Videophotometric skin capillaroscopy for assessment of microvascular disturbances

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PREFACE

The present study was carried out during the years 1986-1989 at the Vascular Research Laboratory, Department of Surgery, Aker Hospital and the Microvascular Laboratory, Department of Medicine, Karolinska Hospital, Stockholm. This article is based on the following publications referred to by their Roman numerals:

I. *Rosén, L., Östergren J., Fagrell, B. & Stranden, E.:* Skin capillary blood cell velocity in preeclampsia. The effect of plasma expansion. Int J Microcirc: Clin Exp 1989, *8*:237-244.

II. *Rosén, L., Östergren J., Stranden, E. & Fagrell, B.:* Mechanisms for edema formation in normal pregnancy and preeclampsia studied by measuring skin capillary dynamics. Int J Microcirc (in press).

III. *Rosén, L., Östergren J., Fagrell, B. & Stranden, E.:* Skin microvascular circulation in the sympathetic dystrophies evaluated by videophotometric capillaroscopy and laser Doppler fluxmetry. Eur J Clin Invest 1988, *18*:305-308.

IV. *Rosén, L., Östergren J., Roald, O. K., Stranden, E. & Fagrell, B.:* Bilateral involvement and the effect of sympathetic blockade on skin microcirculation in the sympathetic dystrophies. Microvasc Res 1989, *37*:289-297.

V. *Rosén, L., Fagrell, B., Eriksson, S-E. & Sjölund, A.:* Evaluation of a completely computerized cross-correlation technique for measuring capillary blood cell velocity in humans. Microvasc Res (submitted).

INTRODUCTION

Intravital capillaroscopy techniques make it possible to study and quantify dynamic phenomena in single capillaries of the human skin. *Zimmer* et al. (1963) and *Zimmer* and *Demis* (1964) were the first to use the television microscopy technique to evaluate capillary circulation of the skin in man. *Bollinger* et al. (1974) refined the technique to measure blood cell velocity in human capillaries (CBV). Introduction of the cross-correlation technique greatly facilitated such measurements (*Intaglietta* et al. 1975, *Silva* and *Intaglietta* 1974, *Fagrell* et al. 1977a and *Fagrell* et al. 1977b).

Skin capillaries in the distal parts of fingers and toes are positioned parallel to skin surface (*Davis* and *Lawler* 1958). This anatomical feature supplies the means to measure CBV with videophotometric capillaroscopy.

Preeclampsia is characterized by hypertension and proteinuria. The condition is associated with placental insufficiency and intrauterine growth retardation. This state is partly attributed to rheological and generalized hemodynamic disturbances (*Buchan* 1982, *Gallery* et al. 1979). Preeclampsia has therefore been regarded as a *multiorgan-hypoperfusion* syndrome with signs of increased blood viscosity, increased total peripheral resistance and reduction of both plasma volume and cardiac output (*Müller* 1981, *Hobbs* et al. 1982, *Mathews* and *Mason* 1974, *Schwartz* and *Retzke* 1982). Plasma expanders are effective in counteracting these rheologic and hemodynamic disturbances (*Gallery* et al. 1979, *Rasmussen* et al. 1984).

Sympathetic dystrophies are a general description of clinical conditions with similar symptoms and signs following trauma to an extremity or other diseases such as myocardial infarction, cervical osteochondrosis and cerebrovascular disease (*Poplawski* et al. 1983, *Kozin* et al. 1976, *Rowlingson* 1983). The syndrome is characterized by pain, cutaneous edema, dystrophic changes of the skin, joint stiffness, sudomotor and *vasomotor instability* (*Kozin* et al. 1976, *Poplawski* et al. 1983). The nature of this vasomotor instability is not completely known. Involvement of the sympathetic nervous system has been suggested, but has not been thoroughly investigated (*Miller* and *DeTakets* 1942, *Poplawski* et al. 1983, *Rawlingson* 1983).

The purpose of the present investigation was to assess the applicability of different tests performed by videophotometric capillaroscopy. Based on patophysiologic disturbances patients with sympathetic dystrophies and preeclampsia were selected to elucidated the tests.

AIMS OF THE STUDY ARE:

1. a) To measure the skin capillary blood cell velocity (CBV) in preeclamptic patients during basal condition and during post-occlusive reactive hyperemia (PRH).
   b) To measure the effect on CBV variables of dextran 70 infusion to these patients.
2. To determine the pattern of CBV fluctuations at rest and the effect of venous stasis on CBV in healthy subjects, in women with normal pregnancies and with preeclampsia, two conditions often associated with cutaneous edema.
3. a) To describe skin microcirculation in sympathetic dystrophies at rest.

