Physiological measurement of Raynaud's phenomenon and peripheral microvascular disorders: from research into clinical practice

Friday 17th May 2002

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Medical Infrared Thermography

Saturday 18th May 2002

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FRIDAY 17TH MAY 2002

PHYSIOLOGICAL MEASUREMENT OF RAYNAUD'S PHENOMENON AND PERIPHERAL MICROVASCULAR DISORDERS: FROM RESEARCH INTO CLINICAL PRACTICE

8.50 - 9.15 Registration and coffee, Sheila Sherlock Centre common room

9.15 WELCOME

SESSION 1: THE CLINICAL PICTURE.

Chair: AJ MacGregor

9.20 **The microvasculature in Rheumatology**
AL Herrick

9.40 **The clinical presentation and natural history of Raynaud's phenomenon**
N Kumar

10.00 **The epidemiology of Raynaud's phenomenon**
AJ MacGregor

10.20 **Vibration white finger**
T Lees

10.40 - 10.55 Coffee and exhibitors: common room

SESSION 2: PROVOCATION STUDIES

Chair: K Ammer

10.55 **Thermal and mechanical provocation tests for Raynaud's phenomenon and Vibration White Finger**
EFJ Ring

11.15 **Primary, secondary Raynaud´s phenomenon and vibration induced white fingers: Are they all the same ?**
K Ammer

SESSION 3: THERMOGRAPHIC TECHNIQUES AND TEMPERATURE MEASUREMENT 1

Chair: EFJ Ring, JM Engel

11.35 **The 'distal-dorsal difference': a thermographic parameter by which to differentiate between primary and secondary Raynaud's phenomenon**
ME Anderson

11.55 **Mean relaxation velocity after cold challenge - a selective parameter for diagnosis in peripheral vascular diseases**
JM Engel

12.15 **Assessment of Raynaud's phenomenon with a hand held infra-red scanner**
JR Harding

12.35 **The use of portable radiometry to assess Raynaud's phenomenon: a practical alternative to thermal imaging.**
KJ Howel

12.55 – 1.45 Buffet lunch and exhibitors: common room

SESSION 4: THERMOGRAPHIC TECHNIQUES AND TEMPERATURE MEASUREMENT 2

Chair: EFJ Ring, JM Engel

1.45 **The use of thermographic criteria to identify Raynaud's phenomenon in a population setting**
L Cherkas

2.05 **Vibration disease - thermological proof of vibration induced vasospasm**
JM Engel

SESSION 5: OPTICAL TECHNIQUES 1

Chair: F Khan, N Harris

2.25 **Image analysis of nailfold capillary patterns from video sequences**
TL Moore

2.45 **Photoplethysmography as a tool for assessing the microcirculation**
J Allen

3.05 **Iontophoresis and factors affecting responses measured by laser Doppler**
R Gush

3.25 **Laser Doppler flowmetry in the assessment of Raynaud's phenomenon**
F Khan

3.45 – 4.00 Tea and exhibitors: Common room

SESSION 6: OPTICAL TECHNIQUES 2

Chair: F Khan, N Harris

4.00 **Comparison of microvascular blood flow changes in the fingertips of Raynaud's phenomenon patients and normal subjccts following cold challenge**
MD Aldridge

4.20 **A laser Doppler imaging protocol for patients with connective tissue disease**
N Harris

4.40 **Variable wavelength laser Doppler imaging (LDI) in Raynaud's phenomenon (RP) – A new technique by which to study microvascular pathophysiology**
ME Anderson

SESSION 7: CLINICAL TRIALS

Chair: AL Herrick

5.00 **Topical application of a novel nitric oxide generating system in patients with severe Raynaud's syndrome**
A Tucker

5.20 SESSION 8: OPEN FORUM DISCUSSION

Standardisation of measurement protocols for study of the peripheral microcirculation

Chair: EFJ Ring, N Harris

5.40 CLOSE OF MEETING

THE CLINICAL PRESENTATION AND NATURAL HISTORY OF RAYNAUD'S PHENOMENON

N Kumar

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Raynaud's Phenomenon is a common condition that affects around 5% of the population. Patients may consult their General Practitioners, Rheumatologists or even Vascular Surgeons for help and advice. Of particular interest to Rheumatologists is the association of Raynaud's with the autoimmune rheumatic diseases.

