A critique of a UK standardized test of finger rewarming after cold provocation in the diagnosis and staging of hand–arm vibration syndrome

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Background
Accurate diagnosis and staging of hand–arm vibration syndrome (HAVS) is important in health surveillance of vibration-exposed workers and the substantial number of related medico-legal cases. The measurement of the rewarming rate of fingers after cold provocation to the hands (CPT) has been suggested as a useful test in diagnosing HAVS.

Aim
To investigate the diagnostic value of a standardized version of the CPT test using a 15°C cold challenge for 5 min applied in the recent compensation assessment of UK miners.

Methods
Analysis of a subset of UK miners assessed at our unit, together with data from a small repeatability study of the standardized CPT in normal subjects.

Results
Rewarming time in the CPT was significantly lower in those subjects classified as vascular Stockholm stage 0 compared with Stockholm stages 1–3 combined, but did not discriminate between the stages of abnormality. Using the suggested cut-off in the CPT test, the sensitivity and specificity were calculated as 43 and 78%, respectively. Receiver operator characteristic analysis suggested that the rewarming time of highest accuracy gave a sensitivity of 66% and specificity of 59%. In 10 miners who reported unilateral hand blanching, there was no significant difference in CPT measurements between blanching and non-blanching hands. Repeat CPT measurements in normal subjects suggested mean differences of 52 and 107 s for each hand, and the Bland–Altman coefficient of repeatability was ~600 s for all fingers.

Conclusion
Single application of this standardized CPT test may have limited value in diagnosing the vascular component of HAVS in an individual.

Keywords
HAVS; vibration-induced Raynaud’s phenomenon; vibration white finger

Introduction
Hand–arm vibration syndrome (HAVS) is characterized by vascular, neurological and musculo-skeletal changes to the hands and arms. The severity of vascular and neurological damage has been described by use of the internationally agreed Stockholm Workshop scale [1,2]. Vascular changes are evidenced by blanching of the
fingers in response largely to cold or the damp, but may also occur under stress. It reflects a vibration-induced Raynaud’s phenomenon. The diagnosis of HAVS relies heavily on the anamnestic reporting of symptoms with an appropriate history of exposure to vibration. A number of physiological and psychophysical tests have been used in many countries in attempts to confirm the reported symptomatology and define the degree of abnormality in digital vascular function [3–7] and neurosensory deficit [8,9]. These tests, in various forms, have been used in the UK in epidemiological research studies, clinical assessment and medical-legal cases. A large number of workers historically exposed to hand–arm transmitted vibration in British coalmines have been evaluated recently at a number of centres for compensation claims. This evaluation was initiated by the Department of Trade and Industry (DTI), and is being performed at a number of centres using an agreed standardized clinical and laboratory procedure. The vascular damage was assessed by medical interview of the subject about the reported vascular symptoms; a standardized cold provocation test (CPT) that monitors the recovery of skin fingertip temperature after a cold challenge to the hands [10] was also performed.

Members of the medical review panel overseeing the miners’ assessments recently reported an initial analysis on vascular diagnosis from ~20 000 evaluations [11]. They reported that the standardized CPT test correlated very poorly with the overall staging of disease severity using the Stockholm scale and helped little in the assessment of the vascular element of HAVS, which relies heavily on self-reporting of symptoms. Such a conclusion may have significant implications for the wider use of this quantitative test of vascular function as currently standardized. The authors rightly highlighted possible biases and problems within their data set, including potential positive bias in symptom reporting amongst those claiming compensation, some suggested or anecdotal evidence of ‘symptom coaching’ of subjects, and the large number of physicians and technicians involved at multiple different centres, which may lead to apparent increased noise in the data.

We performed a similar analysis, but used a narrower cohort with less possible biases. We compared CPT measurements with both the reported extent of finger blanching and final vascular Stockholm scale grading in the first 1000 miners who were assessed at our HAVS unit after the start of the DTI scheme. Although part of the medical review panel’s data, this subset was assessed by far fewer physicians and technicians under a central management structure to ensure quality control of assessments, and at a time when the likelihood of coaching on symptomatology may have been at an insignificant level. Importantly, we also present a limited amount of additional data based on within-subject repeatability data using the standardized CPT technique in subjects with no past exposure to vibration or history of Raynaud’s phenomena.