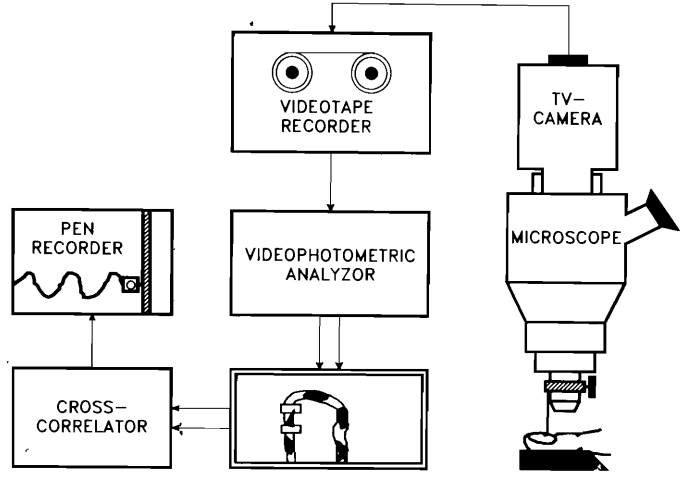

Fig. 1. Schematic presentation of equipment for videophotometric capillaroscopy. CBV measurements are based on the standard temporal cross-correlation technique.

b) To measure the effect of stimuli increasing the arteriolar tone (cold exposure, lowering of the hand) which depends on sympathetic nerve activity.
c) To investigate the possibility of bilateral involvement in sympathetic dystrophies by studying skin microcirculation in the asymptomatic hand.
d) To measure the effect of sympathetic blockade on skin microcirculation in the affected hand of patients with sympathetic dystrophies.

4. To evaluate correlations of CBV measurements performed by a new computerized technique (Capi-Flow^{R}) and the standard cross-correlation (IPM) technique.

MATERIAL AND METHODS

Fourteen patients with preeclampsia aged 21-34 years (median 28 years), fulfilled the prerequisites to be enrolled in the study. As control subjects 15 women, aged 20-34 years (median 27 years) with normal preg-

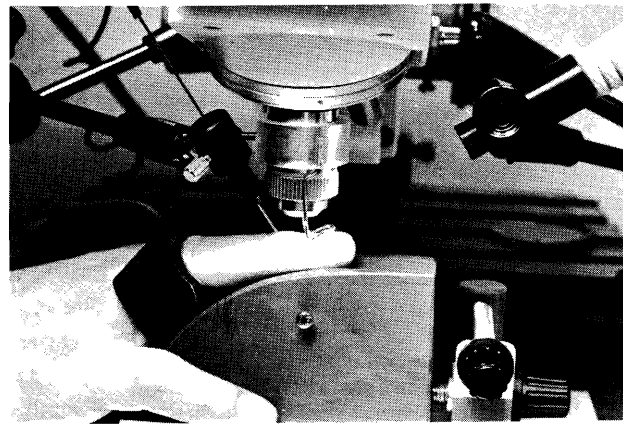

Fig. 2. The finger is placed under the objective of the microscope. A small metal bracket attached to the objective is used to stabilize the finger.

nancies and 14 non-pregnant women, aged 24-39 years (median 29 years), were studied. All pregnant women were in the third trimester of pregnancy.

Fifteen patients, aged 43-71 years (median 51 years), with sympathetic dystrophies were studied. They were all in the late phase of the disease. The control group consisted of 12 subjects, aged 31-65 years (median 41 years). All patients with sympathetic dystrophies were studied on at least two different occasions.

Twenty-three healthy subjects, aged 11-51 years (median 31 years), were included to study vasomotor activity.

Videophotometric capillaroscopy (Fig1). The third or fourth finger was placed on a modified stage of a Leitz epi-illumination microscope (Fig. 2). The nailfold area of the finger was positioned under the lens at the level of the sternal notch. A metal bracket attached to the objective of the microscope was adjusted to rest on the nail with a slight pressure to minimize movements of the investigated area. A 50W mercury lamp illuminated the nailfold at an angle of approximately 45° to the skin surface. To prevent heat from the lamp to influence skin temperature the light was transmitted through a heat absorbing filter. A green filter was used to increase contrast between blood cells and the surrounding tissue. A drop of paraffin oil was applied to the skin to increase its transparency and minimize reflexes from the skin surface. A video camera (Hitachi model HV-725) mounted on the microscope and connected to a monitor produced images of nailfold capillaries which were videotaped (Panasonic AG 6200 video recorder) for subsequent analyses. During playback the capillary images were displayed on a monitor at a final magnification of 250x. A dual channel videophotometric analyzer (Model 202, IPM San Diego, USA) measured the average level of illumination in the two independent square areas (windows) positioned on the capillary loop. The videophotometric windows produce analog voltages directly proportional to the light intensity within the windows (Fig.3). Variations of optical density in the windows are due to passage of erythrocytes, leukocytes and plasma gaps. The inter-window transit time of identical or similar signals is inversely proportional to CBV. By the cross-correlation technique (IPM) signals are computerized producing a continuous read-out of CBV (*Silva* and *Intaglietta* 1974, *Fagrell* et al. 1977a, *Tomkins* et al. 1974). The velocity curve was produced on a Mingograf 34 chart recorder and velocity variables manually calculated.