This brief session will look at the clinical presentation and natural history of Raynaud's Phenomenon. Associated conditions will be outlined with potential hazards if unrecognised by the clinician. Finally an overview of treatments available will be given.

THE EPIDEMIOLOGY OF RAYNAUD'S PHENOMENON

AJ MacGregor

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Raynaud's phenomenon (RP) has a worldwide distribution. However, problems of definition and classification present a major challenge to accurately characterising its occurrence. Estimates of prevalence vary widely, ranging between 1 and 15%. Most studies show a consistent female excess. Although the prevalence of RP is reported to be higher in colder climates, temperature variation does not fully explain the observed geographical variation, and other risk factors are implicated. Genetic variation has an important contribution to susceptibility, as evidenced by an increased recurrence risk among relatives of affected cases and by concordance studies in twins which have indicated a heritability for the disease of around 50%. A range of constitutional and environmental risk factors have also been associated with the disease including body mass index, the presence of underlying cardiovascular diseases, and alcohol consumption. These effects may be modified by sex. RP is a common manifestation of a range of inflammatory and non-inflammatory diseases and can result from mechanical stresses (such as those caused by pneumatic equipment) and from the use of drugs. The proportion of subjects presenting with RP in isolation who progress to develop systemic disease is small and has been estimated to be as low as 0.2% per year. The risk of autoimmune disease rises in the presence of antinuclear antibodies and in those with nailfold capillary changes. RP itself may be a specific manifestation of a more widespread vasospastic process that includes migraine, atypical angina and pulmonary hypertension.

VIBRATION WHITE FINGER

T Lees

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Vibration white finger is a common clinical condition amongst manual workers who are exposed to the use of hand held vibrating tools. It is a prescribed disease within the Social Security Regulations (1985) and workers with the condition may claim disability payments from the Department of Social Security or may pursue litigation against their employers.

There are three components to the condition of vibration white finger, (or more accurately named as hand-arm vibration syndrome). These are vascular, neurological and musculo-skeletal, with the commonest symptoms being intermittent finger blanching due to vasospasm, tingling and numbness of the fingers and loss of manipulative dexterity.

The diagnosis of this condition is difficult and is based largely on patient history and examination. There are two common scales of disability used to grade patients with this condition and these are the Taylor Pelmear Scale and the Stockholm Workshop scale. The differential diagnosis includes primary Raynaud's disease, carpal tunnel syndrome, other neurological conditions e.g. diabetic neuropathy, and cervical spondylosis.

Many neurological and vascular tests exist that have the potential to aid the diagnosis of this condition but many of these require the subjective response of the patient and have a low sensitivity and specificity. Tests include thermal aesthesiometry, vibrotactile threshold, cold provocation, and the Purdue Peg Board Test. The use and benefits of these investigations remain controversial although more data relating to their use may soon be available from the widescale testing of miners currently claiming compensation.

THERMAL AND MECHANICAL PROVOCATION TESTS FOR RAYNAUD'S PHENOMENON AND VIBRATION WHITE FINGER

EFJ Ring

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Provocation tests to induce a thermal challenge to the extremities have been developed by a number of investigators who require an objective assessment of the response to a thermal stress. Skin temperature can be monitored by contact and non contact methods. Thermocouples fixed to the skin have been used to monitor fingertip temperature. Infrared thermal imaging or infrared radiometry allows the skin temperature to be measured without contact. This is efficient as the skin is a highly efficient black-body radiator.

All thermal detection techniques require the subject to be stabilized in a temperature controlled environment. The imaging technique has advantages in the speed by which the temperature distribution can be captured. It also provides possibilities for dynamic recording of thermal reactions as most modern systems operate at video rate – 50 frames per second or higher [1]. Modern thermal imaging systems can give temperature resolution up to 0.01°C, with spatial resolution resolving 1mm spot target at 0.5 meter.

Most investigators use similar techniques and agree on the need for standardization and equilibration of the patient prior to a thermal provocation test. After a baseline thermal image, thermal challenge usually involves immersing the hands (and feet in some cases) in water at a fixed temperature for a fixed time period. A mild challenge, water at 20°C for 1 minute is favoured by a number of centres in Rheumatology, especially with connective tissue diseases. The recovery is monitored in a reasonably short time (10-20 minutes).

