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Electronic Infrared Thermography as a Method of Assessing Herpes Labialis Infection

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The purpose of this study was to ascertain the applicability of infrared thermography to study the natural history of herpes labialis lesions. Since thermography is capable of detecting changes not visible to the naked eye, then it may be of value in complementing clinical examination of the various stages of herpes labialis. In addition, thermographic imaging is quantitative and therefore allows for an accurate assessment of temperature changes accompanying the disease process, both within patients and between patients.

Ten female patients suffering from herpes labialis were studied (mean age 25 ± 5 years). In all cases herpes simplex virus Type 1 was isolated by the HEP-2 technique. No treatment was instituted and patients were clinically assessed and thermographically imaged daily from the prodromal phase through to resolution. A marked temperature increase (1°C minimum) was observed within hours of the prodromal phase and maintained until day 4. As the lesions progressed to vesicle formation, the central area of the vesicle was noted to be cooler due to the insulating effect of the fluid. Even by day 6 a significant 0.5°C temperature increase over background was present at the involved site and this returned to normal within 8 to 10 days. The area of thermographic involvement was three to four times larger than the clinical area of involvement (60–100 mm^2 versus 20–25 mm^2).

To assess reproducibility, we also studied patients through two additional untreated herpes labialis episodes. The prodromal phase was reproducible thermographically and characterised by a temperature increase of 1.42°C ± 0.2°C. Thermographic imaging may represent a new approach to quantifying disease activity in herpes labialis, particularly in the subclinical prodromal stage.

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Body temperature has been used as diagnostic evidence of underlying pathophysiological changes throughout the development of medicine. Becquerel and Breschet were among the first to identify that the temperature of inflamed areas was higher than that of non-inflamed areas (1). This relationship between localised areas of hypo/hyperthermia and disease states has led to ongoing interest in the application of thermal measuring techniques to a variety of disease conditions (2–5). Due to technical developments, such as more sensitive detectors and image analysis systems, techniques such as infrared thermography have reached a very high standard of performance. Infrared thermography is defined as the recording of the temperature of a body by means of infrared radiation emitted by the surface of that body at wavelengths between 0.8 μm and 1 mm (6). The human body is an almost perfect emitter of infrared radiation, with maximal emission around 8–10 μm wavelengths. As homeotherms, humans continually generate heat; this heat production can be categorised as minimal, food inducible and regulatory, which relates to basal metabolism, A.T.P. breakdown with food conversion and enhanced muscular activity or non-shivering thermogenesis, respectively. This heat must be released to the surroundings so that the core temperature stability is maintained. The transfer of heat to the surroundings occurs via four different mechanisms, namely conduction which is the exchange of heat between adjacent spatially fixed particles, convection which is the transport of heat by moving particles namely blood and/or air currents, evaporation which employs heat transfer associated with the transition from the liquid to gaseous phase and finally radiation which is the radiant exchange of heat without a material heat carrier. Therefore in steady state conditions, the heat produced within the body and heat loss to the surroundings are in equilibrium. Within stable ambient conditions of 18–25°C, with no convective air currents or external radiation sources, the principal mechanism to achieve thermal equlibrium between a body and its environment is via radiation (7). However, it must always be noted that skin temperature is not constant and is affected by a number of variables including environmental conditions, skin vasculature, circadian rhythms, physical workload, metabolic state, drug effects and the individual's psychological state. These conditions must be eliminated or standardised before proceeding with any thermographic recording.

Our interest was therefore to assess the role of infrared thermography as a methodology for the quantification of the herpes labialis lesion. This condition is one of the most common viral infections to affect humans (8). The clinical stages of herpes labialis infection are well recognised as extending from a prodromal period lasting for a matter of hours to 1 to 2 days and terminating with the appearance of small vesicles, which develop at the mucocutaneous junction of the lips. The duration of this phase is variable per individual but normally after some 2 to 5 days the vesicles rupture and the lesions crust over. Complete resolution of the condition takes 7 to 14 days. Due to the location of the lesions, this disease is readily accessible for thermographic imaging.

The aim of this study was to assess the role of infrared thermography as a means of quantifying recrudescent herpetic lesions in terms of the heat emitted throughout the stages of untreated episodes of infection. The opportunity was also taken to assess the reproducibility of thermal radiance of two further untreated episodes.

