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CHAPTER 11

TECHNOLOGY REVIEW: THE NEUROMETER® CURRENT PERCEPTION THRESHOLD (CPT)

INTRODUCTION

The American Association of Electrodiagnostic Medicine (AAEM) undertook this technology review based on AAEM member inquiries received in the Executive Office regarding the Neurometer® Current Perception Threshold (CPT). The Neurometer® CPT is a device for evaluating and quantifying sensory function which has been available in the medical market place for some years. The AAEM is currently undertaking a review of the general topic of quantitative sensory testing (QST), and technology reviews of other specific methodologies and instruments are anticipated in the future.

The Neurometer® CPT is a transcutaneous electrical stimulator which delivers sinusoidal electrical stimuli via surface electrodes at frequencies of 5 Hz, 250 Hz, and 2000 Hz, and at a current intensity range of 0.01 to 9.99 milliamperes. It is the only commercially available instrument applying this technology to the evaluation of sensory nerve function. Patients are asked to identify the presence or absence of the stimulus through a forced choice protocol. After an initial tentative threshold is determined, stimuli are presented that vary around the presumed threshold to confirm threshold stability and replicability. To prevent guessing, results are verified with placebo stimulation. The placebo stimulation is given by turning off all current without informing the patient and presenting these absent stimuli. Therefore, determination of threshold requires consistent patient response. The threshold of perception is the measured response. The testing procedure requires a brief time to perform (the promotional literature suggests 15 to 20 minutes), uses few consumable supplies, and will print out results in a standard format. The instrument weighs 12 pounds (including rechargeable batteries) and includes software for the analysis of information.

Scientific publications and information from promotional literature report the usefulness of this instrument for the detection, screening, diagnosis, and management of diseases of the peripheral nervous system. Capabilities attributed to the instrument in the literature include the:

1. Detection of axonal and demyelinating peripheral neuropathies (specific conditions include those associated with diabetes,[5-7,9,10,13,14,19,20,23,25-28,30,32,35,36,38-41,44,48-51,53] uremia,[3,18,31,53-55] organophosphate pesticides,[13] heavy metals,[13] vinca alkaloids,[31] hyperthyroidism,[33] cisplatin toxicity,[33] HIV infection,[17,33,47] Lyme disease,[33] leprosy,[34] hereditary conditions,[33] primary biliary cirrhosis,[21,22] and other toxins[43,56]).

2. Detection of carpal tunnel syndrome (CTS),[8,15,16] cervical radiculopathy,[33] lumbosacral radiculopathy,[16,33] tarsal tunnel syndrome,[33] reflex sympathetic dystrophy,[33] fibromylagia,[42] and neuroma.[33]

3. Ability to selectively measure and quantitate the response to stimulation of different size sensory nerve populations (the 2000 Hz stimulus is described as specific for measuring the response of A-beta fibers, the 250 Hz for A-delta fibers, and the 5 Hz for type C fibers).[5,12,24-30,40,45,51-53]

4. Differentiation of mononeuropathies from polyneuropathies (including enhanced sensitivity for the detection of ischemic mononeuropathies) through multisite testing.[4,34,39]

5. Quantification of hyperesthetic and hypoesthetic conditions.[11,15,16,25,46,53]

METHODS - REVIEW OF PUBLISHED ARTICLES OR ABSTRACTS

Criteria for Review and Literature Search Methods

Studies utilizing the Neurometer® CPT for the detection and diagnosis of peripheral nervous system disorders

Developed by the American Association of Electrodiagnostic Medicine (AAEM) Equipment and Computer Committee (1993-1996): George D. Baquis, MD; William F. Brown, MD, FRCP(C); Joseph T. Capell, MD; Vinay Chaudhry, MD; Didier Cros, MD; Bernard R. Drexinger, MD; Jeffrey B. Gelblum, MD; James M. Gilchrist, MD; Andrew J. Gitter, MD; Andrew J. Haig, MD; Wayne A. Hening, MD, PhD; Kenneth H.Z. Isaacs, MD; Daniel H. Lachance, MD; Robert L. Magnuson, MD; John M. Ravits, MD; James J. Rechtien, DO, PhD; Joseph J. Sciortino, MD; James F. Selwa, MD, MBA; Robert W. Shields Jr., MD; A. Robert Spitzer, MD; Frederick M. Vincent, MD; and David Walk, MD. Additional assistance provided by John C. Kincaid, MD, 1997-1998 AAEM Equipment and Computer Committee Chair.

Key words: *neurometer® • current perception threshold*

published through February 1, 1998, were reviewed. A Medline text-word search ("neurometer" or "current perception threshold") revealed 26 articles. Other articles were obtained through cross-referencing bibliographies from already obtained articles and from lists provided by the manufacturer. This search yielded 44 articles (original investigations or case reports) and 115 abstracts, textbook chapters, or review articles. The staff of the AAEM, Mayo Clinic Library, and Baystate Medical Center Library assisted with obtaining articles, some of which were only obtainable from large reference libraries. References not obtainable through these sources were requested directly from the manufacturer of the Neurometer® CPT.

The criteria used for the evaluation of these publications were modified from those used by the AAEM Quality Assurance Committee for the evaluation of CTS[1] and from the consensus report[37] on QST of the Peripheral Neuropathy Association.

The 6 criteria used in the evaluation are:

1. A prospective study.

2. Independent ascertainment of the clinical condition evaluated by the Neurometer® CPT.

3. A detailed description of methodology (sufficient to permit replication).

4. Attention to testing conditions that could potentially affect the results.

5. A suitable reference population from the same laboratory (obtained either concurrently or previously in the same laboratory).

6. Criteria for abnormality obtained from the reference population and defined in statistical terms. This last criterion allows comparison of a given procedure with other procedures.

