

Diameter, Thickness, Area, and Volume of Skin-Prick Histamine Weals

Measurement of Skin Thickness by 15 MHz A-mode Ultrasound

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Twelve healthy persons were prick-tested on the volar forearm with three concentrations of histamine chloride (0.1 mg/ml; 1.0 mg/ml; 10 mg/ml) and an isotonic sodium chloride control. Weal diameters were measured, and skin thickness representing weal thickness was measured by high frequency ultrasound. Relative increases in weal parameters as measured and calculated between weak and strong concentrations of histamine (0.1 and 10 mg/ml) were: mean diameter 139%, weal thickness 46%, tangential area 443%, cross-sectional area 218%, and weal volume 680%. All the parameters of weal size measured and calculated showed significant differences between the three concentrations of histamine. However, a better distinction might be obtained by calculating weal volume. Coefficients of variation ranged from 12–28% for the weal diameter, 11–14% for the weal thickness, 24–53% for the tangential area, 14–39% for the cross-sectional area, and 23–55% for the weal volume. The increase in thickness was correlated to weal diameter up to a diameter of 5 mm ($r = 0.64$; $P < 0.001$), after which weals only expanded tangentially. Weal thickness as measured by ultrasound is a potentially important parameter in experimental studies of inflammatory skin reactions. With this new technique it is possible to compare with normal skin and skin treated with solvent for control. For routine prick-testing of patients with allergy, measurement of weal diameter is still a valid and easy method.

Key words: Allergy; histamine; weal; prick test; skin; thickness; ultrasound.

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The skin prick test is often used for evaluating allergic diseases. Attempts have been made to develop accurate and standardized methods (1, 2, 4, 6).

A positive prick test is normally interpreted by measuring the largest and smallest diameters of the weal with a ruler, and, occasionally, by calculating the surface area. Recently, accurate and objective measurement of the full thickness of the skin became possible by high frequency ultrasound (3). The ultrasound technique of measuring skin thickness compared favourably with a radiographic method (3, 12). However, the radiographic method cannot be applied to smaller areas of skin. In 1980–81 we

constructed an improved 15 MHz A-mode ultrasonic biometric ruler, which we used for quantification of scleroderma (systemic and localized), psoriasis, and patch test reactions in patients with contact dermatitis (7, 8, 9, 10). Quantification of patch test reactions by the ultrasound technique was superior to laser Doppler flowmetry, because vasodilation was already at a maximum in the weak positive reactions (+) (11).

In this study the size of histamine weals, induced by skin-pricks with three different concentrations, was evaluated. Experiments included measurement of weal thickness by ultrasound and calculation of weal volume.

MATERIAL AND METHOD

Twelve healthy persons (5 women, 7 men) participated in the study. Their mean age was 42.9 years (range 21–62). Three persons were excluded because of a weal reaction to the sodium chloride control or because of a paradoxical negative reaction to one of the histamine concentrations.

Skin prick test was performed on the volar side of the right forearm. Three tests with different concentrations of histamine chloride (0.1 mg/ml; 1 mg/ml; and 10 mg/ml) and a control with sodium chloride (9 mg/ml) were performed in each patient. The disposable "allergy pricker" of Dome/Hollister-Stier® with a point length of 1.0 mm was used: the pricker was jabbed with moderate force through the drops at an angle of 90° to the skin and lifted, and the drops wiped off (6).

The weal reactions were recorded between 10 and 15 min after skin prick. The contours of the weals were outlined with a fine fibre-tip pen and transferred to paper by means of tape. The largest diameter and a smaller diameter perpendicular to this were measured with a steel, precision ruler.

The skin thickness of the weal centre and an area of normal skin at least 2 cm from the weal were measured by our 15 MHz A-mode ultrasound scanner. The transducer was unfocused at a diameter of 5 mm. Instead of a water bath, a gelatine plug hardened with glutardialdehyde was prepared rendering quick measurements possible (Fig. 1). The weal surface was covered by few drops of water and the probe lightly applied. The pulse transit time and reflected signal amplitude were displayed on a cathode ray tube with the electronic distance indicator adjusted for skin measurements, and photographed. For calculation of skin thickness an acoustic velocity of 1518 m/sec was used as described by Daly & Wheeler (4). Examples of measurements performed by our apparatus are shown in Fig. 2. The skin thickness could be read from the photographed tube image with an approximate accuracy of 0.05 mm. Previous reproducibility studies showed standard deviations from 0.05 to 0.09 mm and coefficients of