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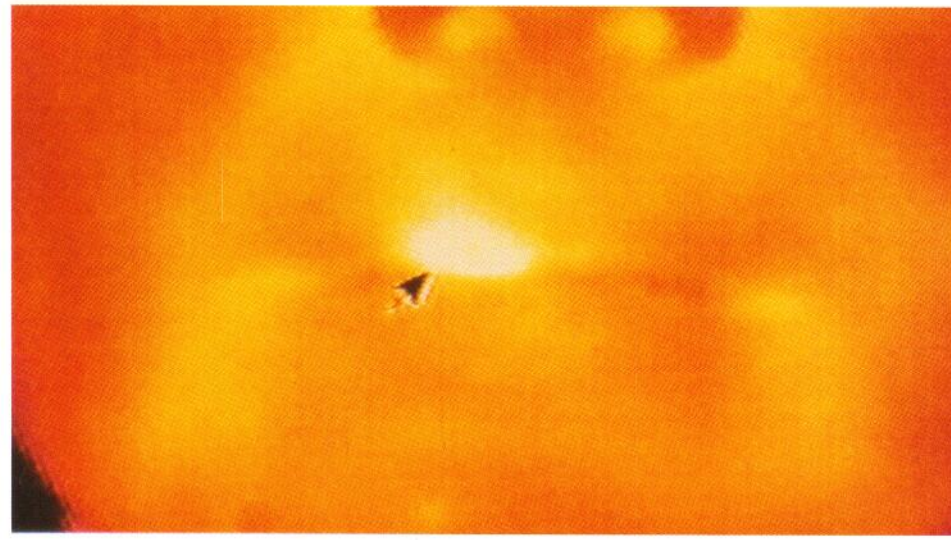


Fig. 1a. Facial thermogram of a subclinical developing prodromal herpes labialis lesion at a focal length of 0.5 m. The lesion site is right of centre on upper lip. The localised increase in temperature is seen as a lighter shade indicated by the cursor arrow.

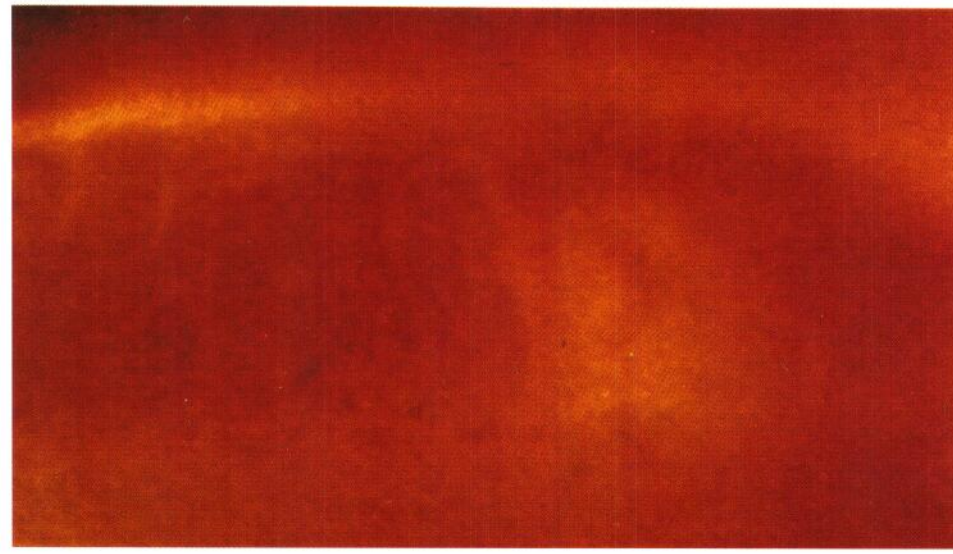


Fig. 1b. Thermogram of developing prodromal lesion site (< 1 h after patient recognition). The image is a close-up of the lesion using a macro lens set at a focal distance of 0.05 m. The position of the lesion is left of centre on the lower lip. The intense white, "hot", area to the right of the lesion on this image corresponds to the naturally warmer areas at the lip junctures; these are normal thermal patterns for these areas.