SUMMARY OF THE LITERATURE

General Issues

1. Most of the published articles involve studies correlating the performance of the Neurometer® CPT to results obtained from standard nerve conduction studies (NCSs) (or other diagnostic techniques) within populations of affected individuals with known diseases. Differing and conflicting conclusions are drawn from several of these evaluations; examples include the usefulness of the Neurometer® CPT for the evaluation of CTS[8,15,16] and for the assessment of diabetic associated peripheral neuropathy.[5-7,9,10,13,14,19,20,23,25-28,30,32,35,36,38-41,44,48-51,53] The studies frequently show abnormalities in Neurometer® CPT measures that correlate with NCS results (or other means of evaluating nerve deficits). The Neurometer® CPT findings in these studies are often more numerous or pronounced than those abnormalities on NCS testing. However, there is the fundamental problem of what constitutes an appropriate standard against which to measure the Neurometer® CPT (for example, NCS values cannot be used as the standard if the Neurometer® CPT is being compared to these values). Another problem with the technique is that it elicits multiple measures (thresholds for 3 frequencies at each site), and any abnormality detected during the assessment of a diffuse or multifocal condition is considered significant. This causes a problem when multiple measures are being compared. Also, there is a tendency in the literature to arbitrarily assign various degrees of deviation from a normal population as grades of severity.[15,16,36,53] These grades do not add any additional information. Some of the reports use ratios of sensory threshold values.[15,16,53] These ratios are difficult to interpret given the current state of knowledge about this technique.

   The following issues were apparent in the Neurometer® CPT literature, however, these same comments apply to other applications of QST as well.

2. Since the Neurometer® CPT test requires an intact sensorimotor system from the sensory receptor to the motor speech area (to signal stimulus detection), a report of abnormal sensory perception lacks localizing value and can reflect abnormality at any site along this pathway. Therefore, the technique is limited in its ability to distinguish between anatomic sites of peripheral nerve injury. For example, it is not possible with the Neurometer® CPT to distinguish between distal median nerve entrapment, proximal median nerve injury, or cervical radiculopathy, since these may all cause the same Neurometer® CPT abnormality.

3. Unlike an NCS, which requires only minimal patient cooperation, the Neurometer® CPT test requires active patient participation. In the absence

of cooperation (due to physical or motivational limitations, including a failure to follow instructions) the Neurometer® CPT test will generally fail to result in a reproducible score. This limitation excludes certain classes of patients from investigation (such as children, those too weak to communicate, and the comatose patient).

4. The influence upon current perception threshold of central nervous system diseases, conditions which affect sensory perception such as local cutaneous diseases, or painful states not due to nerve pathology has not been established.

Specific Issues

1. Evidence supporting the ability of the Neurometer® CPT to selectively measure the function of different nerve size nerve fiber populations is based primarily upon studies correlating stimulation frequency with results from other examination techniques (such as thermal threshold and vibration threshold) in diseased patients or studies on normal volunteers undergoing spinal anesthesia.[24] However, there is a problem regarding what constitutes an appropriate way to validate these studies. It is not clear what constitutes an appropriate standard against which to test this hypothesis. For instance, it is possible that different classes of sensory fibers are being stimulated simultaneously, resulting in the subjective sensations described by the patient.[37] (The only study examining the relationship between CPT measures and pathologic nerve specimens shows no correlation between myelinated nerve fiber density and current perception threshold.[49])

2. Although normal values for Neurometer® CPT measures are reported, it is unclear if these values depend upon accumulated studies or have been obtained by a systematic program for establishing normal values. Also, the source of these values is not easily gleaned from the publications that were reviewed. For instance, Weseley, Sadler, and Katims[54] report in a table for normal values, "healthy CPT measures (n=84)" and reference this to 2 earlier papers.[13,14] The referenced papers however do not report the tabular data. The papers describe testing "44 normal volunteers" and "60 normal volunteers," respectively, and report normal data only in a graphical format. The same table is presented by Weseley, Liebowitz, and Katims.[53] This paper, however, indicates that the values are derived from "60 neurologically healthy subjects."[53] These values are then referenced to 2 publications,[12,13] 1 of which does not mention or present the tabular accumulation of normative data and was not referenced by Weseley and colleagues.[12] The other reference was 1 of those referenced by Weseley and colleagues.[13] This same table is also presented by Katims, Rouvelas, Sadler, and Weseley,[16] but describes "N=137," and incorporates into the table of normal values "n=68" published by Appenzeller and colleagues.[2] Therefore, it is not possible to know from the literature if patient evaluations for the different conditions to which usefulness of this technique has been attributed have been performed over the same sites or with the same techniques used for obtaining normal values. This is a significant limitation when attempting to interpret the published studies examining the usefulness of the Neurometer® CPT for assessment of patients with diabetes, uremia, CTS, and the other described applications. In addition, there is little published information about reliability of test results between operators and the replicability of results between testing times.

3. Unlike an NCS, which provides information on conduction velocity and amplitude across a number of proximal and distal nerve segments, the Neurometer® CPT provides only 1 set of values for each site studied. Therefore, the location and type (axonal or demyelinative) of peripheral nerve pathology is less clear with Neurometer® CPT testing compared to NCSs to which needle electromyography (EMG) may add nonredundant information.

4. Evidence supporting the ability of the CPT evaluation to quantify hyperesthesia, as well as hypoesthesia, is based upon the assumption that detection of stimuli that fall either below or above the reported normal ranges represent the former or latter condition, respectively. This assumption forms the basis of several published reports.[15,16,53] However, "in hypersensitivity states, threshold may be reduced, normal, or increased, but typically, as the stimulus strength is gradually increased above threshold, perception increases abnormally in magnitude, kind (an altered

sensation), or both."[37] Testing and validation of this assumption using the Neurometer® CPT has not been described.

Safety

There have been no reports of adverse effects or injury in association with performance of Neurometer® CPT studies by personnel trained in the use of this equipment. The test procedure appears to be safe when performed by trained and experienced medical personnel.

RECOMMENDATIONS

Determination of current perception threshold has the potential for evaluation of patients with peripheral nervous system diseases resulting in altered cutaneous sensation. This type of testing could potentially complement needle EMG and NCSs, to assist with evaluating treatment response or disease progression after a diagnosis is made. However, conflicting information and methodologic problems exist regarding the utility of the Neurometer® CPT for the diagnostic evaluation of specific disease conditions such as CTS and polyneuropathy. Future research is needed to establish statistically expressed normal values and to demonstrate the sensitivity and specificity of the Neurometer® CPT data.