In Vibration White Finger, a thermal stress is part of an accepted protocol where immersion of the hands for 5 minutes in water at 15°C has been shown to lower digital systolic pressure by 40% [2]. In the author's experience, it has been possible to show a reduction in thermal recovery in affected fingers after a mild stress at 20°C in a few cases. However, exposing the fingertips to a vibrating surface has yielded more dramatic effects, which can be monitored by infrared thermal imaging. More work is required to examine the range of frequencies and duration of experimental exposure before the systematic establishment of a normal range of responses, which could be used as part of a screening or test procedure for clinical studies.

References

1. Ring EFJ Thermal Imaging of Skin Temperature. in Non-Invasive methods and the skin, (Serup, Jemec eds) Chapter 18, 457-471 CRC London

2.Noel B Pathophysiology and Classification of the Vibration White Finger- Int Occup Environ Health 2000 73:150-155

PRIMARY, SECONDARY RAYNAUD´S PHENOMENON AND VIBRATION INDUCED WHITE FINGERS: ARE THEY ALL THE SAME ?

K.Ammer

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The diagnosis of Raynaud´s phenomenon is based on episodic triphasic changes of skin colour, mostly provoked by coldness. Decreased temperature of the fingers and the poor ability to cope with a cold environment have become a surrogate sign for vaso-spastic disease. However, subjects showing skin changes and those with low finger temperatures may be two different entities, with a large overlap of symptoms. This becomes obvious from the fact that sufferers from primary Raynaud´s disease often present with a normal reaction to a mild cold water challenge.

The hand-arm vibration syndrome is an accepted disorder in industrial and occupational medicine. Such a diagnosis entitles the sufferer to claim compensation in most European countries and in the USA. Work exposure to vibrating tools may affect the peripheral nerves and the vascular tone. In contrast to the typical sequence of colour changes from white, through blue, to red in Raynaud´s phenomenon, only blanching of the fingers is required to establish vibration induced vasospastic disease. Symptoms of nervous involvement such as tingling or numbness may appear together or precede the vascular signs of the disease. The interaction between nerve damage and vasospasm is still under debate.

Thermal images of typical cases classified as primary, secondary Raynaud´s phenomenon and of vibration induced white fingers will be presented. The coincidence of changes of skin colour and the occurrence of diagnostic thermal gradients of the fingers will be discussed.

THE 'DISTAL-DORSAL DIFFERENCE': A THERMOGRAPHIC PARAMETER BY WHICH TO DIFFERENTIATE BETWEEN PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON

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2 Arthritis Research Campaign Epidemiology Unit, University of Manchester Medical School, Manchester, Ml3 9PT.

*Aim*To evaluate a) all parameters measured during thermographic testing of patients with Raynaud's phenomenon, and b) the hypothesis (suggested from a pilot study from our group), that a temperature difference of >1°C (fingers cooler than dorsum) between fingertips and dorsum of the same hand (distal-dorsal difference or DDD) at 30°C room temperature suggests underlying structural vascular disease. The latter may help to differentiate between primary RP (PRP) and RP secondary to systemic sclerosis (SSc).

Patients and Methods:We carried out a retrospective analysis of case notes and thermography results of patients who had attended our vascular laboratory for standard thermographic testing of the hands (imaging at 23°C and 30°C room temperatures, plus cold challenge).

Results

	SSc	PRP	Total
DDD>1^0C at 30^0C (1 or more digits)	31	8	39
DDD£ 1^0C at 30^0C (all digits)	14	48	62
Total	45	56	101

A DDD>1°C at 30°C has 86% specificity and 69% sensitivity in identifying the patient with RP secondary to SSc. On logistic regression (age /sex/ smoking adjusted), individual DDD (at 23 and 30°C) and rewarming curve parameters were significantly different for the PRP and SSc groups. Combined logistic regression of all DDD and rewarming curve variables plus age yielded
a) older age,
b) DDD>1°C at 30°C and
c) smaller maximum rewarming curve gradient.

Conclusions: A DDD>1°C°at 30°C is reasonably specific for underlying structural vascular disease and, in combination with older age of patient, may complement other investigations in alerting the clinician to an increased likelihood of underlying connective tissue disease.