METHODS AND MATERIALS

The patients were all staff members of the Royal Victoria Hospital who suffered from recrudescent herpes labialis. All were requested to attend the School of Clinical Dentistry for enrolment in the trial. Ten patients were studied after giving informed consent. All were female, mean age 25 ± 5 years, and all underwent the same study protocol.

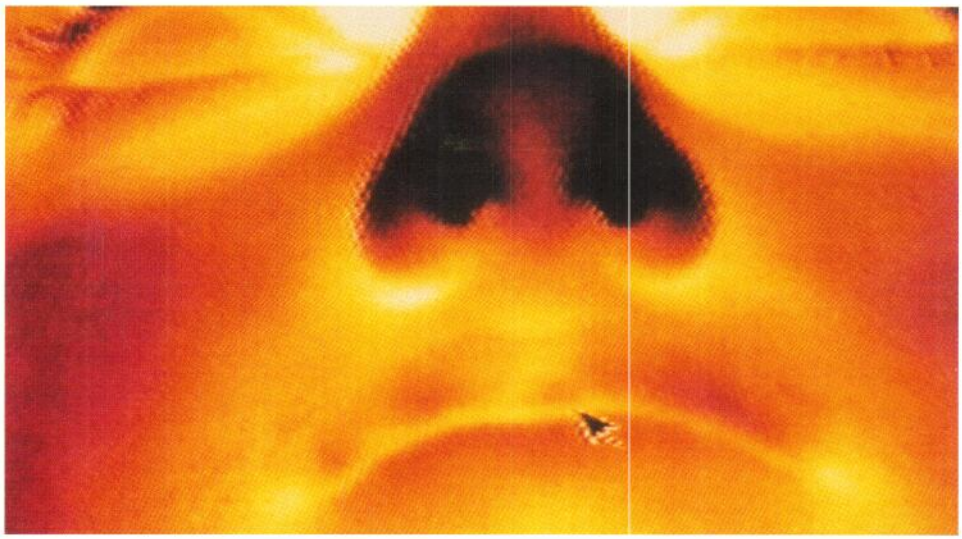
Each patient attended at the onset of the prodrome usually within 1 to 2 h. They were assessed by the clinician for (a) stage of lesion recorded as prodrome, vesicle or crust and (b) clinical area of lesion (mm^2). For each active episode swabs were taken from recently ruptured vesicles and placed in viral transport media. Virus isolation and culture were confirmed using the HEP-2 technique. The infrared thermographic imaging system used was the Agema 900 thermovision system (Agema Infrared Systems AB, Danderyd, Sweden). All patients were requested to refrain from eating, smoking and strenuous physical exercise before examination. Facial cosmetics were removed and lesions were not treated. On arrival patients were thermally stabilised in a room with a constant environment ($20°C \pm 1°C$) for 20 min. No radiation sources were present and air convection was minimised. Subsequent visits were requested to be at a similar time of day. For thermographic assessment two images were recorded and stored, one at a focal length of 0.5 m (Fig. 1a) and one at a focal length of 0.05 m (Fig. 1b). These thermograms were used for quantitative assessment. Several parameters were recorded using the system software: firstly the maximum temperature within the symptomatic region and secondly the background temperature, i.e. normal tissue temperature, and finally the thermally active area in mm^2. All patients underwent the same study protocol and were assessed daily until complete clinical and thermographic resolution. Each patient attended the clinic, for thermal assessment of their developing lesion, during the first 8 h of their next two subsequent prodromal stages. This allowed each patient's thermal variability between active episodes to be observed.

Statistics

Fisher's exact test was used for paired comparisons. p-values of < 0.05 were considered significant.