1. Reference values need to be established for well characterized and representative populations. Values should be available for each of the sites used for patient testing. Reference values should be expressed as either mean ± a number of standard deviations (when values are normally distributed or so transformed) or as percentile values (providing sufficient numbers of control subjects are studied). The effects of potentially influential variables such as age and temperature should be characterized so that appropriate adjustments can be considered.

2. Reproducibility and interoperator variability of Neurometer® CPT normal values need to be established and expressed statistically in control subjects and patients with specific diseases.

3. The sensitivity and specificity need to be established and compared to an appropriate standard (for example, by studies comparing Neurometer® CPT data to the final diagnosis of CTS in patients and a group of healthy control subjects with a full clinical and electrodiagnostic evaluation).

4. Studies are needed to analyze the cost and outcome when Neurometer® CPT data is used for evaluating treatment or disease progression.

The ultimate value of the Neurometer® CPT in the settings to which it is suited will also depend upon comparison of its usefulness against other methods of QST. This may involve assessment of the sensitivity and specificity of the different methodologies to which it is compared, as well as a cost-benefit analysis.

Although the abstracts, textbook chapters, and review articles describe many of the useful features attributed to this instrument, the reviewers concluded that information in these publications is insufficient to make conclusions about the usefulness of this form of sensory testing at the present time.

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DEFINITIONS

Safety: A judgment of the acceptability of risk in a specified situation, e.g., for a given medical problem, by a provider with specified training, at a specified type of facility.

REFERENCES

Abbreviations: alcoholic noninsulin dependant diabetes mellitus (A-NIDDM); cephalic evoked noncutaneous sensations (CENS); central nervous system (CNS); current perception threshold (CPT); carpal tunnel syndrome (CTS); hemodialysis (HD); human immunodeficiency virus (HIV); nerve conduction testing (NCT); newly diagnosed noninsulin dependent diabetes mellitus (ND-NIDDM); noninsulin dependent diabetes mellitus (NIDDM); polychlorinated biphenyl (PCBs); polychlorinated dibenzofurans (PCDFs); polychlorinated dibenzo-p-dioxins (PCDDs); peripheral nervous system (PNS); standard deviation (SD); transcutaneous electrical nerve stimulation (TENS); transcutaneous nerve stimulation (TNS).

1. American Association of Electrodiagnostic Medicine Quality Assurance Committee. Jablecki CK, Andary MT, So YT, Wilkins DE, Williams FH: Literature review of the usefulness of nerve conduction studies and electromyography for the evaluation of patients with carpal tunnel syndrome. *Muscle Nerve* 1993; 16:1392-1414.
2. Appenzeller O, Wood SC, Appenzeller T: Pentoxifylline, altitude, and peripheral nerve function. *Ann Sports Med* 1988; 4:286-288. Criteria Met (2/6: 1,6) CPT was measured on mountain climbers at Lhasa, Mt. Everest Base Camp, and at Camp I. There was no measurable effect of altitude on CPT values. The number of climbers is not specified. Determination of CPT in Beijing is reported in Figure 2 but is not included in the methods section. This is a brief report, and the presented information about testing conditions and test reproducibility under these extreme conditions is limited. A normal values table is presented, N = 68.
3. Avram MW: Severe neuropathy in urban dialysis patients: Neurological complications in chronic uremia management. *Contemp Dialysis Nephrol* 1994; 15:22-23, 34. Criteria Met (0/6) The prevalence of polyneuropathy is described in a HD population and evaluated in 60 nondiabetic and 35 diabetic patients by measurement of CPT. CPT is correlated with serum metabolic measures and dialysis treatment. Severe neuropathy is defined as "...an anesthetic response at one of the three frequencies measured." The methods are brief and testing conditions are not presented. Controls are not presented. CPT is used to define the study population, and there is no independent ascertainment of diabetic and uremic polyneuropathy.
4. Chado HN: The current perception threshold evaluation of sensory nerve function in pain management. *Pain Digest* 1995; 5:127-134. This review includes a graph of normal CPT data.
5. Dent MT, Ward JD, Ryder REJ: Testing for diabetic neuropathy; part 1, somatic nerve function. *Practical Diabetes* 1992; 9:24-28.