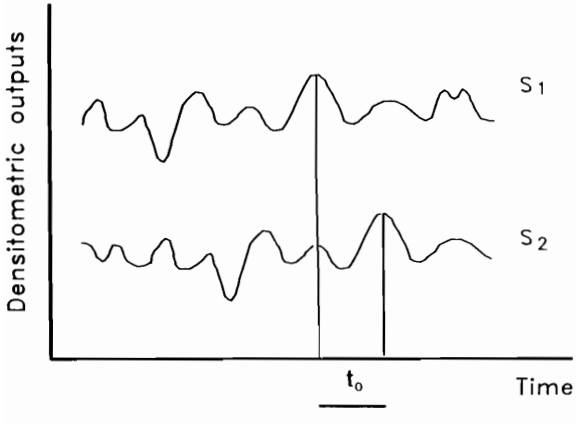

Fig. 3. Videodensitometric outputs (s_1, s_2) from the two photometric windows placed on the capillary loop. The time delay between identical signals is t_0.

Cross-correlation (CapiFlow^R)

Temporal correlation. The two densitometric windows are positioned on the capillary loop with a certain distance (d) apart. The passage of blood cells produces similar signals (s_1, s_2) in the two windows. Signals from the downstream window (s_2)

is delayed relative to signals from the upstream window (s_1) with a time t_0 (Fig. 3). The velocity (v) can be expressed as:

$$v=d/t_0.$$

Time delay between signals can be determined by displacing s_2 until the best fitness is achieved to s_1. This displacement equals the time delay between signals. To assess and quantify this fitness a correlations function is used. The cross-correlation function (R) as a function of an assumed time delay (τ) is defined mathematically:

$$R(\tau) = \int s_1(t) \cdot s_2(t+\tau)dt$$

The two signals are multiplied with varying τ and integrated over a time T. An example of a cross-correlation function is shown in figure 4. The peak in the cross-correlation function corresponds to the time delay t_0. A correlation coefficient (r) is used to describe the degree of correlation. The correlation coefficient varies between 0-1 indicating respectively no correlation between signals and identical signals.

Spatial correlation

This is a distance related, not a time related, cross-correlation technique as described above. A line is positioned along the capillary axis. The intensity along the line can be described by an intensity function $i_1(x)$. After a time interval t_0 the intensity along the line has changed to a new intensity function i_2x due to a continuous capillary flow. During a known time interval the blood cells have moved a certain distance x_0. This displacement can be measured by moving $i_2(x)$ to achieve the best approximation to $i_1(x)$. Analogous to temporal correlation a spatial correlation function can be defined, and the peak in the spatial correlation function corresponds to the displacement x_0.

CBV measurements performed by computer analyses (CapiFlow®) (Fig. 5 and 6). Velocity measurements are performed by a computer (PC-AT) with a CapiFlow video RAM card (CF-RAM-1) (V). The two photometric windows, generated by the computer, can be moved in tandem by the computer mouse and positioned onto a capillary with clearly visible plasma gaps. Desired capillary velocity variables are selected from the menues and subsequently presented to the operator on the computer screen. CBV can be measured by both temporal and spatial correlation. If correlation function drops below a certain limit or the position of the photometric windows is changed, CBV will not be recorded.

Capillary velocity variables were determined as follows:

1. *CBV at rest (I-V)* was calculated as the mean velocity during 60-120 s (12 measurements per 60 s). The standard deviation (SD) of these velocity values reflects the

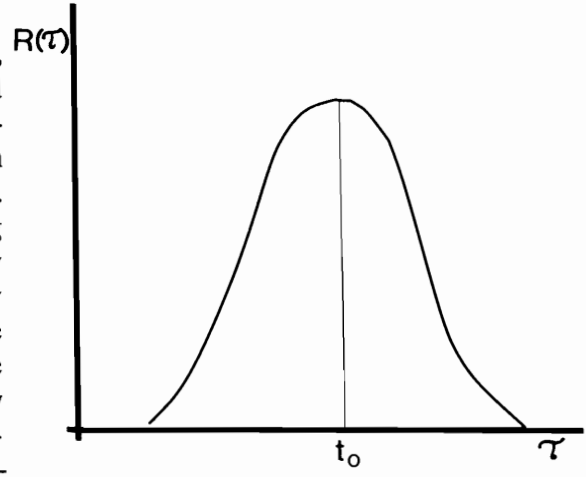

Fig. 4. An example of a cross-correlation function where the peak corresponds to the time delay (t_0) between identical signals obtained from the two photometric windows.

