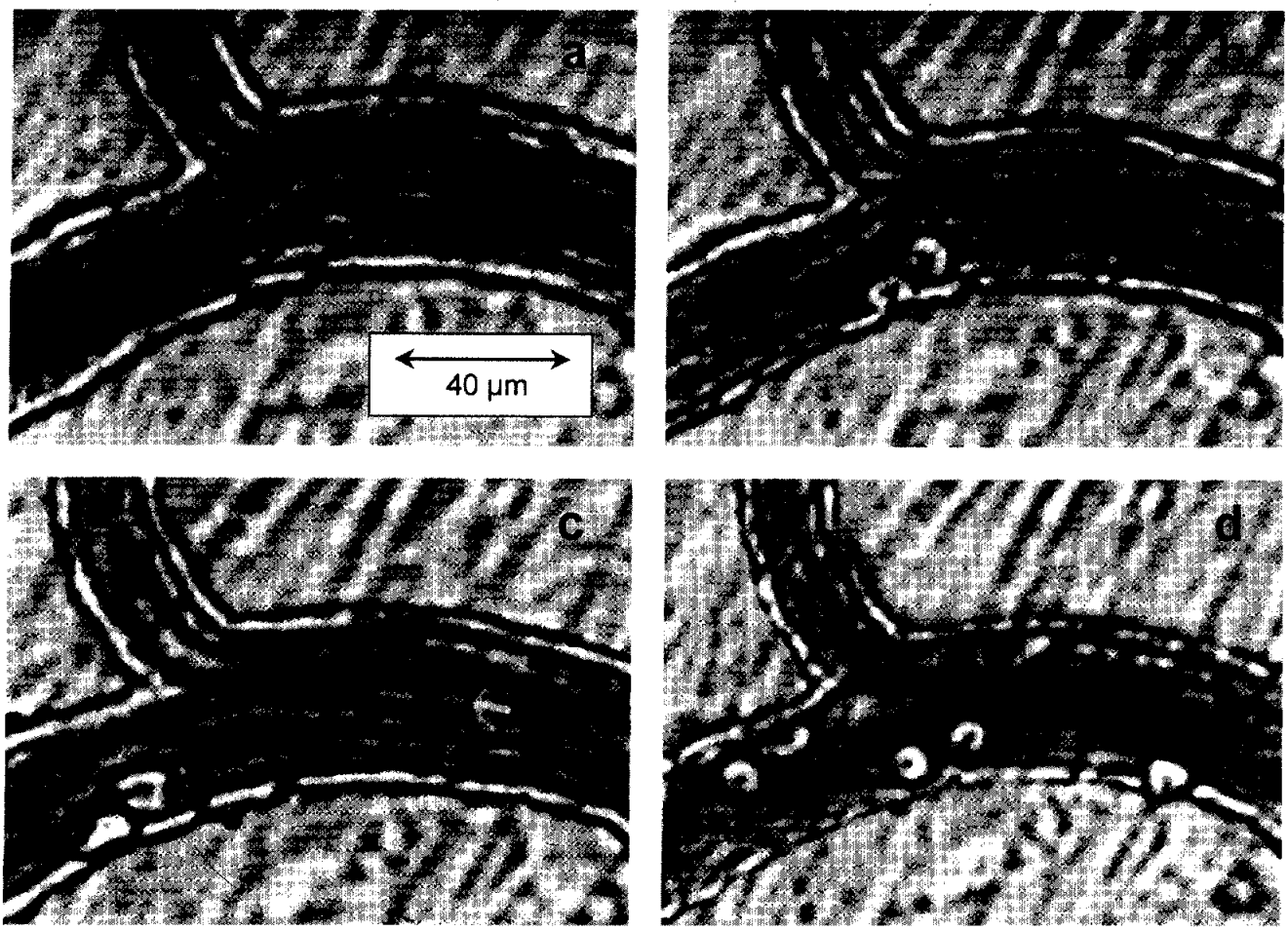

Figures 3a – 3d. *Vital microscopic examples of changes in behavioral characteristics of white blood cells of a volunteer before and after mistletoe extract injections from the same microvascular section (derma / injection point) mf 1/8000 s; venule junction. Condition of the roll-off and adhesion phenomena of the white blood cells before mistletoe extract injection on day 0 (a) and after mistletoe extract injection on day 1 (b), on day 3 (c) and on day 5 (d).*

were used; the injection was applied into a defined fold of the skin; the injection angle was 90°; there were no injuries to blood vessels by the injections; the same bolus volume V = 1ml was used; the injection time was t = 10s.)