We report these data to help give further insight into the value of this specific, single standardized CPT measurement in helping to diagnose and stage the severity of the vascular element of HAVS.

**Methods and populations**

The study cohort comprised the first 1000 miners and ex-miners undergoing the standardized assessment at the Health and Safety Laboratory, Sheffield, as agreed under the DTI compensation scheme. This number of miners and ex-miners from a number of different geographical mining areas were investigated within the initial 4 month period of the DTI compensation scheme. At later times within the compensation scheme, concerns were raised about possible coaching of some subjects on answers to questions within the assessment.

Essentially, after quantitative tests to investigate neurosensory deficit, each subject would undergo a clinical examination by a physician who had undergone a minimum of 2 days of specialist training on a formalized assessment scheme for HAVS. This included a clinical questionnaire, based around the initial use of non-leading questions, followed by more detailed interrogation, both of which were used to elicit the recent history of blanching and to ascribe a blanching score [12]. This blanching history, in conjunction with a work history of exposure to vibration and past relevant health parameters, together with other diagnostic procedures carried out largely to exclude confounding vascular diseases, was used to stage the subject according to a modified Stockholm scale. Modification to this scale was by defining an ‘early’ and ‘late’ division to the neurosensory stage 2. After the clinical examination, a standardized CPT was performed using a 15°C cold water challenge to the hands for 5 min and subsequent monitoring of finger skin temperature for 10 min after removal from the cold water bath [10]. Calibrated thermocouples were attached by surgical tape to the volar surface of the fingertips. Subjects’ hands were covered in appropriately sized, long-wristed, thin plastic gloves during the cold immersion. They were taped to the wrist in such a manner to avoid trapping of air during immersion. The gloves were removed during the post-challenge monitoring of temperature. Time (in seconds) to rewarm by 4°C was used as the output metric from this test. Environmental conditions in the air-conditioned building were closely controlled during the subjects’ attendance at the assessment unit. Normative data (mean ± 2 SD) for the time to rewarm by 4°C were supplied as part of the standardized test and were used at all assessment centres, <300 s being defined as normal and >600 s significantly abnormal. All
CPT measurements were undertaken by trained technical staff and the method was audited regularly.

We restricted analysis of our miners cohort to those ≤65 years of age, subsequently to a smaller number of miners who reported no finger blanching and also to a much smaller subgroup who reported significant blanching on one hand only.

Repeatability data on the standardized CPT test were available from a small study commissioned to look at the immediate influence of a UK-permissible daily dose of vibration exposure on CPT and finger systolic blood pressure measurements. Eight subjects with no history of occupational vibration exposure or Raynaud’s phenomenon on careful questioning had undergone the standardized CPT measurements on two consecutive days prior to a 20 min vibrational exposure to frequency weighted acceleration of 13.7 m/s² to one hand. Thus, duplicate CPT measurements were collected on eight subjects after a 16 h vibration-free period under carefully controlled environmental conditions.

Statistical analyses used included the Bland–Altman test for test repeatability [13,14], receiver operator characteristic (ROC) analysis for definition of test characteristics (sensitivity and specificity) [15,16], correlation analysis reporting Pearson coefficients and t-tests. Log transformation of data was performed for statistical analyses where the original data had been shown to better fit a log distribution.

Results

Of the 1051 male miners assessed during June and September 1999, 727 were ≤65 years old and formed the study population. The median age was 54 years (range = 33–65 years) and all subjects had been exposed to vibrating tools during work at British Coal for between 3 and 45 years (median = 22 years). Stockholm scale vascular staging was carried out separately for each hand; prevalences were ~10, 11, 46 and 33% for vascular Stockholm stages 0–3 inclusive. There was close agreement in vascular staging between hands (contingency coefficient = 0.83). One-way analysis of variance suggested that the mean recovery time for the CPT was significantly lower in those subjects classified as Stockholm stage 0 compared with Stockholm stages 1–3, but did not discriminate between the three Stockholm stages (1–3), suggesting abnormality.

