Quantitative Sudomotor Axon Reflex Test in Normal and Neuropathic Subjects

P. A. Low, MD,* P. E. Caskey, MSEE,† R. R. Tuck, MBBS, PhD,* R. D. Fealey, MD,* and P. J. Dyck, MD*

We have quantified postganglionic sweat output in human subjects resulting from axon reflex stimulation using acetylcholine electrophoresis. Dehumidified nitrogen of controlled temperature and flow rate was passed through an acrylic plastic chamber placed over a defined area of skin. Sweat droplets were evaporated; humidity change was sensed by a narrow-range humidity sensor housed in a temperature-controlled compartment and was plotted on a chart recorder. The time integral (area under the curve) was continuously integrated and converted to absolute units using a derived equation. Because stimulation and recording were simultaneous, an accurate determination of the latency of the sweat response was also possible.

Quantitative sudomotor axon reflex tests were performed on the left forearm and foot of 33 female and 29 male normal subjects aged 11 to 69 years. Acetylcholine, 10%, was electrophoresed for 5 mA-minutes in the forearm and 10 mA-minutes in the foot, and recording was continued for an additional 5 minutes. The mean sweat output in males was 2.7 and 3.0 times that in females in forearm and foot, respectively ($p < 0.0001$). Studies in selected autonomic neuropathies confirm that quantitative sudomotor axon reflex tests will detect postganglionic sudomotor abnormalities sensitively and reproducibly.

Low PA, Caskey PE, Tuck RR, Fealey RD, Dyck PJ: Quantitative sudomotor axon reflex test in normal and neuropathic subjects. Ann Neurol 14:573–580, 1983

The sympathetic postganglionic neuron may be involved in the dysautonomias [22, 36] or as part of a generalized peripheral neuropathy [23]. A useful index of sympathetic innervation is the integrity of exocrine sweat gland function, because this gland is innervated by sympathetic cholinergic fibers whose function is abolished by sympathectomy [19]. Modern techniques for quantitating postganglionic sudomotor function have not been developed as rapidly as similar measurements of motor and sensory function, however [3]. Recent suggestions that abnormalities of small myelinated and unmyelinated axons are more easily reversed than are abnormalities of large myelinated fibers in treated patients with diabetic neuropathy [15, 16] highlight the need for improved quantitation of postganglionic autonomic function to permit early detection of dysautonomia and to monitor more accurately the course of autonomic neuropathies and their response to treatment. We have recently developed methodology to record sweat output in human subjects accurately, reproducibly, and dynamically with simultaneous axon reflex stimulation using a quantified stimulus.

Methods

Subjects

The quantitative sudomotor axon reflex test (Q-SART) was studied using 62 healthy volunteers with no neurological illness or dermatological disease. Their ages ranged from 11 to 69 years. There were 29 males and 33 females; the age difference between the sexes was not significant (mean ages: males, 38.0 ± 17.8 [standard deviation]; females, 37.6 ± 18.0). In addition to reviewing the coded diagnosis to exclude subjects with diseases known to affect autonomic function, we administered to all healthy subjects a detailed questionnaire concerning medications, injuries, disease, and levels of alcohol intake that might impair autonomic function.

The patient group consisted of 20 patients with peripheral neuropathies and 4 patients who had undergone surgical sympathectomies for extremity pain. All patients were examined by at least one of the neurologists. Electromyography and nerve conduction studies were performed on 19 of the 21 patients with neuropathy. Thermoregulatory sweat tests (TST) were performed on 12 of 24 patients. Sural nerve biopsy was done on 7 of the 21 neuropathic patients.

Patient data are summarized in Table 1. These patients fell into three categories. Category A included patients 1 to 11, who had peripheral neuropathies thought to be associated with active axonal degeneration. Patients were assigned to category A if they fulfilled at least two of the following criteria: (1) prominent positive symptoms (burning pain and paresthesias), (2) nerve biopsy evidence of prominent axonal degeneration, and (3) electromyographic evidence of prominent fibrillation potentials in the lower extremities. Category B included patients 16 to 24, who by the criteria just listed were not thought to have active axonal degeneration. Category C included patients 12 to 15, who had had surgical sympathectomies.

From the *Autonomic Reflex Laboratory, Department of Neurology, and the †Section of Engineering, Mayo Clinic and Foundation, Rochester, MN 55905.

Received Jan 28, 1983, and in revised form Apr 5, 1983. Accepted for publication Apr 12, 1983.

Address reprint requests to Dr Low.