6. Drobny E, Rendell M, Dovgan D, Bergman T, O'Donnell G, Katims J: Mapping diabetic sensory neuropathy by constant current perception threshold (CPT) testing. *Diabetes* 1989; 38(suppl 2):29A.
7. Evans ER, Rendell MS, Bartek JP, Bamisedun O, Connor S, Giitter M: Current perception thresholds in ageing. *Age Ageing* 1992; 21:273-279. Criteria Met (3/6: 1,3,6) Clinical neurological examinations (a symptom score and a physical examination score) were studied in 40 healthy elderly and 31 healthy volunteers, and in 25 elderly diabetic and 37 young diabetic patients. There results were correlated with CPT results. The symptom and physical examination scores are used to define the patient groups. CPT values are not found to differ significantly between younger and older healthy subjects. The study is presumed to be prospective. No comment is made regarding blinding of each study portion. Reproducibility of each of the scores is assumed to be the same as that reported in other studies but is not addressed for the patients in this study. No comment is made regarding validation of the symptom and physical examination scoring technique or whether the patients were age and sex matched with controls. Data is presented as correlation coefficients.
8. Franzblau A, Werner RA, Johnston E, Torrey S: Evaluation of current perception threshold testing as a screening procedure for carpal tunnel syndrome among industrial workers. *J Occup Med* 1994; 36:1015-1021. Criteria Met (4/6: 1,2,3,6) A prospective study of 84 automobile parts manufacturing plant workers participating in a worksite screening program to estimate the prevalence of CTS. This included a self-administered question survey, limited physical examination, limited electrodiagnostic testing, and CPT testing. The test performance characteristics (sensitivity, specificity, and predictive value) of CPT were believed to be low compared to electrodiagnostic measurements and self-reported symptoms of CTS. The study was prospective, and the methods and testing were described (surface temperature was controlled for during electrodiagnostic testing but is not mentioned for CPT testing). Criteria used for the clinical diagnosis of CTS are clearly described. The source of electrodiagnostic study normal values is not stated. The CPT manual is referenced as the source of CPT testing methodology and normal values. Precise CPT testing conditions are not included.
9. Gavin LA: A comprehensive approach to sidestep diabetic foot problems. *Endocrinologist* 1993; 3:191-203. Criteria Met (0/6) CPT is briefly mentioned in this review of diabetic foot care.
10. Guthrie D, Gomes R, Guthrie R, Topham B, Childs B, Parks L: Neuropathy in children who have diabetes mellitus. *Diabetes* 1989; 38(suppl 2):560.
11. Katims JJ, Appenzeller O: Differential susceptibility to noxious stimuli: Exercise-associated insensitivity to pain. *Neurology* 1986; 36(suppl 1):306.
12. Katims JJ, Long DM, Ng LKY: Transcutaneous nerve stimulation. Frequency and waveform specificity in humans. *Appl Neurophysiol* 1986; 49:86-91. Criteria Met (1/6: 1) A summary of the sensations experienced and described by 52 healthy volunteers who experienced cranial TNS. The data is presented in a figure containing 9 graphs (not all data is presented for review). The authors conclude that "...nervous tissue is capable of discriminating the wave form parameters of an electrical stimulus." It is not possible to determine if all the patients experienced all the phenomena described. The examiners are not blinded. The designation "bilateral cranial TNS" is confusing since the article only describes stimulation at one site. The authors assume that the sensations described result from direct "nervous tissue" stimulation.
13. Katims JJ, Naviasky EH, Ng LKY, Rendell M, Bleeker ML: New screening device for assessment of peripheral neuropathy. *J Occup Med* 1986; 28:1219-1221. Criteria Met (1/6: 6) The purpose of the study is not explicitly stated. CPTs are evaluated in 33 diabetic patients and 54 normal persons. The authors conclude that CPT is a "...sensitive quantitative measure of sensory function." The test setting is not described (the photograph in the article of an individual being tested appears to be an outdoor setting). Clinical characteristics that define the peripheral neuropathy and normal groups are not described. It is not stated whether the groups are age and sex matched. Independent ascertainment of clinical condition is not provided for comparison with the CPT values. Normal data is displayed as a graph (44 "normal volunteers").
14. Katims JJ, Naviasky EH, Rendell MS, Ng LKY, Bleeker ML: Constant current sine wave transcutaneous nerve stimulation for the evaluation of peripheral neuropathy. *Arch Phys Med*