Blanching scores were calculated according to Griffin [12] and reflect the extent of subjectively reported blanching in fingers. ROC analysis was carried out for each hand, using the Stockholm vascular staging (0 versus 1–3) as the disease discriminator and the average CPT recovery time by 4°C for the four fingers. Figure 1 shows the plot of right-hand rewarming times categorized by normal and abnormal vascular Stockholm Workshop staging. Using the 300 s cut-off, the sensitivities for the right and left hands were 42.6% [95% confidence interval (CI) = 37.6–47.2%] and 43.7% (95% CI = 38.9–48.1%), respectively; specificities were calculated as 80.5% (95% CI = 65.1–91.2%) and 75.5% (95% CI = 61.7–86.2%). The ROC areas under the curve were 0.656 and 0.625, respectively, where 0.5 reflects chance and 1 perfect diagnosis. Further ROC analysis suggested that the rewarming time of highest accuracy, i.e. minimum false negatives and false positives, was 173 s, with a sensitivity of 65.8% and specificity of 58.5%.

Similar ROC results were obtained using the Griffin blanching scores to discriminate disease from the non-disease state. Correlation analysis on each hand between average CPT for the four fingers and the blanching score showed no significant relationship (r = 0.0392 and 0.0577; P > 0.2). Therefore, these data on the complete cohort suggest that the CPT was a poor predictor of final diagnosis or the extent of self-reported finger blanching.

Thirty-one miners who underwent CPT measurements had reported in the clinical assessment that they did not suffer any finger blanching. Their median (range) age and potential length of exposure to vibrating tools median were 46 (34–65) and 19 (11–38) years, respectively. Ages and length of exposure were not significantly different to the 727 workers in the full cohort. Five of the 31 subjects had mean rewarming times for four fingers above the normal range on both hands, and a similar number had at least one finger above the normal range (Figure 2). There was a strong correlation between the mean rewarming time of the fingers on each hand (r = 0.9163, P < 0.0001) in these subjects. Ten subjects were identified who had a blanching score of 0 on one
hand and a blanching score of 8 or above on the other. In all 10 cases, the hand with reported abnormality was their dominant hand. Eight of these subjects had CPT measurements and a blanching score of between 8 and 21 on the hand where blanching was reported, suggesting that at least two fingers were affected. A paired, one-tailed t-test comparing mean CPT measurements between the non-blanching hand and the abnormal hand showed no significant difference ($P > 0.2$), suggesting that the CPT test did not reflect the self-reported differences in blanching between hands.

Repeatability of CPT measurements in eight normal, volunteer subjects was assessed by calculating the mean difference in time to rewarm by $4^\circ$C and the coefficient of repeatability for the four fingers on each hand. Due to technical difficulties, results for the hand of one volunteer were not available (subject 6, right hand day 1). The mean differences on the hands were 52 and 107 s, and the coefficient of repeatability was ~600 s (Bland–Altman test). These data suggested that there was no systematic difference between the first test and the repeat measurement, but that wide variability could be noted, given that the upper limit of normality was 300 s and the length of the test did not extend beyond 660 s. The extent of the variability in this small but carefully controlled study can be seen in Figure 3. Three subjects showed large decreases in mean recovery time on both hands from day 1 to day 2, and one volunteer showed a reverse pattern. Three subjects showed relatively small variation between repeat measurements.

**Discussion**

Our analysis of a restricted data set of UK miners...
claiming compensation agrees with the report of Lawson et al. [11] on a wider data set (20 000 cases). Using ROC analysis, which is considered a fundamental tool in defining the value of a clinical diagnostic test [16], Lawson suggested that the CPT measurement of finger rewarming is not a valid tool for diagnosing the vascular component of HAVS and also that seasonality in measurement did not affect outcome. His quoted ROC analysis area under the curve (0.55) is very similar to our figure (0.63–0.66), and we found relatively poor levels of test specificity and particularly sensitivity (~78 and 43%, respectively). The poor sensitivity reflects the likelihood of false negatives. This relatively poor level of sensitivity and associated positive predictive value may be particularly important if this standardized CPT test is applied diagnostically in other occupational cohorts, where the level of vibration-induced vascular disease would hopefully be considerably lower than in the cohort of UK miners applying for compensation.