ASSESSMENT OF RAYNAUD'S PHENOMENON WITH A HAND HELD INFRA-RED SCANNER

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Raynaud's phenomenon is an intermittent abnormal spasm of the peripheral arterioles of the limbs after exposure to cold or emotional stimuli, resulting in painful or cold digits and clumsiness. Will et al demonstrated in 1992 that average finger to wrist temperature indices of minus 4 or greater acquired from an infra-red radiometric camera are indicative of Raynaud's phenomenon. Infra-red cameras and their inherent hardware and software can be expensive and inconvenient for use in the Outpatient Clinic or General Practitioner setting.

The aim of this study was to compare the temperature index obtained with a thermal imaging camera with that obtained using a hand held infra-red temperature scanner.

20 patients with suspected Raynaud's phenomenon undergoing thermological examination in a specialist clinic using an infra-red camera (Agema Thermovision 782) were also assessed using a hand held infra-red temperature scanner (Exergen Dermatemp). A temperature index was calculated for each hand using measurements before and 10 minutes after a cold challenge (immersion of gloved hands in water at 20 degrees C for 1 minute), using the average temperature of the fingers minus the wrists for the thermal image and the average of 12 finger minus 8 wrist temperature measurements taken with the infra-red scanner.

12 out of the 20 patients assessed by the infra-red camera and by the hand held infra-red temperature scanner demonstrated index values of minus 4 or greater indicating Raynaud's phenomenon. The hand held infra-red scanner gave a comparable result to the 'Gold Standard' of assessment with the infra-red camera. This could allow the use of hand held infra-red temperature scanners in Outpatient Clinic or General Practitioner settings, providing appropriate staff training is given, and a suitable environment is available for thermal assessment.

THE USE OF Pthursday15ORTABLE RADIOMETRY TO ASSESS RAYNAUD'S PHENOMENON: A PRACTICAL ALTERNATIVE TO THERMAL IMAGING.

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*Department of Rheumatology, Royal Free Hospital, Pond Street, London NW3 2QG UK

Obectives: To compare the performance of a portable radiometer with thermal imaging and to assess the potential for radiometry to provide a practical alternative for assessing vascular responsiveness in Raynaud's Phenomenon.

Methods: Subjects comprised 18 patients with diagnosed Raynaud's Phenomenon (RP) and 19 non-RP subjects. A thermal imager (Starsight) and a portable radiometer (Cyclops) measured digital temperature at baseline and the subsequent drop and rise in temperature following a cold challenge test.

Results: The intra-class correlations between the two instruments for all three measures exceeded 80%. The overall performance of each instrument was almost the same, with the Starsight thermal imager correctly classifying 84% of subjects as RP or non-RP and the Cyclops portable radiometer correctly classifying 86% of subjects. The sensitivity of the thermal imager was 83%, compared with 89% sensitivity for the portable radiometer, with the specificity of both instruments 84%. The positive and negative predictive values of the thermal imager were 83% and 84% respectively; the comparative values for the portable radiometer being 84% and 89%.

Conclusions: Both instruments performed equally well and the differences between them in their absolute measurements did not influence their ability to detect RP. Portable radiometry provides a practical, cheap, accurate and reliable alternative to thermal imaging and has the potential to be applied to a range of clinical and epidemiological settings.

THE USE OF THERMOGRAPHIC CRITERIA TO IDENTIFY RAYNAUD'S PHENOMENON IN A POPULATION SETTING

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Obective: To assess the value of thermographic measurements of digital skin temperature after cold challenge in classifying subjects with Raynaud's Phenomenon (RP) in subjects ascertained from a population setting.

Methods: 175 subjects with RP (reporting a history of two or more colour changes including white on exposure to cold) and 404 normal subjects were subjected to a 60-second cold challenge test, with water at 15°C. Digital temperature measurements were taken at baseline, immediately post-immersion and 10 minutes after immersion using a portable radiometer.

Results: The average temperature of the fingers of RP subjects at baseline was significantly lower than that of normal subjects (28.30 ± 0.26°C v 29.97 ± 0.15°C, $p<.01$: t-test). Baseline skin temperature was a significant predictor of RP; however, the fall in temperature on immersion and the subsequent rewarming rate provided no additional information. Only 4% of normal subjects had baseline digital temperatures below 24°C. The majority of subjects reporting symptoms of RP did not have particularly cold hands.