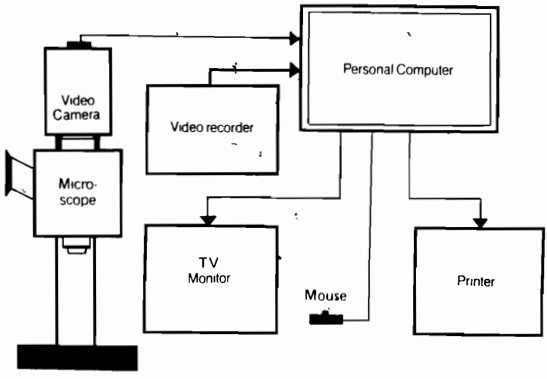

Fig. 5. Schematic presentation of the equipment for the computer based videophotometric capillaroscopy.

cyclic fluctuations of CBV dependent mainly on vasomotor activity in the pre-capillary vessels.

2. *Post-occlusive reactive hyperemia (PRH) response (I, V).*
Arterial occlusion was achieved by rapid inflation of a cuff applied around the base of the finger. Suprasystolic pressure (200 mmHg) was maintained for 60 s and then instantaneously released. The PRH response was described in the following terms:

i) Maximal post-occlusive peak CBV (pCBV).
ii) Time from cuff release to pCBV.

3. *Response to venous occlusion (II, V).*
A cuff around the base of the finger was abruptly inflated to 50 mmHg and the pressure maintained for 30 s. CBV was measured during the period of venous occlusion.

4. *Response to cooling of the contralateral hand (III, IV).*
The contralateral hand was immersed in ice-water for 60 s, while CBV was simul-

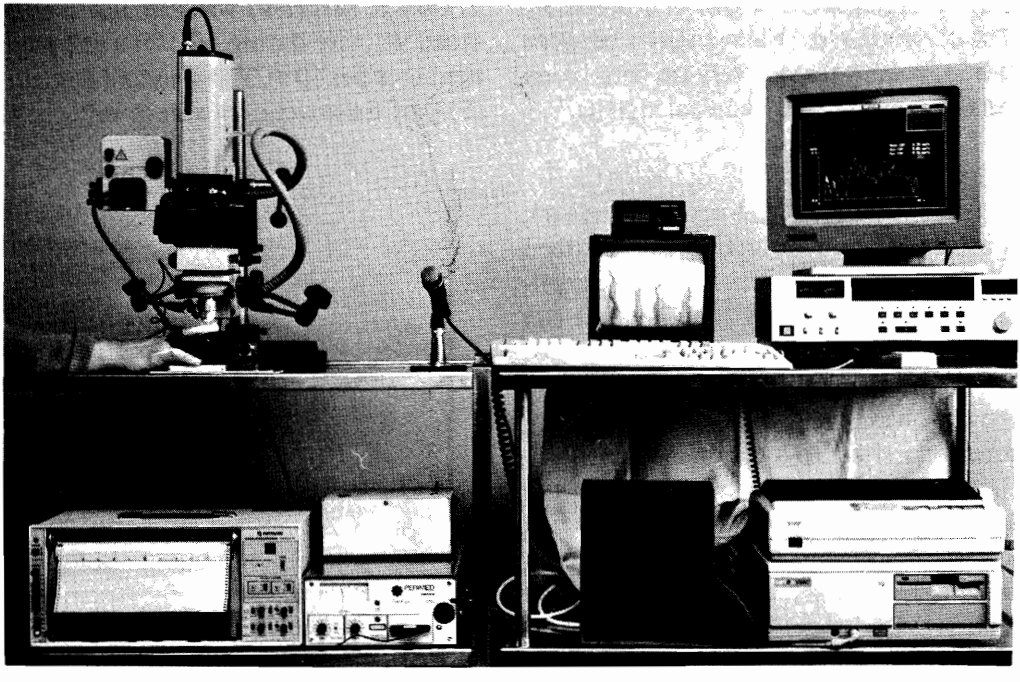

Fig. 6. Experimental setup, showing the vital capillary microscope, the CapiFlow system and the Periflux laser Doppler fluxmeter.

taneously recorded in the ipsilateral hand. CBV changes from basal values less than or equal to 5 % during provocation tests were defined as no change.

Laser Doppler Fluxmetry (III, IV).
By means of a 2mW helium neon laser Doppler fluxmeter (Periflux[R], Perimed, Sweden) laser Doppler flux (LDF) was measured in the same region of the finger as investigated by videophotometric capillaroscopy. The laser Doppler fluxmeter was only combined with capillaroscopy for studying patients with sympathetic dystrophies.

RESULTS AND GENERAL DISCUSSION

Videophotometric capillaroscopy has several advantages:

* The method is noninvasive and does not disturb normal physiological events in the capillary bed.
* It is continuous which allows dynamic studies of capillary flow.
* Quantitative values are obtained specifically from nutritive skin capillaries.
* Videotaping allows analyses at later occasions.

In the present study the limitations of the method were reaffirmed:

* Only a few capillaries can be visualized simultaneously on the monitor to measure CBV.
* Only capillaries in the nailfold area and some distal parts of the extremity can be visualized. This, however, is of minor importance since most peripheral circulatory disturbances manifest themselves in fingers and toes.
* In some subjects capillaries cannot be visualized due to an intransparent epidermal layer.