Rehabil 1987; 68:210-213. Criteria Met (2/6: 1,6) The purpose of the study was to "describe the quantitative characteristics" of skin CPT by studying 60 healthy individuals, 34 patients with diabetic neuropathy, 29 patients in an alcohol detoxification program, and 11 patients with nondiabetic neuropathy. The authors conclude that CPT offers promise for initial screening of patients with sensory neuropathies. The screening criteria for the normal patients consisted of a brief history and limited examination. The population from which they are chosen is not stated. The criteria for defining the presence and severity of polyneuropathy in patient groups is not provided. The CPT is not compared to any other peripheral nerve function measurement technique. This study presents information from preselected patients and does not assess the instrument's ability to screen any specific patient populations. Normal data is displayed as a graph (60 "normal volunteers").

15. Katims JJ, Patil AS, Rendell M, Rouvelas P, Sadler B, Weseley SA, Bleecker ML: Current perception threshold screening for carpal tunnel syndrome. *Arch Environ Health* 1991; 46:207-212. Criteria Met (1/6: 6) CTS questionnaires, physical examinations, and CPT were measured on 16 self-referred assembly line workers with hand pain from an Ohio food processing factory. The questionnaire is referenced in the article, but is not presented. Questionnaire raw data are not presented (other than to indicate that some patients were believed to have conditions precluding them from participation in this study). General aspects of the clinical examination methodology are described but specific information is not stated. Only brief descriptions of the clinical characteristics are presented. A table of normal CPT values is presented, N=137. It is not clear if the study is prospective.
16. Katims JJ, Rouvelas P, Sadler BT, Weseley SA: Current perception threshold. Reproducibility and comparison with nerve conduction in evaluation of carpal tunnel syndrome. *ASAIO Transactions* 1989; 35:280-284. Criteria Met (1/6: 6) CPT measurements are obtained on 29 "stable dialysis patients" with renal failure resulting from a variety of causes including diabetes mellitus. These are compared to median and peroneal nerve conduction velocities and amplitudes. The authors conclude that "...repeated CPT determinations are consistent and are diagnostic for CTS." The description of methodology is confusing ("Standard NCT was conducted bilaterally from the digital median and peroneal nerves on all subjects..."), and distal latency median sensory nerve conduction values for evaluation of focal median neuropathy at the wrist are not utilized. Methods to discriminate between distal nerve conduction or CPT abnormalities that result from uremic polyneuropathy, diabetic polyneuropathy, and distal entrapment neuropathy are not addressed (it is possible that abnormality on CPT could reflect multiple etiologies). A normal value table represents previously obtained normal values in an unmatched group of patients, N=137. A questionnaire was completed by patients to identify symptoms of CTS; the questionnaire and the data from it are not presented or referenced. The criteria used for the diagnosis of CTS are not described.
17. Katims JJ, Taylor DN, Wallace JI, Bekesi JG, Masdeu JC: Current perception threshold in HIV-positive patients, in *Proceedings of the Neurological and Neuropsychological Complications of HIV Infection, Satellite Conference of the 5th International Conference on AIDS.* 1989, p 39.
18. Katims JJ, Taylor DN, Weseley SA: Sensory perception in uremic patients. *ASAIO Transactions* 1991; 37:M370-M372. Criteria Met (1/6: 1) CPT was evaluated on 19 chronic HD patients with "...bilateral testing of median and ulnar nerves on the distal phalanx of the second and fifth digits." Data from "...cephalic evoked noncutaneous sensations (CENS), which are centrally mediated..." is also presented. Electrical current was delivered to the skin from 1 cm diameter cotton electrodes on clips applied to the anterior and posterior surface of earlobes. " The subjects verbal reports of experienced sensations..." are described (cranial stimulation) and compared to CPT data. The authors conclude that CPT is a "...sensitive and easy to administer test of PNS sensory function for the purpose of assessing the adequacy of dialysis in chronic hemodialysis patients; the CENS examination also may prove useful in this regard." Only a brief summary of data is presented. There is no comparison or control group, comparison of test methodology to other validated testing procedures, presentation of normal data, or detailed description of patient clinical characteristics or testing conditions.
19. Kempler P, Kadar E, Marton A, Vargha P, Hermanyi Z, Keresztes K: Sensory nerve dysfunction in NIDDM and in newly diagnosed NIDDM detected by the Neurometer®: Relation to autonomic function, in Hotta N, Greene DA, Ward JD, Sima AAF, Boulton AJM (eds): *Diabetic Neuropathy: New Concepts and Insights.* New York, Elsevier Science Publishing Co 1995. Criteria Met (0/6) CPT and tests of autonomic function were examined on 22 patients with NIDDM, 6 patients with ND-NIDDM, and 12 healthy subjects. The authors conclude that CPT permits the diagnosis of sensory dysfunction early in the course of diabetes and in NIDDM. This appears to be the same data presented by Kempler P, and colleagues at the 22nd Congress of the International Society of Internal Medicine (Prior presentation not referenced in this publication).
20. Kempler P, Keresztes K, Marton A, Váradi A, Hermanyi ZS, Márczy V, Kádár É, Vargha P: Evaluation of current perception threshold (CPT) by the Neurometer®: A diagnostic tool to detect early abnormalities of peripheral sensory nerve function in non-insulin-dependent diabetes mellitus, in Varro V, de Chatel R (eds): *Proceedings of the 22nd Congress of the International Society of Internal Medicine.* Bologna, Italy, Monduzzi Editore, SpA, 1994, pp 765-768. Criteria Met (2/6: 5,6) CPT and tests of autonomic function were evaluated in 22 patients with NIDDM, 6 patients with ND-NIDDM, and 12 healthy subjects. They conclude that the use of the Neurometer® CPT "...permits the diagnosis of sensory neuropathy..." in patients with ND-NIDDM. It is not stated whether this is a prospective study, definitions of the patient populations are not presented, methods are brief, and testing conditions are not presented.
21. Kempler P, Váradi A, Kádár É, Szalay F: Autonomic and peripheral neuropathy in primary biliary cirrhosis: Evidence of small fibre damage and prolongation of the QT interval. *J Hepatol* 1994; 21:1150-1151.
22. Kempler P, Váradi A, Pap A, Kádár É, Vargha P, Hermányi ZS, Márczy V, Gálffy G, Szalay F: Comparative evaluation of autonomic and peripheral sensory nerve function in primary biliary cirrhosis. *Z Gastroenterol* 1993; 31:336.
23. Lee Y, Robinson M, Wong N, Chan E, Charles MA: The effect of pentoxifylline on current perception thresholds in patients with diabetic sensory neuropathy. *J Diabetes Complications* 1997; 11:274-278. A 1-year randomized double-blind parallel group placebo-controlled clinical trial of pentoxifylline for treatment of diabetic polyneuropathy. Effectiveness measured by evaluating glycated hemoglobin, blood pressure, and CPT. No medication effect on diabetic sensory neuropathy was detected by CPT.
24. Liu S, Kopacz DJ, Carpenter RL: Quantitative assessment of differential sensory nerve block after lidocaine spinal anesthesia. *Anesthesiology* 1995; 82:60-63. Criteria Met (3/6: 1,3,6) CPT was measured in 6 different volunteers undergoing spinal anesthesia over the L2,3 dermatomes. It was assumed that the different stimulation frequencies selectively stimulate specific fiber sizes population. The authors conclude, based upon CPT data, that sensory nerve blockade characterized by the order of return of tactile sensation to touch, pinprick, and cold is due to the different recovery profiles of A beta, A delta, and C fibers. The study was not blinded, details of cutaneous testing are not described, and normal values for CPT are not presented. The selectivity of lidocaine for

specific nerve populations is assumed, but the possibility of simultaneous block of more than one fiber size population cannot be excluded.