Table 1. Patient Data

Patient No., Sex, Age	Diagnosis	Dysautonomia	Thermoregulatory Hypohidrosis		Q-SART					
					Forearm			Foot		
			Peripheral[a]	Regional[b]	Latency (min)	Volume ($\mu l/cm^2$)	Abnormal Result	Latency (min)	Volume ($\mu l/cm^2$)	Abnormal Result
1, M, 44	Diabetic neuropathy; mild distal sensorimotor involvement	−	+	−	0.8	4.2	±	2.4	0.23	+
2, M, 56	Diabetic neuropathy; painful autonomic neuropathy	+	ND		0.9	2.2	±	1.9	1.4	−
3, F, 34	Idiopathic painful autonomic neuropathy	+	−	+	6.0	0.04	+	. . .	0	+
4, F, 11	Idiopathic painful relapsing neuropathy	−	ND		−	0	+	. . .	0	+
5, M, 62	Monoclonal gammopathy with neuropathy	−	ND		1.8	1.87	−	. . .	0	+
6, F, 56	Idiopathic painful neuropathy	−	−	−	0.7	0.56	±	0.8	0.57	±
7, F, 41	Idiopathic asymmetrical painful neuropathy	−	− (mild)	−	1.0	3.15	−	3.9	0.08	−
8, F, 58	Idiopathic asymmetrical painful neuropathy	−	−	−	2.3	0.01	+	. . .	0	+
9, F, 46	Monoclonal gammopathy with asymmetrical painful neuropathy	−	− (right foot)	−	1.8	0.73	−	. . .	0	−
10, F, 65	Amyloid neuropathy; small fiber > large fiber involvement	±	−	+	1.9	1.49	−	. . .	0	+
11, M, 66	Amyloid neuropathy; associated polycythemia rubra vera	+	−	+	1.2	4.19	−	2.6	0.91	+
12, M, 75	Right lumbar sympathectomy 5 wk previously	−	−	−	ND	ND	ND	. . .	0	+
13, M, 73	Right lumbar sympathectomy 2 yr previously	−	ND		ND	ND	ND	. . .	0	+
14, F, 16	Left lumbar sympathectomy 3 yr previously	−	ND		2.2	1.53	−	. . .	0	+
15, M, 53	Right thoracic sympathectomy 10 mo previously	−	−	+	0.5	2.02	±	ND	ND	ND
16, F, 13	Guillain-Barré syndrome	±	ND		1.7	0.79	−	2.1	2.77	−
17, M, 40	Chronic inflammatory demyelinating neuropathy	−	ND		2.4	1.00	−	1.7	3.90	−
18, M, 49	Chronic inflammatory demyelinating neuropathy	−	ND		1.8	1.52	−	3.1	1.48	−
19, M, 24	Chronic inflammatory demyelinating neuropathy (? inherited)	−	ND		1.5	2.10	−	. . .	N	−
20, M, 43	Chronic inflammatory demyelinating neuropathy	−	ND		1.7	3.56	−	1.6	3.24	−
21, M, 32	Chronic inflammatory demyelinating neuropathy	−	−	−	1.4	3.11	−	1.3	6.89	−

Table 1. (Continued)

Patient No., Sex, Age	Diagnosis	Dysautonomia	Thermoregulatory Hypohidrosis		Q-SART					
					Forearm			Foot		
			Peripheral[a]	Regional[b]	Latency (min)	Volume ($\mu l/cm^2$)	Abnormal Result	Latency (min)	Volume ($\mu l/cm^2$)	Abnormal Result
22, F, 64	Subacute combined degeneration	±	ND		0.6	3.6	±	1.0	0.84	–
23, F, 62	Monoclonal gammopathy with neuropathy	–	ND		ND	ND	ND	1.3	1.15	–
24, F, 25	Familial dysautonomia	+	–	–	1.1	4.26	–	0.7	4.83	–
Control subjects (5th to 95th percentile)										
Male					1.0–2.4	1.04–3.99		1.0–3.3	1.01–5.73	
Female					1.0–2.4	0.14–2.10		1.3–4.1	0.11–3.11	

[a]Sock and glove pattern of hypohidrosis.
[b]Anatomical regions and usually extensive hypohidrosis.

Q-SART = quantitative sudomotor axon reflex test; M = male; F = female; + = present; – = absent; ± = equivocal, transient, or mild; ND = not done; N = normal study but no accurate values.