To achieve a typical local reaction the test individuals were initially injected with 0.1 mg mistletoe extract twice at an interval of 2 days between the injections; 2 days after initial applications they received an injection of 1.0 mg/mL mistletoe extract. Before the first injection (day 0) baseline values were taken and thereafter (days 1 to 12) measurements were performed daily. The time of injections (1:00 am) and the time of measurements (7:00 pm) were standardized.

The following defined conditions were required of the subjects: no alcohol, no coffee, no tea, no caffeine containing soft drinks for 12 hours before the examination; at least 6 hours of sleep a day, 2 hours acclimatization before the measurement; blood pressure and heart rate as well as breathing frequency according to rest conditions; room temperature ~22° C.; relative air humidity ~75%; comparable weather conditions during the entire trial period; measurements taken in a seated position.

The investigation methods allowed measurement of defined characteristics:

a) systemic characterisation of circulation and temperature regulation;
b) geometric and dynamic characterisation of the functional condition of the microcirculation in various areas of target tissues;
c) immunological/behavioral characterisation of white blood cells in the microvascular networks in various areas of target tissues;
d) secreted proteins of white blood cells in various areas of target tissues.

The *accompanying systemic investigations* included standardized measurements of the systolic blood pressure (RR_{syst}), of the heart rate (Hf), and of the body basal temperature (rectal $T_{rec,}$).

The *microcirculatory investigations* were carried out in various areas of target tissues (defined volume V = 1200 µm3). The time of measuring (t = 0.d 60) and KIRCHHOFF junctions (nodal points) perfused with blood cells were determined in the microvascular networks of the target volumes. All microvessels (arterioles, capillaries, venules) with diameters d < 40 µm, as well as the initial lymph stream, were included.

Microcirculatory data were obtained simultaneously in various areas of target tissues of well-known immunological activity as follows.

A - Derma injection point, 15 mm from the injection point (near Tela subcutanea); B – Derma thorax area, defined measurement point (near Tela subcutanea); C – Gingiva, upper jaw, left incisor, frontal (near Sulcus); D – Rectum defined measurement point, Canalis analis passage (mucous, muscle)