RESULTS

All patients successfully attended for clinical and thermographic assessment from prodromal stage to resolution. Viral culture was positive for herpes simplex Type 1 in all patients. In the prodromal phase there was an increase in temperature over the symptomatic area of $1.6°C \pm 0.5°C$, with the mean duration of the prodromal phase extending from 7.25 ± 3.4 h. Thermographically the prodromal phase is demonstrated in Fig. 1a and b. This temperature increase was maintained throughout the



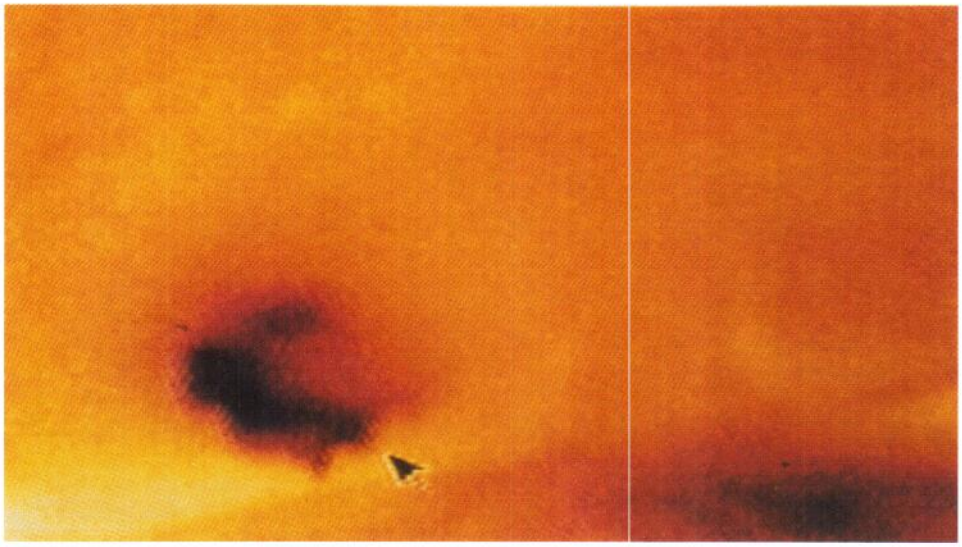


Fig. 1c. Thermogram of a vesicular herpes labialis lesion. The lesion is on the centre of the upper lip and can be seen as a "lighter", warmer area with a "darker", colder centre. This colder area is due to the fluid filled vesicles.
Fig. 1d. Thermogram of a herpes labialis lesion in the crusting stage. The crust, as indicated by the cursor arrow, is seen as a central darker area within an area of increased temperature.

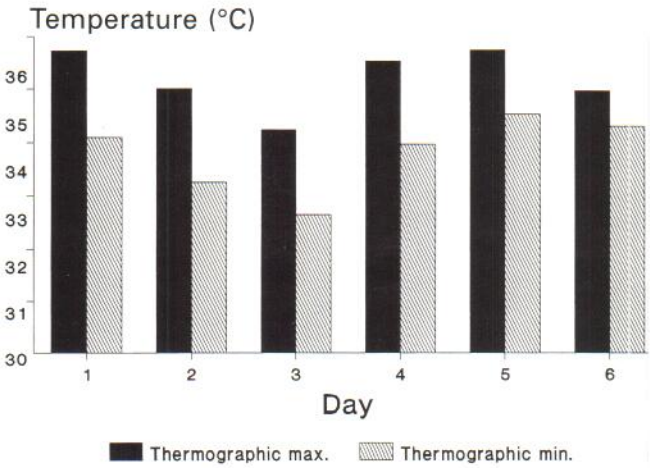


Fig. 2. Bar chart illustrating the mean maximum (active) and minimum (background) temperatures for the 10 patients' active episode of recurrent herpes labialis from day 1 through to day 6.

vesicle phase, the difference being that the central area of the vesicle became colder (Fig. 1c), presumably due to the insulating effect of the fluid. During crusting the central area became even colder due to separation of the surface epithelium (Fig. 1d).

The mean maximum and minimum temperatures for the 10 patients' active lesions from day 1 through to day 6 are shown in Fig. 2. These are the mean temperatures recorded within the active lesion areas. As the condition progresses through the

Table I. *Mean maximum and background temperatures for 10 patients over 6 days*

Day	Mean maximum temperature (°C)	Standard deviation	Mean background temperature (°C)	Standard deviation
1	35.72	1.12	34.1	0.86
2	35.00	1.68	33.2	1.70
3	34.20	1.67	32.6	1.62
4	35.57	0.66	34.0	0.67
5	35.73	0.76	34.5	0.50
6	34.95	0.21	34.3	1.00