We accept that using a cohort applying for HAVS compensation that still relies heavily on anamnestic reporting of symptoms is open to positive bias and may cause difficulties in defining the true diagnostic value of any test. However, three further analyses strengthen our concerns about the value of the CPT test as currently standardized. First, in the miners who reported no history of finger blanching (thus positive bias in symptom reporting is unlikely), there remains a relatively high prevalence of abnormal CPT measurements, which suggests that the test specificity may not be good. Conversely, it could be argued that this suggests that the CPT test is reflecting pre-symptomatic vascular abnormality. Secondly, in the small number of miners who reported no finger blanching on one hand but significant blanching on the other, the quantitative CPT test failed to detect this difference between the hands. Thirdly, our data from a small repeatability study on two consecutive days suggested that the measurement can be highly variable with respect to the suggested normal range for the standardized CPT test. There was no evidence to suggest that the short vibrational exposure or pre-testing equilibration conditions influenced the level of repeatability in these volunteer subjects.

Therefore, we consider that relatively high levels of intra-individual variability in the CPT measurement may influence the lack of diagnostic power found in the miners cohort. The exact mechanism causing vibration-induced Raynaud’s phenomenon is still unclear. Both central responses, largely from the sympathetic nervous system, and local vascular damage in the hand may be involved [17]. Finger rewarming after a cold challenge to the hands is related to changes in finger blood flow, but is under complex control [18]. Poor finger rewarming may reflect peripheral damage in the digital arterial and vascular system, caused by the chronic absorption of vibrational energy, or the influence of the central sympathetic nervous system on vascular tone. Environmental acclimatization prior to testing may not be able to lessen an overriding but variable influence of central nervous system control mechanisms, in contrast to the effects of local, vibration-induced digital vascular damage on CPT. The nature of the cold challenge may influence the balance of these two influences. The strong agreement we saw in rewarming time between hands, not only in the miners but also in the volunteers, on each occasion of testing suggests that perhaps this standardized CPT test reflects very closely the central sympathetic response to the cold challenge. The use of CPT testing, albeit carried out under a wide variety of conditions, such as the temperature and duration of cold challenge and the indices of recovery, has been used extensively in the study and diagnosis of HAVS since the 1980s [7,19]. Often the emphasis in the published use of CPT measurements has been in distinguishing between groups of controls and cases [20,21], rather than as a diagnostic tool for the individual subject. However, the review by Lindsell and Griffin [19] of literature for CPT tests suggests a wide range of apparent test sensitivities and specificities for diagnosis of the individual. It is interesting to note that the large majority of published CPT tests reviewed by Lindsell and Griffin used cold challenges to the hands of <15°C. Some published data have suggested good sensitivity and specificity in their particular form of CPT test. Gautherie [3] reported a diagnostically useful CPT test, but used a complex set of algorithms to analyse both the pre- and post-challenge temperatures profiles. Coughlin et al. [5] have recently reported, albeit in a small study where all the cases where graded at Stockholm scale 3, substantially better test sensitivity and specificity than we found using the standardized CPT. Coughlin et al.’s study used a shorter but more severe cold challenge of 5°C for 1 min and recorded finger temperature by infra-red thermography, which gave the possibility of looking at temperature gradients along the finger.

We suggest that great care should be used in interpreting a single result from this standardized CPT in diagnosing the vascular component of HAVS for an individual. Further work is necessary to investigate the value of CPT in its various forms, and other vascular tests such as finger systolic blood pressure, in diagnosing HAVS. This should be done with regard to the criteria that would be applied to any clinical laboratory diagnostic test. Importantly, this work should use subjects who are being studied for health surveillance purposes rather than medico-legal purposes. This should help reduce bias in such studies. There is an ongoing need to accurately stage the extent and severity of the vascular component of HAVS without relying heavily on anamnestic reporting by the subject. In this context, we note the comments that have been made concerning problems with the vascular
staging in the Stockholm Workshop scale [22,23]. Such a test would aid not only diagnosis, but also the clinical management of individual workers within the workplace who already have some symptoms of HAVS. Often, in these cases, informed and regular decisions may need to be made concerning redeployment or continuing vibration exposure where there may be substantial remunerative implications for the worker. In these cases, the ability to quantitate accurately the degree of vascular damage would be useful. We suggest that this standardized CPT test as currently formulated and used in the UK miners’ compensation assessments may be useful for discriminating between groups of workers, but it does not meet the criteria usually associated with clinical diagnosis tests applied to an individual.

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Reference