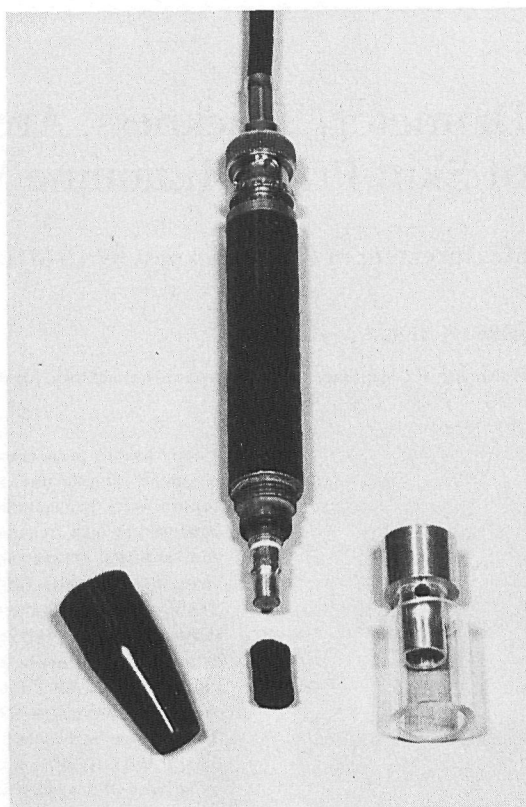


Fig. 1. Probe with 15 MHz transducer for ultrasound measurement of skin thickness. Gelatine plug (middle) and conical headpiece (left). Devices for measurement under water bath (right); cylindrical bath is fastened to the skin surface by double adhesive tape.

variation from 4.6 to 6.8% in non-diseased skin (8).

Calculation of weal areas and volume

The tangential area (TA) of the weals parallel to the skin surface and the cross-sectional area (CSA) were calculated assuming an elliptic contour and assuming the full-thickness of the skin to represent the weal thickness.

$$TA = 1/4 \times \pi \times d \times D = 0.7854 \times d \times D$$

$$CSA = 1/2 \times \pi \times \frac{d + D}{2} \times t = 0.3927 \times (d + D) \times t$$

HISTAMINE WEALS

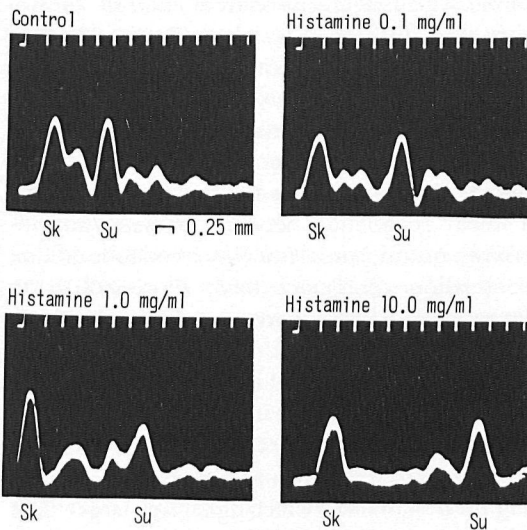


Fig. 2. Examples of ultrasound A-mode images of histamine weals. Skin thickness is calculated from the time-interval between the skin surface echo (Sk) and dermis-subcutaneous tissue interface echo (Su), using ultrasound velocity in skin = 1518 m/sec. In the upper margin: electronic indicator of distance – distance between two points = 0.25 mm.

(d = smallest diameter, D = largest diameter, t = weal thickness).

The volume (V) was calculated assuming a weal shape of an ellipsoid of revolution.

$$V = 4/3 \times \pi \times \frac{d}{2} \times \frac{D}{2} \times \frac{t}{2} = 0.5236 \times d \times D \times t$$

Statistical methods

Statistical analysis was performed by Student's t -test. Probabilities of <0.05 were considered significant. The relation between mean weal diameter and weal thickness was analysed by linear regression.