1. CBV at rest (Fig. 7)
CBV varies with e. g. precapillary vascular resistance and skin temperature. Consequently, individual CBV varied considerably in healthy subjects (0.10-1.20 mm/s) as well as in patients with preeclampsia and sympathetic dystrophies. CBV measured in one capillary is therefore an unreliable parameter of total skin nutritional capillary circulation, and has little value for individual comparisons. In groups of subjects median CBV varied to a lesser extent than individual values. The range of median CBV values obtained from healthy controls was 0.44 mm/s-0.70 mm/s. *Fagrell* et al. (1977b) found a mean CBV at rest of 0.65 mm/s in twelve healthy subjects with an average skin temperature of 30.4 °C and similar values have been found by others (*Bollinger* et al. 1974, *Östergren* 1984). Values can be compared and conclusions drawn in groups of subjects investigated under the same conditions.

CBV was reduced in the affected hand of patients with sympathetic dystrophies (III, IV) but increased following sympathetic blockade (IV) indicating an increased sympathetic vascular tone. Decreased CBV has been found in several conditions, e. g. Raynaud phenomenon, acrocyanosis, leukemia, associated with increased blood viscosity and/or constriction of precapillary resistance vessels. (*Bollinger* et al. 1976, *Dintenfass* 1982, *Jacobs* 1985, *Östergren* et al. in press). CBV was not reduced in preeclampsia (I, II) which presumably is associated with both increased blood viscosity and vascular smooth muscle tone. Factors tending to reduce perfusion may be counteracted by

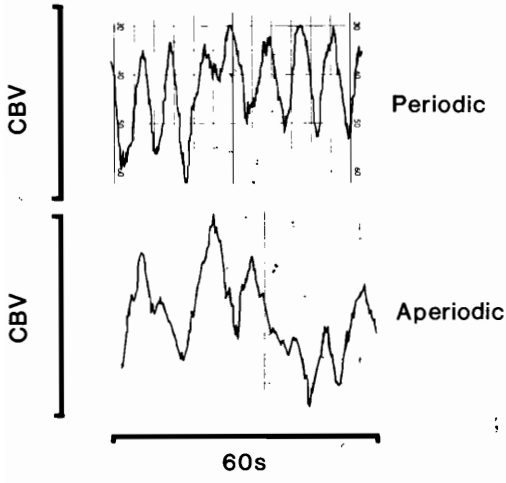

Fig. 7. CBV curves recorded from two healthy subjects. The tracing illustrate periodic and aperiodic flow pattern.

the increased arterial blood pressure in these patients.

Following infusion of dextran 70 CBV at rest increased significantly (I). This may be attributed to hemodilution reducing the whole blood viscosity (*Dawidson* et al. 1980), increased cardiac output and reduced peripheral resistance secondary to plasma expansion (*Heilmann* and *Siekmann* 1983, *Schwartz* and *Retzke* 1982).

Vasomotion

In healthy subjects CBV at rest was not constant but fluctuated most often in a periodic manner at a frequency of 3-10 cycles per minute (Fig. 7) (II) as has also been reported earlier (*Fagrell* et al. 1980). In some subjects cessation of flow at irregular intervals («on-off flow») is seen (*Bollinger* and *Jäger* 1981). This periodicity is probably caused by spontaneous, rhythmic variations in the diameter of precapillary resistance vessels, so-called vasomotion (*Funk* and *Intaglietta* 1983). Vasomotion was first observed by *Jones* (1852) who described the rhythmic contractions of small veins in a bat wing. In several animal studies vasomotor activity was shown to be present in small arteries and arterioles of the skin, muscle, intestinal serosa and mesentery and several other tissues (*Funk* and *Intaglietta* 1983, *Schmidt-Schönbein* et al. 1981). The amplitudes of velocity fluctuations were positively correlated to CBV at rest (II). *Funk* et al. (1983) reported that vessels with periodic changes in diameter have lower resistance than vessels acting as rigid tubes with the same average diameter. Vascular resistance is gradually reduced by an increasing amplitude of periodic changes in vessel diameter. A pulsatile microcirculation therefore has a lower resistance than an inactive, non-pulsatile microcirculation (*Colantuoni* et al. 1984). Hence, skin microcirculation seems to be regulated not only by dilatation or constriction of precapillary resistance vessels but also by vasomotor activity (II). The stimulus trigging increased amplitude of vasomotor activity may be a progressive increase of intravascular pressure associated with dilatation of precapillary vessels (II). This is concordant with the hypothesis that vasomotion originates from groups of vascular smooth muscle cells with pacemaker properties which can be modulated by humoral, local metabolic, nervous and physical stimuli (e. g. intravascular pressure). *Fagrell* (1983) found that the pattern of velocity fluctuations differed even in adjacent nailfold capillaries indicating that structures responsible for vasomotion are located close to the arteriolar limb of the capillary. This is in accordance with the fact that two vessels with the same order of branching may have different frequency and amplitude of vasomotion (*Colantuoni* et al. 1984).