25. Masson EA, Boulton AJM: The Neurometer®: Validation and comparison with conventional tests for diabetic neuropathy. *Diabet Med* 1991; 8 Symposium: S63-S66. Criteria Met (0/6) This study compares CPT obtained using the Neurometer® to study 22 "normal control subjects" with 59 "diabetic patients with and without conventionally defined neuropathy." The hypothesis to be tested is not explicitly stated. The study groups are not defined and the testing conditions and methodology are not described. Data are presented as 2 sets of graphs and it is unclear if the data represent control or diabetic patients.
26. Masson EA, Fernando D, Veves A, Boulton AJM: A critical independent evaluation of the 'Neurometer®' in the assessment of diabetic peripheral neuropathy. *Diabetes* 1989; 38(suppl 2):130A.
27. Masson EA, Fernando DJS, Veves A, Boulton AJM: Independent evaluation of a novel device for assessment of diabetic neuropathy. *Diabetologia* 1989; 32:515A.
28. Masson EA, Veves A, Fernando D, Boulton AJM: Current perception thresholds: A new, quick, and reproducible method for the assessment of peripheral neuropathy in diabetes mellitus. *Diabetologia* 1989; 32:724-728. Criteria Met (2/6: 1,5) The study evaluates CPT in 31 healthy subjects and 90 diabetic patients (separated into 3 groups). The CPT results in the different groups are compared to each other and correlated with thermal threshold (thermoaesthaesiometer), vibration reception threshold (biothesiometer), and peroneal motor conduction velocity. The authors conclude that CPT "...provides useful discrimination between neuropathic and non-neuropathic clinical groups and may offer an indication for risk of foot ulceration in diabetic patients." A general description of methodology is provided, but details of testing conditions are not described. Considerable overlap exists for testing of all groups. The effect of breakdown of skin integrity on CPT values is not discussed. The correlation of CPT and sensory testing is presented as a table, but the non-CPT sensory test data are not included.
29. McAllister RMR, Urban LA, Dray A, Smith PJ: Comparison of the sensory threshold in healthy human volunteers with the sensory nerve response of the rat in vitro hindlimb skin and saphenous nerve preparation on cutaneous electrical stimulation. *J Hand Surg Br* 1995; 20:437-443. Criteria Met (4/6: 1,3,5,6) An in vitro rat skin-saphenous nerve preparation was utilized to measure the electrical stimulation thresholds of A beta, A delta, and C nerve fibers. Fiber size was defined by conduction velocity range. A constant current square wave stimulus generator delivered single 1 Hz frequency pulses through a bipolar electrode of 10 or 150 ms duration in the current range 0.1 to 50 mA, recording over the saphenous nerve with Ag/AgCl electrodes. The same assembly was used to determine "psychophysical" thresholds ("tingling," "prickling") in 12 healthy volunteers, but the current range was extended to 100 mA. The threshold of electrical stimulation of the rat preparation was then compared to the threshold of stimulation needed to evoke the "psychophysical" thresholds. The authors concluded that "tingling" sensation is due to recruitment of A beta fibers and that sharp "pricking" occurs with recruitment of A delta fibers. The study does not describe selection criteria of normal subjects, blinding, skin temperature, reproducibility of human results, relationship of skin characteristics to perception, or the large range of variability of stimulus threshold perception in normal volunteers.
30. Meijer JWG, Tack CJJ, Netten PM, Lutterman JA: Current perception threshold testing; A reliable method to quantify diabetic neuropathy?. *J Intern Med* 1992; 1:53.
31. Mittman N, Avram MM: Management of uremic peripheral neuropathy, in Nissenson AR, Fine RN (eds): *Dialysis Therapy*. 2d ed. Philadelphia, Hanley & Belfus 1993, pp 277-279.
32. Moss K, Holewski JJ, Adams S, Grunfield C: Comparison of aesthesiometry, biothesiometry and neuroselective current perception threshold test to quantify sensory deficit in diabetic sensory neuropathy. *Diabetes* 1989; 38(suppl 2):136A.
33. Neurometer® CPT Clinical Applications, Int-Med New Port Richey, Florida, 1993.
34. Neurotron Inc: *Neurometer® CPT Quantitative Sensory Nerve Tester.* Baltimore, MD, 1989-1991.
35. Olmos PR, Cataland S, O'Dorisio TM, Casey CA, Smead WL, Simon SR: The Semmes-Weinstein monofilament as a potential predictor of foot ulceration in patients with noninsulin-dependent diabetes. *Am J Med Sci* 1995; 309:76-82. Criteria Met (5/6: 1,2,3,4,6) The Semmes-Weinstein monofilament was evaluated as a potential predictor of foot ulceration. Patients with NIDDM were evaluated with the filament at 3 sites and with CPT. Groups consisted of patients without ulcers and those with a history of ulcers in the past year. The CPT values were higher in the foot ulcer group than the nonulcer group for all frequencies. The CPT was slightly more sensitive than the filament but also had a higher false positive rate. Overall, both were believed to provide similar results, but the filaments were believed to be easier to administer in routine clinical practice. Normal CPT values were not presented.
36. Pitei DL, Watkins PJ, Stevens MJ, Edmonds ME: The value of the Neurometer® in assessing diabetic neuropathy by measurement of the current perception threshold. *Diabet Med* 1994; 11:872-876. Criteria Met (4/6: 1,3,5,6) CPT was determined for 51 diabetic patients with severe neuropathy and 28 nondiabetic control patients. Diabetic complications of Charcôt joints and foot ulcers affected 26 and 13 patients respectively. Diabetic neuropathy is not defined and Table 1, "clinical and neuropathic details," does not provide any neurological information. Other measures of peripheral nerve function included vibration and thermal sensation to warm and cold. Reproducibility was assessed in 3 patients and 3 controls who were tested at monthly intervals on 4 occasions. The CPT thresholds were increased in diabetic patients compared to control subjects. A large coefficient of variation was noted for CPT testing (greater in diabetic patients than controls). The features suggestive of large fiber or small fiber CPT abnormality did not always correlate with the results of vibration and thermal testing. Testing conditions were not presented.
37. Quantitative sensory testing: A consensus report from the Peripheral Neuropathy Association. *Neurology* 1993; 43:1050-1052.
38. Rendell M, Basmisedun O: Skin blood flow and current perception in pentoxifylline treated diabetic neuropathy. *Angiology* 1992; 43:843-851. Criteria Met (2/6: 1,2) The purpose of the study was "to measure skin blood flow and current perception in diabetic patients with sensory neuropathy following a course of pentoxifylline therapy." The patient group consisted of 24 diabetics (6 of the original group of 30 dropped out) with a polyneuropathy defined by clinical examination and symptoms (the validation of the clinical scales used for assessment of sensory polyneuropathy was not presented). Laser doppler was used to measure skin blood flow. An improvement in blood flow and in CPT values was accompanied by an improvement in the symptom and examination neurologic scores. Diabetic polyneuropathy was not precisely defined and CPT testing conditions were not stated.
39. Rendell MS, Dovgan DJ, Bergman TF, O'Donnell GP, Drobny EP, Katims JJ: Mapping diabetic sensory neuropathy by current perception threshold testing. *Diabetes Care* 1989; 12:636-640. Criteria Met (3/6: 3,5,6) The purpose of the study was "...to see if CPTs could serve as a mapping procedure in surveying the extent of sensory neuropathy." Study subjects are 59 diabetic patients and 44 nondiabetic volunteers. Clinical grading scales are described (scale validation for the measurement of sensory polyneuropathy is not presented). CPT is determined at the same sites used for clinical examination. Repeated examination by CPT to demonstrate

reproducibility is mentioned and footnoted but the details are not presented and it is not clear whether this is assessed in the study groups. The authors conclude that CPT "... should prove valuable for serial quantitation of neuropathy in clinical trials." Diabetic sensory neuropathy is not defined, it is not stated whether the study is prospective, details of testing conditions are not presented, and blinding of examiners and patients is not mentioned.