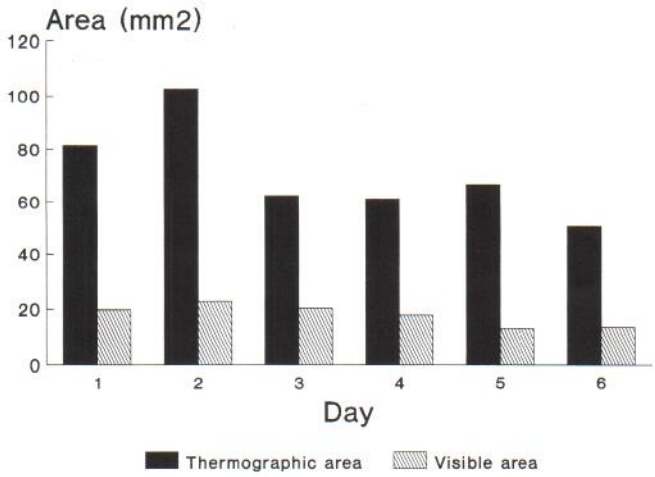


Fig. 3. Differences between the thermographically mean active areas (mm^2) and the observed mean clinical areas (mm^2) for the 10 patients from day 1 through to day 6.

different stages, the difference in temperature (ΔT°) is reduced, though even after day 6 a small ΔT° of approximately 0.5°C is still measurable. Throughout this period the lesions showed an increase in temperature above that of the surrounding skin. There was a reduction in the temperature through days 2 and 3; however, the differences (ΔT°) between maximum temperature and background were not reduced (Table I).

Following the vesicle phase, which had a mean duration of 2.3 days ± 1.2 days, the temperature differences (ΔT°) were decreased but still measurable at day 6. It normally took 8–10 days for the condition to be thermographically normal, with the mean crusting phase being 6.3 days ± 4.2 days. Our second measured parameter was the thermographically visible area of the lesion. The difference between the clinical area and thermographic area was termed ΔAmm^2. Fig. 3 illustrates the difference in measured areas, clinically and thermographically. Here large differences were seen between the two methods. Firstly, the thermographically active area is always far greater than that observed clinically, (especially during the prodromal phase). The clinically evident area is relatively constant, with a slight reduction towards days 5 and 6 as the crusting stage resolves. However, even at day 6 the thermographically active area is still approximately twice as large as the clinical area of the lesion.

Finally the reproducibility of thermal radiance between individual episodes of herpes labialis infection for the 10 patients was undertaken due to the variability in the data when considered with respect to inter-patient comparison. Fig. 4 illustrates the differences observed for the parameter of thermographic area as observed between subjects 3 and 5. These differences in area development, when studied collectively, may mask small but significant changes. Therefore patients returned for thermal assessment of the prodrome stage of their next two active episodes, the results of which are shown in Table II. All patients exhibited an increase in temperature for each episode. Each patient's mean temperature change for the three readings is shown; all were 1°C or more above background. However, the standard deviation about the mean illustrated a marked constancy per individual, with a maximum deviation of only 0.26 of a degree.