Due to vasomotion tissue perfusion, fluid exchange and peripheral resistance fluctuate continuously. Normal vasomotor activity is probably important for optimal fluid exchanges across the capillary wall (*Intaglietta* 1981). Velocity fluctuations were reduced in patients suffering from sympathetic dystrophies associated with cutaneous edema formation (III, IV). Reduced vasomotion has been reported in patients with epidemic meningitis (*Xiu* 1983). Improvement of clinical condition and absorption of edema were associated with the return of vasomotor activity. This indicates that vasomotion is an edema-reducing mechanism (*Xiu* 1983). Vasomotion was not reduced in preeclamptic patients or normal pregnancies (II) which suggests that other disturbances are responsible for the edema seen in these conditions.

2. Post-occlusive reactive hyperemia (PRH) (Fig. 8).

After release of the occluding cuff CBV increased abruptly beyond preocclusive values in controls, preeclamptic patients and women with normal pregnancies (I). CBV reached a maximum (pCBV) approximately 6-8 seconds after cuff release which is in concordance with other studies (*Fagrell* et al. 1977b). During arterial occlusion distal transmural pressure decreases and due to the «myogenic response» vessels will dilate (*Bayliss* 1902, *Folkow* 1964, *Patterson* 1956). Dilation is enchanced by accumulated metabolic substances produced during circulatory arrest (*Folkow* 1964, *Henriksen* and *Paaske* 1980, *Kilbom* and *Wennmalm* 1976).

Time to pCBV was rather constant regardless of skin temperature. The pCBV, however depends on the skin temperature of the area under investigation (*Fagrell* et al. 1977b, *Östergren* 1984). The lower the temperature prior to ischemia the higher the relative increase of pCBV. The PRH response was not disturbed in preeclamptic patients compared to women with normal pregnancies, and it did not change following infusion of dextran 70 (I). A normal PRH response does not exclude hemodynamic and rheological alterations. Increased blood pressure in preeclampsia may probably counteract an impaired PRH response. Abnormalities in the PRH response in skin capillaries have been found in patients with polycytemia, leukemia, diabetes mellitus and atherosclerotic occlusive disease (*Dintenfass* 1982, *Fagrell* et al. 1983, *Tooke* et al. 1985, *Östergren* and *Fagrell* 1985). The delayed time to pCBV in these conditions can be explained by an increased blood viscosity increasing vascular resistance. Additionally, a delay can be ascribed to increased vascular resistance subsequent to structural changes as seen in e.g. diabetes mellitus and atherosclerotic disease (*Tooke* et al. 1985).

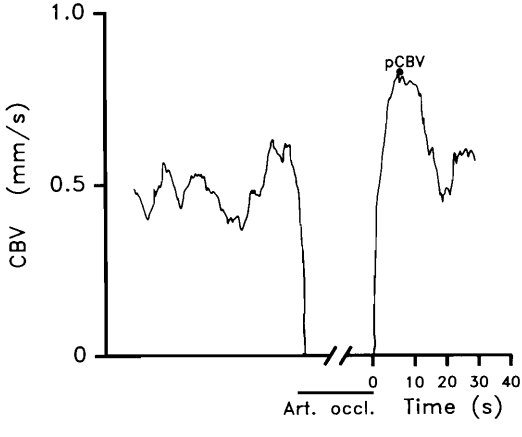

Fig. 8. CBV response to arterial occlusion (PRH) in a healthy subject. Peak CBV (pCBV) during reactive hyperemia is reached after approximately 7 seconds.

3. Response to venous occlusion (Fig. 9). CBV was reduced during venous occlusion in all subjects investigated (II, V). In controls the relative reduction in laser Doppler flux (LDF) response to lowering of the hand (III, IV) was almost similar to CBV decrement during venous occlusion (II). When the limb is lowered beyond a certain level, cutaneous blood flow decreases (*Henriksen* and *Paaske* 1980). A similar response occurs when the transmural pressure is increased 25 mmHg or more by application of an external subatmospheric pressure or venous stasis (*Henriksen* and *Paaske* 1980, *Henriksen* 1977). Decrease of CBV during venous occlusion is a consequence of reduced perfusion pressure across the capillaries due to several factors:

i) Increased venous pressure (*Östergren* et al. 1983).
ii) Activation of a local veno-arteriolar (VA) reflex mechanism elicited by increased transmural venous pressure (*Gaskell* and *Burton* 1953).
iii) An intrinsic myogenic constrictor response in precapillary vessels in response to increased transmural vascular pressure (*Folkow* 1964, *Henriksen* and *Sejersen* 1976).