40. Rendell MS, Katims JJ, Richter R, Rowland F: A comparison of nerve conduction velocities and current perception thresholds as correlates of clinical severity of diabetic sensory neuropathy. *J Neurol Neurosurg Psychiatry* 1989; 52:502-511. Criteria Met (5/6: 1,2,3,4,6) A detailed study was performed of 71 patients with a known diagnosis of diabetic polyneuropathy. Adaptations of the Neurological Symptom Score and Neurological Disability Score, NCT, vibration threshold testing, and CPT were evaluated. Correlations were noted between physical score and symptom score with CPT. The strongest correlation was between physical score and median nerve motor conduction. The authors conclude that CPT may improve the quantitative assessment of diabetic polyneuropathy. The source/reference populations of normal values for CPT and other testing modalities were not described. There was no concurrent comparison control group or comparison group of patients with other causes of polyneuropathy. The problem of what constitutes the "gold standard" for diagnosis of diabetic polyneuropathy exists.
41. Rice BI, Schindler JV: Increased sensory nerve function of the peroneal nerve in response to biofeedback assisted relaxation training in a population with diabetes. *Diabetes* 1982; 41(suppl 1):33A.
42. Romano TJ, Stiller J: Abnormal cutaneous perception in fibromyalgia patients. *Arthritis Rheum* 1988; 31(suppl 1):R44.
43. Shields M, Beckmann SL, Cassidy-Brinn G: Improvement in perception of transcutaneous nerve stimulation following detoxification in firefighters exposed to PCBs, PCDDs and PCDFs. *Clin Ecology* 1989; 6:47-50. Criteria Met (0/6) Seventeen firefighters with acute toxic exposure to PCBs, PCDDs and PCDFs were assessed for CPT "...at the trigeminal, median, and peroneal nerves...." CPT values before and after treatment were compared. Precise timing of the study after toxic exposure is not described. There is no independent ascertainment of condition, quantification of toxic exposure, description of testing conditions, or presentation of normal values.
44. Tack CJJ, Netten PM, Scheepers MH, Meijer JWG, Smits P, Lutterman J: Comparison of clinical examination, current and vibratory perception threshold in diabetic polyneuropathy. *Neth J Med* 1994; 44:41-49. Criteria Met (4/6: 1,3,5,6) Healthy controls (35), diabetic patients without clinical neuropathy (23), diabetics with overt neuropathy (22), and patients with diabetes of duration over 20 years (38) were compared. CPT, vibratory threshold, and neurologic clinical scores were obtained. All tests were performed by 2 observers and inter-observer reproducibility of the clinical scoring system was 26.8%. Patients for each group were reassessed by CPT at 1 - 30 days. Although significant differences were noted in CPT between each group, significant overlap was present between groups. Correlation of symptom or vibration with CPT was weak. Reproducibility was poorer at lower CPT frequencies, especially in the group with deficits. CPT did not reliably discriminate between a group with a high prevalence of disease and healthy controls. The CPT was believed to be of limited value because of high variability and poor reproducibility. Testing conditions were not described and independent ascertainment of diabetic polyneuropathy is lacking.
45. Tay B, Wallace MS, Irving G: Quantitative assessment of differential sensory blockade after lumbar epidural lidocaine. *Anesth Analg* 1997; 84:1071-1075. Criteria Met (2/6: 1,3) CPT was measured over the great toe, knee, umbilicus, and mastoid of patients evaluated with epidural lidocaine and saline placebo. Touch, pinprick sensation, cold sensation, and a visual analog pain scale were also measured. The possibility of simultaneous effect on different nerve fiber size populations is not addressed. Normal values for CPT and validation of cutaneous testing methods are not presented.
46. Taylor DN, Katims JJ, Ng LKY: Sine-wave auricular TENS produces frequency-dependent hypesthesia in the trigeminal nerve. *Clin J Pain* 1993; 9:216-219. Criteria Met (2/6: 1,3) Different frequencies of auricular sine-wave TENS were delivered to 72 healthy volunteers. Baseline CPT was measured at different frequencies and compared to CPT obtained after TENS. The CPT was measured using 1 cm diameter cotton electrodes moistened with water and attached by clips to the medial and lateral aspects of both ears. The TENS current was "passed ear to ear." The CPT was obtained at the patient's TENS treatment frequency. Each subject's CPT for 250 Hz was determined using the TENS device with 2 1-cm gold electrodes, 2 cm apart, with "standard electrocardiography paste as the conducting medium," held in place by surgical tape 1 cm anterior to the left ear tragus. The protocol was double-blinded and prospective. The CPT values obtained after TENS were increased compared to baseline values. The investigators concluded that this corresponds to production of "hypesthesia" by the TENS instrument. However, CPT was not compared to ascertainment of cutaneous sensation threshold by other techniques. The criteria used to select normal volunteers is not presented. The pretreatment CPT (absolute and SD values) for the baseline 5 Hz TENS group appears to be significantly different from the baseline of the placebo TENS group (i.e., is equal to or greater than the CPT values for the after TENS 5 Hz and 2000 Hz post-treatment groups).
47. Taylor DN, Wallace JG, Masdeu JC: Perception of different frequencies of cranial transcutaneous electrical nerve stimulation in normal and HIV-positive individuals. *Percept Mot Skills* 1992; 74:259-264. Criteria Met (0/6) A sine wave cutaneous stimulus of varying frequencies was "applied across the cranium (ear to ear)" at 3 different frequencies, and the response was described by 50 healthy volunteers and 34 HIV positive individuals. Cotton electrodes were moistened with water and held to the anterior and posterior earlobes by clips. The tested subjects described the phenomena they experienced. The testing conditions are not described, little data are presented, reference data are not stated, and there are no statistical methods described.
48. Veves A, Malik R, Townsend C, Thompson S, Boulton AJM: Unmyelinated fibre pathology in diabetic patients with mild neuropathy. *Diabetologia* 1992; 35(suppl 1):16A.
49. Veves A, Malik RA, Lye RH, Masson EA, Sharma AK, Schady W, Boulton AJM: The relationship between sural nerve morphometric findings and measures of peripheral nerve function in mild diabetic neuropathy. *Diabet Med* 1991; 8:917-921. Criteria Met (2/6: 1,2) The morphological findings (mean myelinated fiber density) from the sural nerve biopsy specimens from 15 diabetic patients with mild neuropathy are compared with control biopsies from 8 non-neuropathic nondiabetic subjects. Correlations are examined between these results and vibration, thermal, and CPTs. Diabetic neuropathy was defined by vibration threshold (normal values from 120 healthy subjects) and nerve conduction studies (normal values from 50 healthy subjects). The data were presented as graphs or tables with correlation coefficients. A correlation is present between biopsy myelinated fiber density and sural nerve action potential amplitude, sural conduction velocity, peroneal motor conduction velocity, and median sensory amplitude. No correlation was demonstrated between the fiber density and CPT results. CPT results are presented as mean ± 1SD, and percent of patients with an abnormal test. The precise skin surface location of CPT testing is not described.
50. Veves A, Young MJ, Manes C, Boulton AJM: Differences in peripheral and autonomic nerve function measurements in