Conclusion: Baseline skin temperature can predict the occurrence of RP in subjects drawn from the general population. The cold challenge test itself is of limited additional value for classification. Although objective temperature measurements show little power overall to discriminate between RP and non-RP subjects, detecting low baseline digital temperature may be a useful adjunct to clinical history in classifying the disease

IMAGE ANALYSIS OF NAILFOLD CAPILLARY PATTERNS FROM VIDEO SEQUENCES

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Video capillary microscopy is a valuable tool in the assessment of Raynaud's phenomenon (RP) and systemic sclerosis (SSc). Previous work relied on storage of the output from a video microscope onto VHS videotape and digitizing a single video frame for analysis. The major drawback to this approach is that the capillary walls are transparent with only red blood cells visible; therefore, plasma filled gaps can render the capillaries incomplete at any one instant. A method of integrating information from a number of sequential video frames was developed, based on linear feature detection to register adjacent overlapping nail fold images and build up a composite mosaic image of the capillary network. Capillary dimensions were measured made using electronic calipers.

The new technique provides improved images for qualitative analysis and allows measurement of dimensions in a given individual over time. We are currently assessing the sensitivity and reproducibility of our technique. Results from intra and inter observer variability studies will be presented.

PHOTOPLETHYSMOGRAPHY AS A TOOL FOR ASSESSING THE MICROCIRCULATION

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The optical technique of photoplethysmography (PPG) has been used for many decades to assess a variety of cardiovascular parameters including tissue oxygenation, heart rate, vasomotor function, regional pulsatility and vessel compliance. PPG has several strengths and allows the simple, non-invasive, and low cost measurement of changes in microvascular blood volume with each heart beat. The technique still tends to be employed as a research tool partly because the waveforms obtained can be difficult to describe, and that the interaction processes of near-infrared radiation with tissue are not fully understood. However, the potential information content of the waveforms, the recent improvements in opto-electronic technology, and advancements in computer analysis techniques currently make PPG an accepted tool in the vascular measurement environment. The PPG technique can be used to study waveforms from single or multiple measurement sites simultaneously. For example, good quality pulse waveforms can be obtained from the ear lobes, and the tissue pulps of the fingers and toes. The catchment volume of PPG probes can provide information relating to both the 'nutritional' and 'thermoregulatory' components of the microcirculation. The characteristics of PPG waveforms have been shown by the authors to be body site specific. In healthy subjects the features of bilateral (right and left) similarity and segmental differences (head to foot) are the usual presentation. These features are evident for short term beat-to-beat changes in pulse and also over much longer periods of many minutes - the low frequency 'vasomotor' information contained in the latter is of particular interest in the study of the microcirculation. The authors will also describe the application of the PPG technique both for single site and multi-site assessments. Examples will be given of the measurement

and analysis of PPG pulses for the study of spontaneous and deep inspiratory gasp-induced vaso- constrictor waves, determining the relationships between skin temperature and PPG pulse following a *mild* cold challenge, quantifying bilateral changes in pulse during reactive hyperaemia, and studying multi-site pulse changes with age and in patients with vascular diseases. These examples will consider the methodology of data collection and subsequent PPG pulse analysis. The need for well-considered microvascular measurement protocols will also be highlighted.

IONTOPHORESIS AND FACTORS AFFECTING RESPONSES MEASURED BY LASER DOPPLER

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Iontophoresis is a low voltage, non-invasive technique to overcome the epidermal barrier to get drugs into the skin quickly. The dose of drug iontophoresed depends on the drug, the electric current and the duration. It provides relatively high local concentrations of drug without systemic effect: e.g. 50 microAmps for 20 seconds delivers less than 2 micrograms of acetylcholine (ACh).

Laser Doppler (LD) monitoring or imaging is used to assess the microvascular responses of skin to drugs iontophoresed, often measured through the solution. Many LD/iontophoresis protocols have been described: multi-period protocols enable cumulative dose response curves to be observed over a range of currents and durations (standard protocols have yet to be defined). Routine uses include assessment of endothelial function with ACh and smooth muscle function with sodium nitroprusside. The technique avoids vasodilation due to local trauma, as caused by injection, but the rate of iontophoresis should be limited to avoid the 'galvanic' effect: a non-specific response, recently shown to be related to applied voltage.

Reproducibility of LD measurements during iontophoresis depends on the equipment used and the protocol followed: COV between 6% (MoorLDI) and 40% (2-fibre probe) have been reported.