RESULTS

The mean diameters and the mean thickness of histamine weals are shown in Fig. 3 and Table 1. Differences in diameter between 0.1 and 1.0 mg/ml and between the 1.0 and 10.0 mg/ml concentrations were significant ($P < 0.001$; $P < 0.001$). Differences in weal thickness between

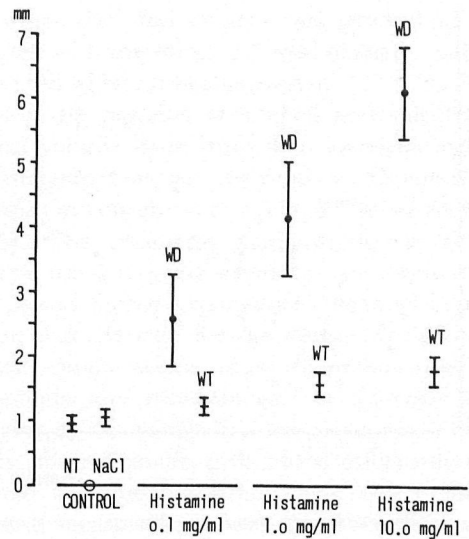


Fig. 3. Weal thickness (WT) and weal diameter (WD) in 12 persons skin-prick tested with histamine in three different concentrations, expressed as mean values $\pm$ SD. Each value of diameter was calculated as the mean value of the largest and the smallest weal diameters. Thickness of control skin not tested (NT) and pricked with isotonic sodium chloride solution (NaCl) is indicated.

non-tested skin and histamine 0.1 mg/ml and between histamine 0.1 and 1.0 mg/ml were significant ($P < 0.001$; $P < 0.001$), while the difference in weal thickness between 1.0 and 10.0 mg/ml concentrations was less significant ($P < 0.05$). The thickness of the sodium chloride control sites tended to be greater as compared with normal skin (n.s., difference in mean thickness 0.104 mm). When the weal

Table 1

Experiments in 12 healthy subjects prick tested with three different concentrations of histamine. Weal diameter and weal thickness in mm

Histamine concentration (mg/ml)	Weal diameter (mm)		Weal thickness (mm)	
	Mean	SD	Mean	SD
0.1	2.54	0.71	1.22	0.14
1.0	4.13	0.89	1.56	0.20
10.0	6.08	0.73	1.78	0.25

Control sites mean 0.95 mm, SD 0.11 mm; NaCl-prick mean 1.05 mm, SD 0.12 mm.

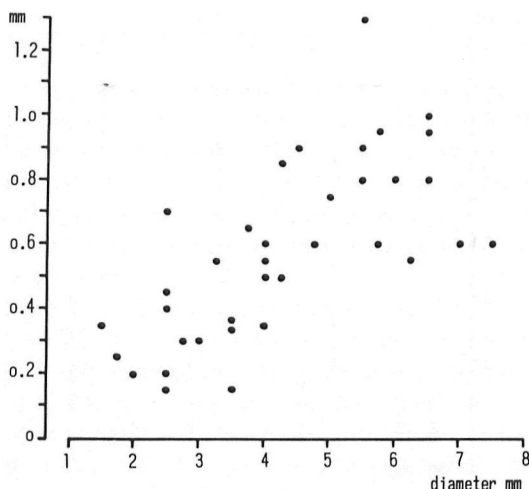


Fig. 4. Relation between mean weal diameter and absolute increase in skin thickness (weal thickness – thickness normal skin) in 12 persons skin-prick tested with histamine in three different concentrations. Correlation coefficient for weal diameter ranging from 1–5 mm = 0.64, $P < 0.001$.

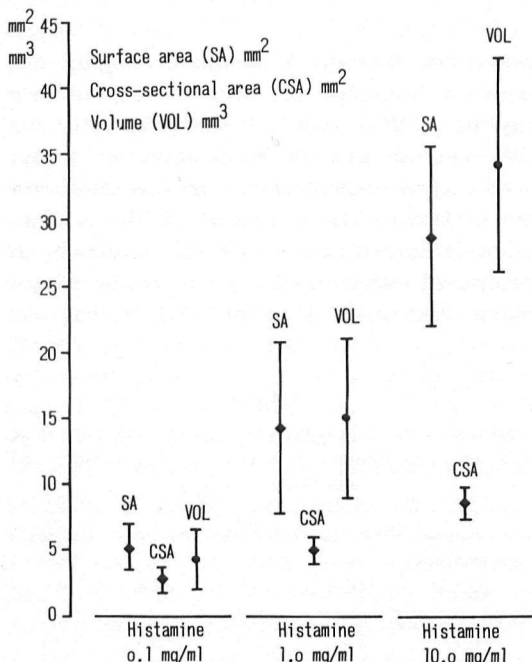


Fig. 5. Tangential surface area (SA), cross-sectional area (CSA) and volume (VOL) of weals of 12 persons skin-prick tested with histamine in three different concentrations, expressed as mean value $\pm$ SD.

thickness with histamine 0.1 mg/ml was compared with that in the sodium chloride control sites, the difference was less ($P < 0.02$) than when compared with normal skin ($P < 0.001$).