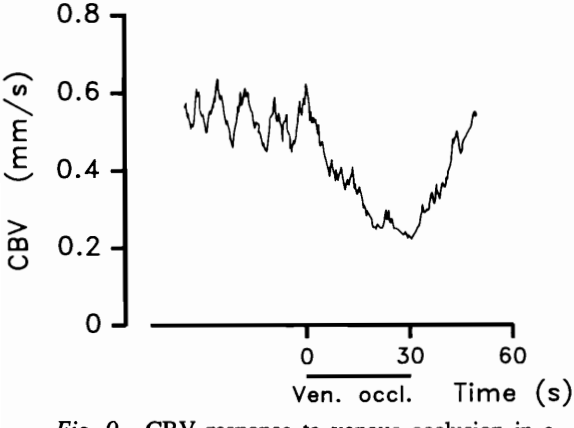

Fig. 9. CBV response to venous occlusion in a healthy subject.

The venous occlusion test was reproducible when performed with three minute intervals (II). Intra-individual differences are considered to be due to random methodological variations. The response to increased transmural venous pressure was impaired in both patients with preeclampsia (II) and symphathetic dystrophies (II, IV). Explanations for an impaired local vasoconstrictor response are numerous. Other studies have found the VA-reflex reduced or abolished probably due to arteriolar dysfunction as a consequence of e.g. accumulation of vasodilating metabolites in ischemic areas and media atrophy in low pressure regions distal to severe arterial stenosis (*Eickhoff* 1980, *Henriksen* 1974). Detrimental effect on the local neurons subserving the VA-reflex, e.g. the diabetic process, may impede the response (*Tooke* et al. 1985). Accumulation of local ischemic metabolites probably inhibits the vascular smooth muscle cells to respond to vasoconstrictor stimuli (*Henriksen* and *Wisborg* 1975, *Stranden* 1984).

One may also suspect vascular structural changes associated with diabetes mellitus and atherosclerotic disease to be accompanied by decreased vascular compliance which hampers the vasoconstrictor response. The mechanisms responsible for the decreased response to increased transmural venous pressure in preeclampsia and sympathetic dystrophies needs further elucidation. Since ischemia is not a clinical feature in these conditions the influence of vasodilator metabolites is hardly essential. It may be suggested that increased arterial blood pressure in preeclampsia counteracts the reduction in cutaneous blood perfusion normally seen following increased

transmural venous pressure. Affection of local sympathetic vasoconstrictor neurons, altered sensitivity of vascular smooth muscle cells to stretch, nervous vasoconstrictor stimuli and structural vascular changes may contribute to the impaired response found in both conditions.

Cutaneous edema in preeclampsia and sympathetic dystrophies may partly be explained by an impaired response to increased transmural vascular pressure. Normally a VA-reflex and an intrinsic myogenic response lead to constriction of precapillary resistance vessels (*Eickhoff* and *Engell* 1982, *Grande* 1979, *Mellander* and *Arvidsson* 1974). The capillary hydrostatic pressure (Pc) is influenced by changes in the ratio between pre- and postcapillary resistance (Ra/Rv). Arteriolar constriction induced by the local VA-reflex increases the Ra/Rv ratio and subsequently reduces Pc (*Henriksen* and *Paaske* 1980). Thus, an intact mechanism counteracts increased filtration of fluid across the capillary wall during increased transmural pressure (dependency, venous stasis) (*Henriksen* 1977, *Henriksen* and *Paaske* 1980).

4. Response to cooling of the contralateral hand (Fig. 10).

When the contralateral hand was immersed in cold water CBV decreased abruptly (III, IV). In some patients the CBV response pattern was similar to that observed during venous occlusion (Fig. 9), while in other patients intermittent cessations of flow were seen (Fig. 10). Skin vessels of the hand and foot are supplied with sympathetic vasoconstrictor nerve fibers (*Feigl* 1974, *Rowell* 1977, *Shepherd* 1984). Cutaneous blood flow is primarily adjusted by variation in sympathetic vasoconstrictor nerve discharge (*Shepherd* 1984). Cholinergic vasodilating nerves to skin blood vessels in the hand have not been found (*Feigl* 1974, *Shepherd* 1984).

During cold exposure cutaneous thermoreceptors are activated and afferent impulses increase the discharge in sympathetic vasoconstrictor fibers to precapillary vessels (*Henriksen* and *Paaske* 1980, *Shepherd* 1984, *Östergren* et al. 1982). Hence, CBV response to contralateral cooling is a test to assess the function of this reflex mechanism. CBV normally decreases abruptly approximately 30-60 % from basal value and maintains this new level during one minute of cooling (III, IV, *Östergren* et al. 1982). Response to cooling of the contralateral hand was bilaterally attenuated or abolished in patients with sympathetic dystrophies (IV). The blockade seems not to be located in the efferent, sympathetic vasoconstrictor nerves since there were signs (decreased CBV and LDF) of enchanced sympathetic nerve discharge in the dystrophic hand (III, IV). The lack of response could also be due to a lesion affecting the peripheral, afferent sensory pathway (*Kozin* et al. 1976). This explanation is hardly plausible since the