In addition to direct measurement (at the site of drug delivery) measurements can be made at adjacent sites to assess axon reflex flare: e.g. to assess peripheral autonomic neuropathy.

Examples of recent applications of LD/iontophoresis will be reviewed.

LASER DOPPLER FLOWMETRY IN THE ASSESSMENT OF RAYNAUD'S PHENOMENON

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A widely used technique for measuring skin microvascular blood flow non-invasively is laser Doppler flowmetry (LDF). The aim of this presentation will be to review the applications of LDF in Raynaud's phenomenon.

The use of single-point LDF to examine skin microvascular function in patients with Raynaud's phenomenon has been used largely for research purposes. Experimental protocols and patient groups have differed in the various studies but nevertheless, the general findings have shown reduced skin perfusion in patients compared with control subjects. The use of scanning laser Doppler imaging has confirmed abnormalities of the skin microvasculature in patients with primary Raynaud's disease and secondary Raynaud's syndrome. However, it has not been possible to distinguish between patients with primary Raynaud's disease and secondary Raynaud's syndrome using either of these techniques because of the large overlap in measurements between groups. Other studies using laser Doppler imaging have shown that rheological factors might be implicated in abnormal cold reactivity.

With respect to endothelial dysfunction and nitric oxide activity, abnormal vascular responses have been reported to both acetylcholine (endothelium-dependent vasodilator) and sodium nitroprusside (endothelium-independent vasodilator) in the digits of patients with Raynaud's phenomenon. One proposed mechanisms for these abnormal responses is increased oxidative stress, which has been known to attenuate nitric oxide activity. Abnormalities in endothelial function and nitric oxide activity have not, however, been a consistent finding, which might reflect the site (e.g. finger v forearm) at which assessment are made in different studies.

While LDF is a very useful instrument for investigating the underlying mechanisms of Raynaud's phenomenon, it still needs to be established whether it has real utility for clinical evaluation.

COMPARISON OF MICROVASCULAR BLOOD FLOW CHANGES IN THE FINGERTIPS OF RAYNAUD'S PHENOMENON PATIENTS AND NORMAL SUBJECTS FOLLOWING COLD CHALLENGE.

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[1] Department of Rheumatology, Royal Free Hospital, London
[2]Regional Medical Physics Department, Freeman Hospital , Newcastle upon Tyne

This study establishes the normal laser-Doppler (LDF) response to cold challenge of the hands, and compares it to that of Raynaud's phenomenon patients.

25 Raynaud's phenomenon patients and 25 sex-matched control subjects have so far been analysed.

After a period of acclimatisation, laser Doppler probes were attached to the pulp of the middle finger of each hand, and each subject was monitored

for five minutes to establish a baseline flux. The subject then immersed both hands in a waterbath at a temperature of 15±1°C for one minute, keeping the laser-Doppler probes in place. The flux was then measured for ten minutes post cold challenge.

To date, analysis has been undertaken on LDF measurements recorded at baseline, one minute and 5 minutes post cold challenge. There was found to be no significant difference in baseline flux between Raynaud's patients and normal subjects. Significant differences in flux were found between Raynaud's and normal subjects at one minute ($P<0.01$) and five minutes ($P<0.05$) post cold challenge. Although differences in erythrocyte speed were not observed at any of these time points, significant differences in cell concentration ($P<0.01$ at all 3 time points) were found.

Flux is the product of red cell concentration and speed. This preliminary analysis suggests that differences in flux levels observed between Raynaud's patients and control subjects arise predominantly from differences between the two groups in red cell concentration. Laser-Doppler concentration may therefore be a more effective measure for discriminating Raynaud's subjects from normals than either the flux or speed signals.