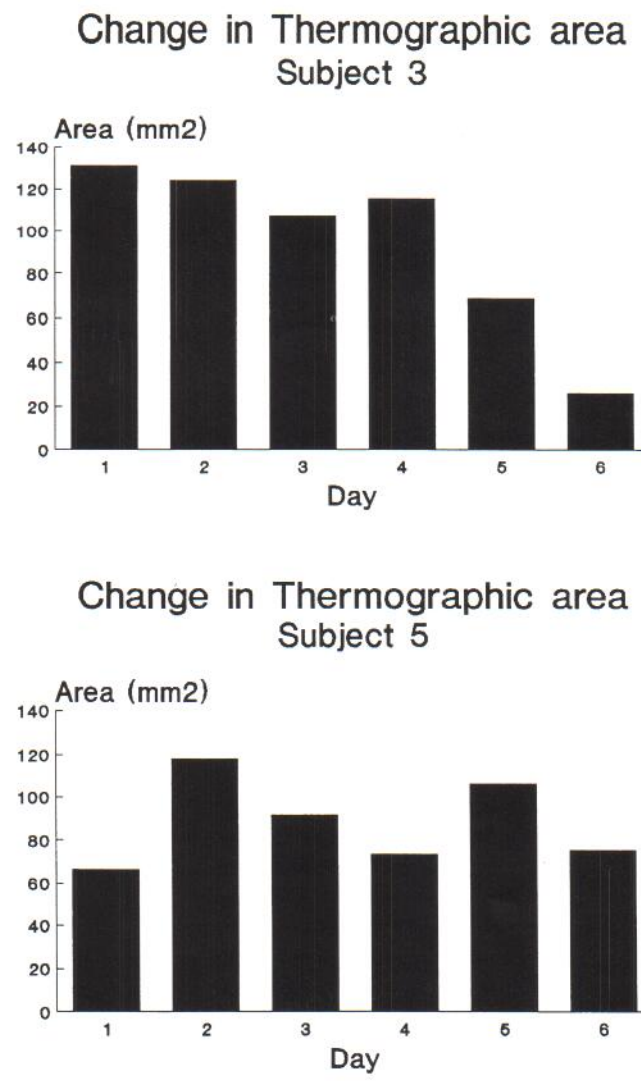


Fig. 4. Bar chart illustrating the differences in the thermographically active area between patient 3 and 5, demonstrating inter-patient variability of results.

Table II. *Mean localised temperature increase for 10 subjects over the prodromal stage of three active lesions*

Prodromal ΔT°C over 3 active episodes		
Patient No	$\bar{x}\Delta T°C$	±SD
1	1.63	0.20
2	1.40	0.20
3	1.70	0.14
4	1.30	0.14
5	1.40	0.26
6	1.37	0.20
7	1.15	0.07
8	1.50	0.20
9	1.70	0.15
10	1.10	0.10

DISCUSSION

The study of herpes labialis infection has previously been based on subjective clinical parameters such as reduction in pruritis and burning (9, 10). This thermographic study, which we believe is the first to be reported, has allowed us to quantify the herpetic lesion development in terms of the heat emitted and is associated with consistently increased temperature above background level. This point is illustrated in Fig. 2, showing the change in temperature for the 10 patients' active lesions from day 1 through to day 6. All 10 patients exhibited a localised increase in temperature on day 1, and collectively the mean $\Delta T°$ was $1.6°C \pm 0.15°C$. However, the timing of thermal assessment is important, since the evolving prodrome is a dynamic process resulting in an increase in temperature with time. Once vesicle formation begins, the cooler areas associated with this delineated active site will reduce the overall increase in $\Delta T°$. This means that any collective assessment must be time-matched, so that prodromal development is assessed at a similar stage. The reduction in temperature at the centre of the developing lesion from day 1 through to day 3 can probably be attributed to the development of the vesicle stage. Two factors may be involved: firstly, the fluid within the vesicles may have an insulatory effect on the heat irradiated; secondly, when the vesicles weep the evaporation of the fluid from the skin may cause a reduction in the temperature site (7). What should be emphasized is the reduction in the $\Delta T°$ between day 3 through to day 6. This gradual reduction signifies the reduction in the inflammatory response and hence indicates that the healing process is progressing. When considering the entire herpetic lesion, the thermographically active area was significantly greater than that observed clinically, but whether or not active virus was present throughout this area is unproven at the present time. Nevertheless from day 3 through to day 6 the difference between the clinical area seen and that observed thermographically (ΔAmm^2) was reduced throughout this time period in an analogous way to $\Delta T°$. However, this larger thermographically active area is obviously related to viral activity and may have implications for topical delivery of anti-viral agents. There is some inter-patient variability in the parameters measured, as can be seen in Fig. 4. To test the reproducibility of $\Delta T°$ and/or ΔAmm^2 each patient returned during two subsequent prodromal phases. Since all attended within 7 to 6 h of recognising the prodromal symptoms, then the time-matching problem was addressed. Thus Table II illustrates that such variations may be minimised, which would be an important consideration therapeutically. In this context identification and quantification of the subclinical prodromal phase is of paramount importance. Electronic thermography therefore offers a new non-invasive method of assessing herpes labialis lesions. Such a technique complements more traditional methods of studying herpes labialis, such as by virus isolation and culture.

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