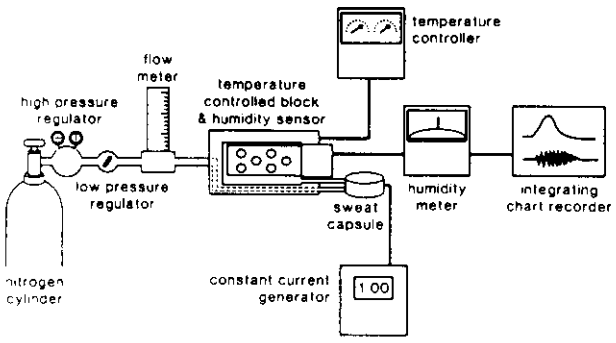

Fig 1. Mayo sudorometer and constant-current generator. See text for details.

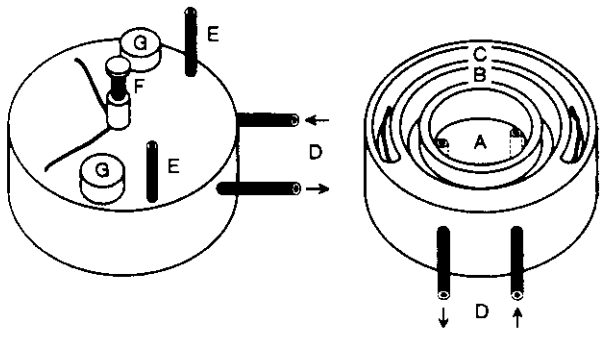

Fig 2. Sweat cell. (A = *recording compartment;* B = *air gap;* C = *acetylcholine well;* D = *gas inlet and outlet;* E = *cannulae for filling acetylcholine well;* F = *anode with extension into acetylcholine well;* G = *attachment posts for straps.*)

Procedures

The sudorometer used is diagramed in Figure 1. Dry nitrogen gas (2 to 5% absolute humidity) was passed through a flow regulator (Fisher Scientific, Minneapolis, MN) and precision flow meter (Lab Crest Scientific, Warminster, PA) at a controlled flow rate (usually 85 cc per minute) into a temperature-controlled stainless steel block housing a narrow-range humidity sensor (Hygrodynamics; American Instrument Co, Silver Spring, MD). The temperature of the block was set at 100°F and controlled by feedback (Yellow Springs Instrument, Model 74, Yellow Springs, OH). The heated nitrogen of known flow rate and humidity, by passing through a sweat cell attached to the skin by an elastic strap, caused total evaporation of sweat produced in the defined area of skin under study. This nitrogen stream of altered humidity returned to the stainless steel block, where relative humidity change (ΔRH) was measured with an accuracy of greater than 0.1% (relative humidity meter, Hygrodynamics). The ΔRH was plotted on a strip chart recorder (Linear, Model 282, Irvine, CA) with simultaneous integration of the area under the curve.

The sweat cell (Fig 2) consisted of a central recording compartment *(A)* 1 cm in diameter surrounded by an air gap *(B)* 1.5 mm wide separating the recording compartment from a semicircular well *(C)* 1.5 mm wide that was filled with 10% acetylcholine (ACh) before application of a constant current. Nitrogen was passed through a gas inlet and outlet *(D)*. The well was filled from above via a cannula *(E)*, and any residual air was forced out a second cannula. ACh was electrophoresed using a constant-current generator designed and constructed at the Mayo Section of Engineering. The circuit will pass up to 6 mA and has a digital display. The anodal current was passed by means of extensions *(F)* into the ACh well. The cathode was a 4 × 6 cm rectangular strip of lead wrapped in flannel and soaked in 150 mM sodium chloride. A stimulus of 1 mA routinely was used. ACh 10% wt/wt (Fisher Scientific) was made twice weekly and stored in a refrigerator at approximately 1°C. Attachment posts *(G)*

were available on the sweat cell to facilitate attachment of the cell to the test site.

All recordings were done in the Autonomic Reflex Laboratory with the subject supine. Room temperature was maintained at 80°F and relative humidity at approximately 50%. Recordings were made at two sites: (1) the left forearm, 25% of the distance from the pisiform bone to the ulnar epicondyle and immediately medial to the palmaris longus tendon, and (2) over the left extensor digitorum brevis muscle. The area was cleaned with soap and water and shaved if necessary. A surface thermistor probe (Bat 8 digital thermometer, Bailey Instruments, Saddlebrook, NJ) was attached adjacent to the sweat chamber. The axon reflex sweat response is optimal near the thermal threshold for sweat activity [9] of about 34.5°C [35]. We warmed the upper extremity to 32°C and the lower extremity to 31°C so as to maintain skin temperatures that were consistent but below the thermal threshold. The stimulus for the forearm was 1 mA for 5 minutes, and the recording was then continued for an additional 5 minutes. The stimulus for the foot was 1 mA for 10 minutes, and the recording was continued for an additional 5 minutes after cessation of the stimulus.