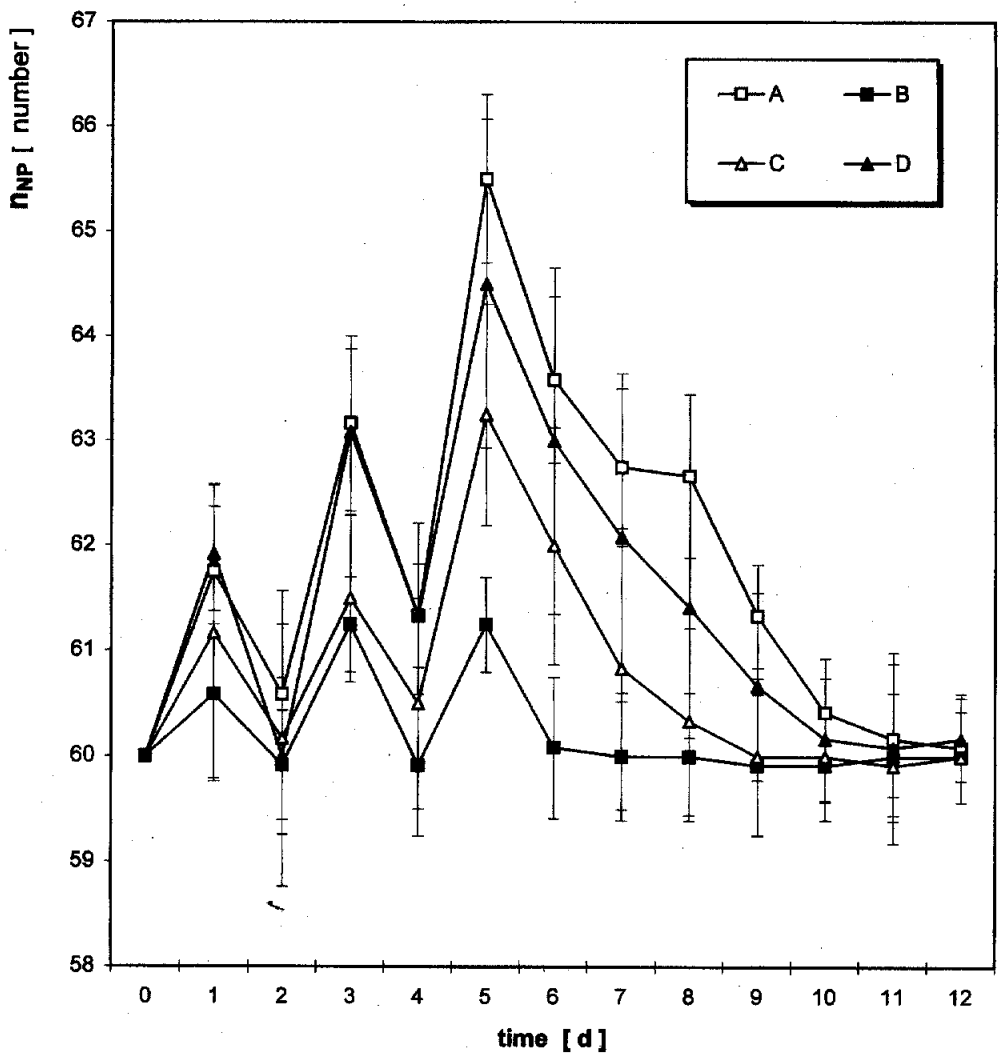

Figure 4. *"Number of blood cell perfused nodal points nNP" (mean values and standard deviations) from the various target tissues: A, derma / injection point; B, derma / thorax; C, gingiva; D, rectum. Abscissa: time (days). Ordinate: number per defined volume unit.*

To analyze 1) functional characteristics of the microcirculation in completely connected microvascular networks, 2)the initial lymph stream and 3) the behavioral characteristics of the white blood cells, an intravital microscopic investigation unit was used with a combined illuminating and radiating process with selective filtering and computer-aided image processing (ZEISS, NIKON, KONTRON system). The combination with a reflection spectrometric investigation unit (SPEX) enabled measurements of the local concentration of a defined protein (Interleukin-1). The diagram of the investigative unit is presented in Figure 1 (25-30). Microphotography (up to 1/8000 s), S-VHS, U-matic and 35mm special cinema film with image frequencies up to 120 images per second (ARRI syste) supported the documentation of the findings.

The following geometric and dynamic characteristics were measured by vital microscopy :

1) Number of blood cell perfused nodal points n_{NP} in a defined network unit.
(Measuring criteria: duration of the condition > 20 seconds, peripheral cases were given a value of + 0.5 or – 0.5, peripheral streaming speed ~ 80 µm/s. Original value at time of measuring
t = 0 n = 60).

2) Tube hematocrit Hk_t.
(Measuring criteria: local hematocrit in a particular microvessel, cell share of the total blood volume).

3) Arteriolar and venular streaming flow Q_{art} or Q_{ven}.
(Measuring criteria: Streaming strength of the red blood cells, the so-called particle stream).

4) Middle streaming flow of the initial lymph Q_L.
(Measuring criteria: interstitial streaming time volumes directly next to the venules).

The immunologically relevant behavioral characteristics of the white blood cells were determined with the help of the vital microscope:

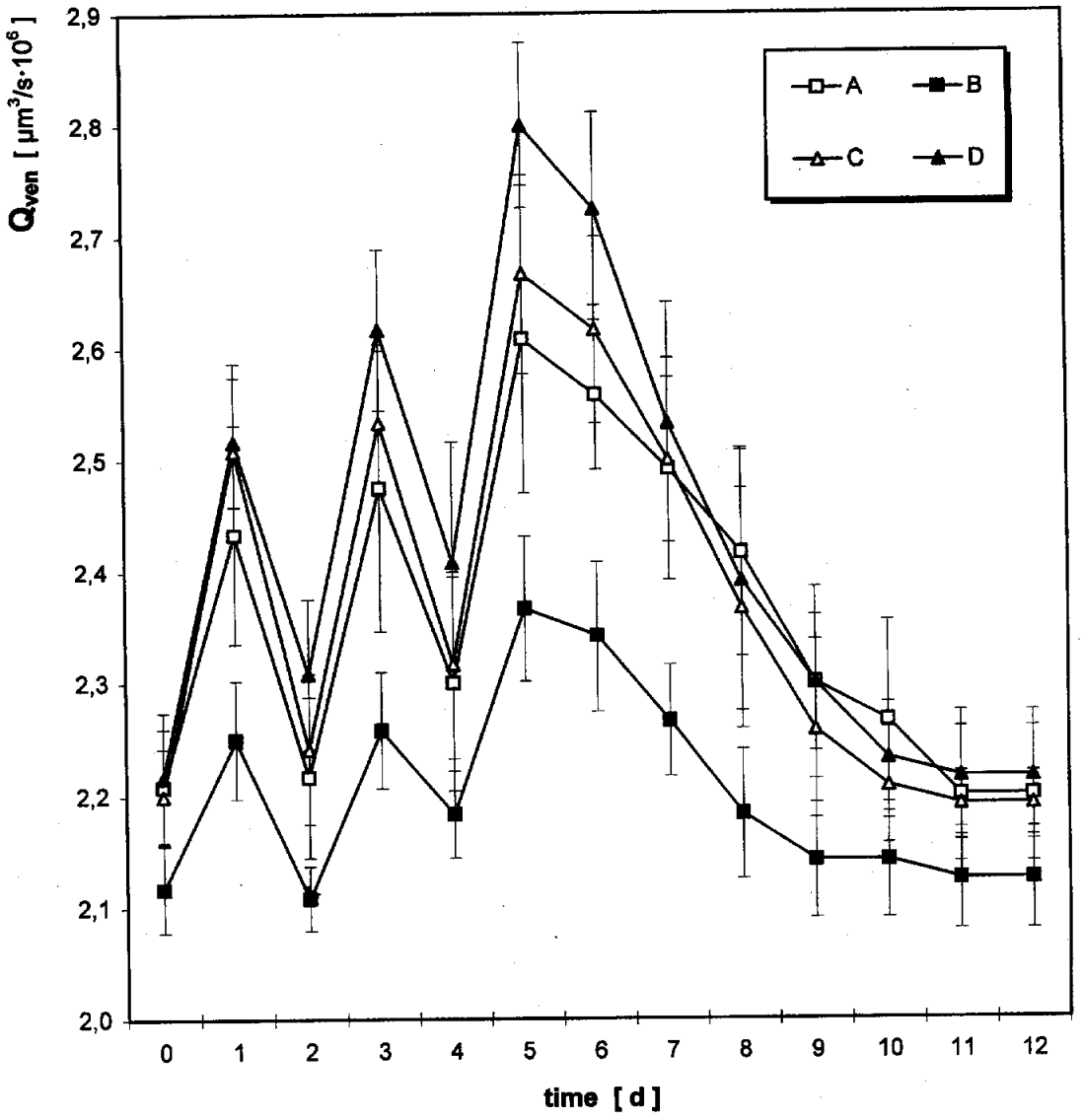

Figure 5. *"Venular streaming flow Qven" (mean values and standard deviations) from various target tissues: A, derma / injection point; B, derma / thorax; C, gingiva; D, rectum. Abscissa: time (days). Ordinate: measuring values in µm3/s.*

1)Number of adhering white blood cells on a defined inner venule wall $n_{WBC/A}$.
(Measuring criteria: the surface involved was a defined venule wall area A = 18000 μm^2 with an axial length l ~ 140 µm and a diameter d ~ 40 µm; the adhesion of the white blood cells to the endothelium lasted longer than 5 seconds).

2) Number of transmigrating white blood cells in a defined tissue volume unit $n_{BC/V}$.
Measuring criteria: all blood cells were counted that had passed the venule wall in the defined tissue volume and time and had reached the extravasal space. Volume unit V = 1200 μm^3.

3) Local concentrations of Interleukin-1 (cIL-1) were determined by a reflection spectrometric unit in the vital microscopically investigated target tissue areas (identical tissue volumes).
(In the identified spectrum each determined amplitude value was arranged on a relative evaluation scale of 0 to 10).

4) Statistical analysis of the collected data. Assuming constant variables in the adequat biometrical sample, the Wilcoxon rank sum test was used.

5) Testing of significance was performed at the significance level a = 5%. For each target tissue the original values at the time t_0 = 0. day were compared with the values of the subsequent analysis $t_n > t_0$.
For analogue times t = t the data of one target tissue were compared with other target tissues.