painful and painless neuropathy: A clinical study. *Diabetes Care* 1994; 17:1200-1202. Criteria Met (3/6: 2,5,6) Groups of male diabetic patients without neuropathy (38), diabetic patients with painless neuropathy (32), diabetic patients with painful neuropathy (52), and 24 healthy subjects were evaluated with a neuropathy symptom score, neuropathy disability score, vibration threshold, thermal discrimination threshold for warm, autonomic function tests, peroneal nerve conduction velocity, and CPT. (The details, including methods and testing conditions, are referenced to other publications and are not described in this paper.) The diagnosis of peripheral neuropathy is based upon the presence of at least 2 of 4 main categories of testing being abnormal. However, it is unclear how the patients were initially selected for each of the clinical groups. CPT values were equally increased in diabetic patients with and without a painful neuropathy.

51. Vinik AI, Suwanwalaikorn S, Stansberry KB, Holland MT, McNitt PM, Cohen LE: Quantitative measurement of cutaneous perception in diabetic neuropathy. *Muscle Nerve* 1995; 18:574-584. Criteria Met (6/6) Groups of 81 diabetic subjects and 31 healthy controls were evaluated with warm and cold thermal threshold, vibration, touch-pressure, and CPT. The study was prospective, sources of patients were indicated, and the methods and testing conditions stated along with statistical methods. The examiners were not blinded. Although a general description is mentioned, no precise definition of diabetic neuropathy is provided. The controls are younger than the diabetic group. The authors conclude that the CPT sensitivity for detecting diabetic polyneuropathy is lower than other technologies tested, and do not find CPT to be fiber size specific when compared to the other testing techniques.
52. Wallace MS, Dyck JB, Rossi SS, Yaksh TL. Computer-controlled lidocaine infusion for the evaluation of neuropathic pain after peripheral nerve injury. *Pain* 1996; 66:69-77. Criteria Met (6/6) A randomized double-blind placebo controlled study of intravenous lidocaine infusion on pain scores, CPT, and pain distribution in patients suffering from peripheral nerve injury pain. The methods and testing conditions are carefully described. Perception was measured at the unaffected ring finger. A significant concentration dependent increase in CPT at 5 Hz and 250 Hz, but not at 2000 Hz was noted. The study did not distinguish between CNS and PNS mechanisms of altering sensation.
53. Weseley SA, Liebowitz B, Katims JJ: Neuropathy of uremia: Evaluation by nerve conduction velocity versus neurospecific current perception threshold. *Nephron* 1989; 52:317-322. Criteria Met (1/6: 6) CPT testing and bilateral peroneal and median motor nerve conduction studies were performed on 34 patients undergoing hemodialysis. Several patients had coexistent conditions which could potentially be associated with polyneuropathy, such as diabetes mellitus. The study does not include clinical neurological assessments, description of testing conditions, and normal laboratory values for NCT. Some of the tabular values fall outside generally regarded physiologic ranges (i.e., patient AE's right median amplitude 49 mV, patient WS's right median amplitude 30 mV). When compared to the patients reported in *ASAIO Transactions* 1988; 34:188-193, the initials of some patients (and data) are virtually identical (Table 4 of each article). This article is not referenced in this paper. A table of normal values from "60 neurologically healthy subjects" is presented.
54. Weseley SA, Sadler B, Katims JJ: Current perception: Preferred test for evaluation of peripheral nerve integrity. *ASAIO Transactions* 1988; 34:188-193. Criteria Met (1/6: 6) CPT testing and bilateral peroneal and median motor nerve conduction were performed on "23 dialysis patients." This appears to be the same patient group from *Nephron* 1989; 52:317-322. Details of clinical diagnosis, clinical examination, testing conditions, and normal nerve conduction values are not described. Some of the data presented in Table 4 fall outside of conventional ranges. A table of normal values is presented (N=84).
55. Weseley SA, Sadler B, Katims J, Goodman AI: Longitudinal assessment of current perception threshold versus nerve conduction velocity in ESRD patients. *Kidney Int* 1988; 33:241.
56. Wisner RM, Root D, Shields M, Beckmann SL: Neurotoxicity and toxic body burdens: Relationship and treatment potentials, in Hashimoto K (ed): *Proceedings of the 1993 International Conference on Peripheral Nerve Toxicity*. Kanazawa, Japan, 1993, pp 49-50. Criteria Met (0/6) CPT evaluation of patients referred for evaluation of exposure to toxic chemicals is described. Evaluation was performed before and after therapy. The CPT methods, testing conditions, patient population, control population, patient diseases, and clinical descriptions of illness are not provided.

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The American Association of Electrodiagnostic Medicine (AAEM) is now the American Association of Neuromuscular & Electrodiagnostic Medicine. The following document was printed in *Muscle & Nerve* before the name change. The name was therefore not updated.