penetration enhancers (39), vehicle effect on percutaneous absorption (40), the appendage contribution to penetration (41), and age and racial differences (42) were all studied with LDF. A decreased percutaneous penetration was recorded in black subjects at various skin sites (43). Circadian differences in penetration kinetics of methyl and hexyl nicotinate were also demonstrated by LDF (44). On the other hand, LDF is not suitable for studying the percutaneous penetration of vasoconstrictive agents such as glucocorticoids (45).

Transdermal delivery utilizing iontophoresis was studied at different sites of the forearms and hands, and vasodilatation was site dependent (46). It was shown that cutaneous vascular responses to iontophoresis of vasoactive agents comprise nonspecific, current-induced hyperemia and specific effects of the administered drug (47).

54.4.1.2 UVB-Induced Erythema

The effect of ultraviolet (UV) light may be evaluated by LDF, but the technique was not adequate for individuals with dark skin (48).

The UVB-induced skin blood flow was monitored using the laser Doppler perfusion imaging technique. It was as sensitive as conventional LDF, but had the many advantages of measuring blood flow over large areas without contact with the skin surface (49). Laser Doppler perfusion imaging was also successfully used for phototesting (50).