The absolute sweat output was calibrated by injecting known volumes of water onto a small square of filter paper contained within the sudorometer. In a typical calibration 0.5, 1, 2, 5, and 10 μl volumes of water are injected sequentially and the area of the ΔRH time curve is regressed against the test volumes. The data are well fitted by a linear regression with typical correlations of $r > 0.9$. We have found this direct calibration more reliable than suggested equations [13, 14].

Data were stored in a computer (HP9845T; Hewlett Packard Data Manipulation and Statistical Analysis Program) and graphically displayed, and group values were tested for normality (skewness, kurtosis, and chi-square goodness of fit). Normally distributed data were compared using a one-tailed Student *t* test. Nongaussian distributed data were analyzed using the Mann-Whitney test. Regression analysis was done using least squares fit (Hewlett Packard General Statistics Program). For evaluation of test reproducibility on different days, the same test was repeated on 10 subjects on another day. The values of each member of a pair were regressed against the other member and least squares fit obtained.

Results

Control Subjects

We initially determined whether the response was caused by ACh and whether it was the result of an axon reflex. We did not encounter leakage of fluid between the stimulating and recording compartments. When isotonic saline was used instead of ACh and the standard stimulus was applied to the forearm, a sweat response was not evoked (Fig 3, "current + saline"). When a current was passed in the presence of ACh, a normal response was evoked (Fig 3, "current + acetylcholine"). In 2 subjects 2% xylocaine was infiltrated circumferentially between the ACh well and the recording compartment. Electrophoresis of ACh failed to evoke a sweat response (Fig 3, "xylocaine infiltration"). In the same subjects a similar infiltration with isotonic

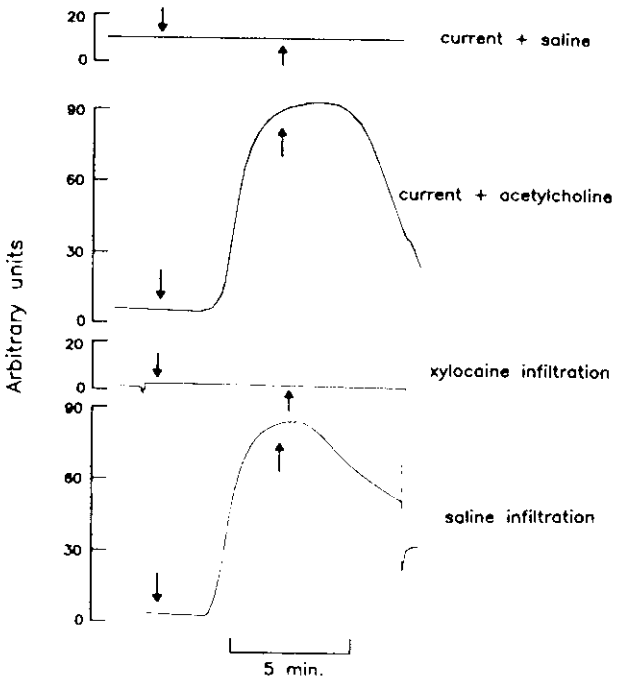

Fig 3. In the first trace (current + saline), *acetylcholine has been omitted and a sweat response has not been obtained. The second trace* (current + acetylcholine) *shows a typical response. In the third trace* (xylocaine infiltration), *local anesthetic infiltration of skin separating the stimulus well and the recording chamber has completely blocked the response. In the fourth trace* (saline infiltration), *infiltration with an identical volume of isotonic saline of the same area of skin has not blocked the sweat response. Arrows indicate onset* (↓) *and cessation* (↑) *of electrophoresis.*

saline (Fig 3, "saline infiltration") did not block the sweat response, suggesting that the block by local anesthetic was a result of its known physiological effects on ionic channel block of the axon rather than any mechanical effect.

We examined the reproducibility of the sweat response obtained on the skin area (marked with an indelible pen) in 3 subjects with minimal, small, and moderate responses, respectively, when the study was repeated on different days. The Q-SART was done on 3, 4, and 7 separate occasions, respectively, and appeared to be quite reproducible (Fig 4A). In 10 subjects (5 men, 5 women, aged 17 to 63 years), the sweat output was measured on two occasions on the same recording site (left forearm) on different days to evaluate day-to-day variability. When the values of the first recording were regressed against the second, a highly significant regression was obtained ($r = 0.95$, $p < 0.001$) (Fig 4B).