A LASER DOPPLER IMAGING PROTOCOL FOR PATIENTS WITH CONNECTIVE TISSUE DISEASE

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Primary Raynaud's phenomenon (PRP) is a condition characterised by reversible episodes of ischaemia, but normal maximum (hyperaemic) blood flow. In contrast, Raynaud's phenomenon secondary to systemic sclerosis (SSc) is associated with irreversible structural changes within the vasculature, abnormal vascular regulatory responses and reduced maximum blood flow. Early detection of vascular changes is an essential element of the diagnosis of these patients and Laser Doppler flowmetry, combined with cold challenge or vasoactive agents, has proved to be a particularly sensitive tool for studies of the vascular dynamics.
We have carried out a review of papers on Medline from 1990, using the terms 'systemic sclerosis and blood flow'. There are more than 20 studies, but there is no consensus as to whether it is possible to discriminate between PRP and SSc using laser Doppler measurements. This is due to differences in the test protocols, small numbers of patients and variations in the type of disease and duration. If we are to make progress with the diagnosis and management of these conditions, there is a clear need for agreed test protocols so that multicentre studies can be carried out. We have developed 4 simple tests based on; cold challenge, vasodilator response to acetylcholine iontophoresis, maximum hyperaemic response and contralateral vasoconstrictor response. The protocol, together with some preliminary results will be presented.

VARIABLE WAVELENGTH LASER DOPPLER IMAGING (LDI) IN RAYNAUD'S PHENOMENON (RP) – A NEW TECHNIQUE BY WHICH TO STUDY MICROVASCULAR PATHOPHYSIOLOGY

ME Anderson[1], TL Moore[1], T King[2], AL Herrick[1]

University of Manchester: [1]Rheumatic Diseases Centre, Hope Hospital, Salford, M6 8HD. UK,
[2] Department of Laser Physics and Astronomy.

Background Different wavelengths of laser potentially allow study of different levels of the microvasculature. Our aim was to use this newly developed research tool to study primary and secondary RP.

Methods We scanned the right hand (dorsum) of 15 control subjects, 15 primary RP (PRP), 10 undifferentiated connective tissue disease (UCTD) and 21 systemic sclerosis (SSc) patients, with standard red (633nm) and specially developed green (532nm) LDI, at baseline (after acclimatisation at 23°C) and after local heating.

Results On both green and red LDI, in comparison to controls, greater flux increases in response to heating were found in UCTD (green $p=0.041$, red $p=0.004$) and SSc (green $p=0.002$, red $p=0.007$) groups, whilst the UCTD group also had lower flux at baseline (green $p=0.048$, red $p=0.001$). On green LDI, greater flux response of the dorsum of the hand in response to heating was found in PRP patients compared to controls ($p=0.015$). [Mann Whitney U]

Conclusions Abnormalities of microvascular flow exist at different levels of the skin in both UCTD and SSc, as greater flux increase in response to heating with both red and green LDI implies relative resting peripheral vasoconstriction of the dermal microcirculation. Green LDI suggests minor abnormalities in resting vascular tone cause decreased flow in the superficial dermal capillaries in patients with PRP. Variable wavelength LDI is an exciting tool for study of microvascular pathophysiology and warrants further investigation.

TOPICAL APPLICATION OF A NOVEL NITRIC OXIDE GENERATING SYSTEM IN PATIENTS WITH SEVERE RAYNAUD'S SYNDROME

A Tucker [1,2], Pearson R [2], Benjamin N[2]

The Ernest D. Cooke Clinical Microvascular Unit [1], St. Bartholomew's Hospital, Department of Clinical Pharmacology [2], William Harvey Research Institute, Bart's & The Royal London School of Medicine and Dentistry.

Aims. The aim of this study was to determine the effect of a topical nitric oxide (NO) generating system on the skin microcirculatory blood flow of the

forearm and fingers of patients with severe primary Raynaud's Syndrome (RS).

Methods. The effect of topical application of NO-generating gel was measured in 20 RS patients and 10 healthy subjects. The NO-generating system was prepared by mixing two solutions. The first KY jelly and sodium nitrite (5% w/w) and the second KY jelly and ascorbic acid (5% w/w). 0.5 ml of each solution was applied and mixed on the skin of the forearms and the finger pulps. The changes in skin microcirculatory volume were measured simultaneously by infra-red photoplethysmography and microcirculatory velocity by laser Doppler fluxmetry against placebo treatment.

Results. Forearm skin blood flow increased markedly following topical application of a NO-generating gel in both healthy volunteers ($p<0.01$) and RS patients ($p<0.001$). Application of NO-generating gel resulted in an increase in the finger pulp microcirculatory velocity in RS patients ($p<0.01$) and the healthy subjects ($p<0.01$), which was sustained after gel removal in the RS patients ($p<0.05$).

Conclusion. This study suggests that although micro-cir culatory function is impaired in primary Raynaud's syndrome, topical application of a NO-generating system is able to restore blood flow to that seen in healthy subjects at rest.