The relation between the diameter of weals and the absolute increase in thickness (thickness weal – thickness normal skin) is shown in Fig. 4. A weal diameter of up to 5 mm showed a linear correlation between diameter and increase in thickness (increase 0.136 mm/mm, correlation coefficient 0.64, $P < 0.001$). In large weals with a diameter > 5 mm the thickness seemed stationary.

The mean tangential area, the mean cross-sectional area, and the mean volume of weals are illustrated in Fig. 5. The tangential area with histamine 10.0 mg/ml was larger than with 1.0 mg/ml ($P < 0.001$), which again was larger than the weal area with histamine 0.1 mg/ml ($P < 0.01$). Differences in cross-sectional area between the three concentrations of histamine were both significant ($P < 0.001$; $P < 0.001$). Differences in weal volume between the three concentrations of histamine were also highly significant ($P < 0.001$; $P < 0.001$). Fig. 5 may give the impression that the increase in weal volume was quantitatively larger as compared with tangential and cross-sectional areas. In Tables 2A and 2B coefficients of variation and the relative increases of the parameters in Figs. 3 and 5 have been calculated.

Ten consecutive measurements performed on one weal (histamine 10 mg/ml) preceded by three measurements under a water bath were as follows: 1.9; 2.0; 1.9 (water bath), and 1.8; 1.9; 1.9; 1.8; 1.6; 1.5; 1.6; 1.3; 1.3; 1.3 (gelatine plug and very light touch). The mean thickness of normal skin was 0.836 mm, SD 0.081 mm. After approximately four measurements weal thickness was thus decreasing due to the very light application of the probe. Measurements lasted approximately 5 min.

DISCUSSION

One finding in this study was that the formation and expansion of cutaneous oedema in well-developed weals is mainly tangential, and thus, under standardised conditions, the routine

reading of weal diameter in prick testing of allergy patients is an easy, simple and accurate method.

Measurement of weal diameter gave good distinction between skin-prick with different concentrations of histamine. Calculation of tangential area added no essentially new information, and provided no improved distinction between the groups.

The thickness of weals was comparatively small. However, measurement of weal thickness by the ultrasound technique had a good reproducibility as coefficients of variation indicated. Measurement of weal thickness is, essentially, an additional parameter for the quantification of weal reactions. Measurement of weal thickness is, considered as a single parameter, of particular interest in weals of small and medium size, i.e. up to 5 mm in diameter, when the weals are expanding in thickness. It is an advantage that comparisons can be made with

normal skin and control skin pricked or injected with the solvent. A weal diameter cannot be read when no weal is present.

Of the parameters studied and calculated, weal volume might provide a somewhat better distinction between reactions to histamine in different concentrations (Fig. 5, Tables 2A and 2B). The seemingly stationary thickness of large weals (Fig. 4) seems to have been compensated by the exponential tangential expansion characteristic of large weals. Calculation of weal volume seems, thus, to combine the advantages and disadvantages of thickness and diameter recordings in a favorable way. Thickness measurements give added information in small and medium-sized weals, where ultrasound measurement has a good accuracy, and diameter measurements give added information in medium-sized and larger weals, where the expansion of weals is tangential and the accuracy of measuring diameter good. Calcula-

Table 2A

Experiments in 12 healthy subjects prick tested with three different histamine concentrations. Coefficients of variation of parameters measured and calculated

Histamine concentration (mg/ml)	Coefficients of variation (%)				
	Weal diameter, mean	Weal thickness*	Tangential area	Cross-sectional area	Volume
0.1	28	11	53	39	55
1.0	22	13	45	21	41
10.0	12	14	24	14	23

* Coefficients of variation in subjects' normal skin was 11%.

Table 2B

Experiments in 12 healthy subjects prick tested with three different histamine concentrations. Mean relative increases in parameters measured and calculated

Histamine concentration (mg/ml)	Mean relative increase (%)				
	Weal diameter, mean	Weal thickness	Tangential area	Cross-sectional area	Volume
0.1/1.0	62	28	171	89	245
1.0/10.0	47	14	100	69	126
0.1/10.0	139	46	443	218	680

tion of weal volume, however, lacks the advantage of weal thickness measurement as a single parameter to allow comparison with normal skin and control skin handled with the solvent.

In conclusion, weal thickness as measured by high frequency ultrasound is an important new parameter for the assessment of weal reactions. Its main interest seems to lie in experimental work, particularly in studies of the effect of inflammatory reaction mediators in normal and diseased skin.

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