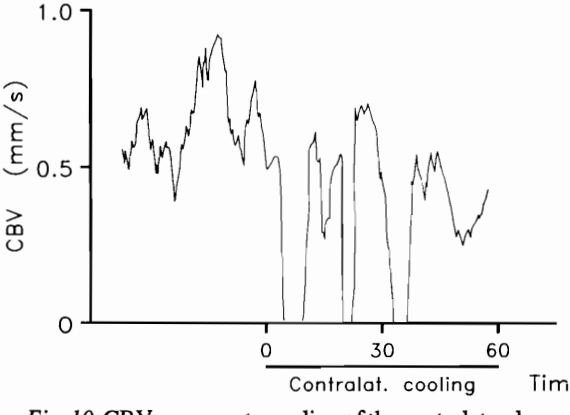

Fig. 10. CBV response to cooling of the contralateral hand in a healthy subject. CBV pattern shows an intermittent cessation of capillary flow (on-and-off flow) during the cooling procedure.

condition can be provoked by diseases such as cerebral apoplexy and cardiac infarction not primarily insulting the peripheral nervous system (*Rowlingson* 1983). Furthermore the patients revealed no overt signs of sensory disturbances (IV). In the chronic stage of the syndrome the effect of sympathetic blockade was absent or negligible. Only in the early stage sympathetic dystrophies can be successfully treated by different procedures for sympathetic nerve interruption (*Rowlingson* 1983).

In the chronic stage even spinal anesthesia fails to abolish pain (*Poplawski* 1983). These findings indicate involvement of the central nervous system in the late phase of the syndrome. It is suggested that an autonomic activity in e.g. hypothalamus or sensory cortex, perpetuates pain and the activity is not altered by input from cutaneous thermoreceptors during the cooling procedure. Consequently sympathetic nerve activity remains unchanged.

Bilateral lack of response to cooling may also be explained by an altered vasomotor reflex behavior. *Blumberg* and *Janig* (1983) found that following lesion of the cutaneous nerves in the cat hind limb the vasoconstrictor neurons were predominantly controlled from the medulla oblongata and not from the hypothalamus as prior to nerve lesion. An altered reflex mechanism could functionally distort or block input from cutaneous thermoreceptors.

CBV measurements performed by the CapiFlow system (V).

Correlations between CBV values obtained by the standard cross-correlator (IPM) system were exceedingly high (CBV at rest: r=0.96, CBV during venous occlusion: r=0.97 and CBV during post-occlusive reactive hyperemia (PRH): r=0.98). The CapiFlow system greatly facilitates measurements compared with the standard IPM system. All commands in the CapiFlow program can be controlled by a few keyboard keys and easily operated with minor technical skill.

Temporal correlation was used to measure CBV in this study (V). Spatial correlation technique does not tolerate minor movements of the capillary as opposed to temporal correlation. This ability makes temporal correlation more suitable for human studies, while spatial correlation can be employed in animal studies where the tissue under the objective can be kept completely immobilized. An advantage of the spatial correlation system is that very low or even retrograde CBV values can be measured.

SUMMARY AND CONCLUSIONS

Videophotometric capillaroscopy was employed to study skin capillary circulation of the finger in healthy subjects, patients with preeclampsia and with sympathetic dystrophies.

Preeclampsia (I, II).

CBV at rest and PRH response were not impaired despite increased peripheral vascular resistance and blood viscosity presumably present in these patients. Our findings therefore do not support the concept of a generalized hypoperfusion syndrome. CBV increased following intravenous administration of dextran 70 which can be due to an increased cardiac output, reduced peripheral vascular resistance and whole blood viscosity. CBV response to

venous occlusion was reduced in pre-eclampsia, and an impaired veno-arteriolar reflex mechanism may therefore contribute to the cutaneous edema formation in dependent regions. Vasomotion was not disturbed compared with non-pregnant women and normal pregnancies, and can be excluded as an edema promoting mechanism.

Sympathetic dystrophies (III, IV).
CBV at rest was decreased in the affected hand of this patient group. The enchanced CBV following sympathetic blockade indicates an increased sympathetic nerve discharge leading to constriction of precapillary resistance vessels. The lack of response to contralateral cooling in both the affected and asymptomatic hand may be a sign of bilateral involvement. This phenomenon may be attributed to disturbances in central nervous mechanisms which also prepetuate clinical features.

In healthy subjects the amplitude of CBV fluctuations, caused by vasomotion, increased with increasing CBV in the range of values measured. Periodic changes of diameters in precapillary vessels (vasomotion) influence flow resistance. Hence, capillary flow seems to be modulated by vasomotion. Optimal fluid exchange between capillaries and the interstitial space depends partly on normal vasomotor activity. Consequently, decreased vasomotor activity may contribute to reduced CBV at rest as seen in the dystrophic hand. Additionally decreased vasomotion in combination with impaired VA-reflex may promote the edema formation.

CapiFlow (V).
CBV was measured during basal condition, venous occlusion and post-occlusive reactive hyperemia. Values obtained by the new computer system (CapiFlow) and the standard cross-correlation technique were highly correlated. CapiFlow represents a refinement of the videodensitometric capillaroscopy technique yielding reliable results.

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