The normal response (see Fig 3) consisted of an abrupt increase in humidity that usually appeared 1 to 2 minutes after the commencement of the stimulus and persisted for several minutes. There was an associated flare response (reflex vasodilatation). Representative normal and abnormal responses are shown in Figure 5.

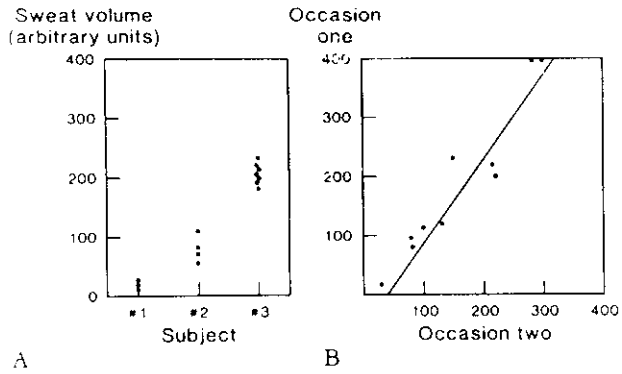

Fig 4. (A) Day-to-day variation in recordings of sweat output from subjects with moderate (#3), small (#2), and minimal (#1) sweat volume. (B) Sweat output (in arbitrary units) on occasion one regressed against the output on a different day for 10 subjects. $Y = 1.36X - 28.78$; $r = 0.95$.

Median latency and volume for sweat output from the forearm were 1.7 minutes and 0.97 $\mu l/cm^2$, respectively, in females for the 10 minutes of recording. Fifth to 95th percentile values were 1.0 to 2.4 minutes and 0.14 to 2.10 $\mu l/cm^2$ for latency and volume, respectively. Corresponding values for males were 1.8 minutes and 2.6 $\mu l/cm^2$ and 1.0 to 2.4 minutes and 1.04 to 3.99 $\mu l/cm^2$, respectively. The latency was not significantly different ($p = 0.17$) between the sexes. The median sweat volume in males of 2.7 times that in females represented a significant difference ($p < 0.0001$).

For the 15 minutes of recording, median latency and volume for sweat output from the foot in females were 2.5 minutes and 1.18 $\mu l/cm^2$, respectively. Fifth to 95th percentile values were 1.3 to 4.1 minutes and 0.11 to 3.11 $\mu l/cm^2$ for latency and volume, respectively. Corresponding values for males were 2.3 minutes and 3.6 $\mu l/cm^2$ and 1.0 to 3.3 minutes and 1.01 to 5.73 $\mu l/cm^2$, respectively. The median sweat output in males was 3 times that in females, and the difference between groups was statistically significant ($p < 0.0001$). The latency was not significantly different between the sexes.

There was no statistically significant reduction in sweat volume with age for either sex (Table 2). In males there was a significant decrease in latency with age in both forearm and foot. The slope for females did not reach statistical significance.

Fig 5. Representative recordings from a normal control female subject (top panel) *and 2 patients. The middle panel shows an absent response in the foot and an unusually large response with reduced latency in the forearm of a patient with neuropathy* (Patient 1). *The bottom panel* (Patient 2) *shows essentially absent responses in forearm and foot. Arrows indicate onset* (↓) *and cessation* (↑) *of electrophoresis.*

Patients with Peripheral Nerve Abnormalities

Ten of the 12 patients (83%) in category A had abnormal Q-SART responses (9 with reduced or absent sweat volume; 1 with the lesser abnormality of a shortened latency). In the forearm, 6 of 11 patients (55%) showed abnormalities (3 had reduced sweat volumes and 3 had a change in latency). These findings support the clinical observation of usually earlier and more severe lower than upper extremity involvement in neuropathies. In contrast, patients in category B had completely normal responses in the foot (9 of 9) and only 1 patient of 7 had a mild abnormality (reduced latency) in the forearm. All 3 patients with lumbar sympathectomies had absent sweat responses in the appropriate foot. The patient who had a thoracic sympathectomy had a normal postganglionic sweat volume but reduced latency. His surgery was thought to be preganglionic and the sympathectomy partial.

Twelve of the 24 patients also had a TST, with areas of hypohidrosis or anhidrosis delineated with alizarin red indicator [24]. Of these 12 patients, 8 were in category A and 8 of 8 had both abnormal TST patterns and an abnormal Q-SART (7 of 8 had reduced or absent sweat volume; 1 of 8 had altered latency) in the foot. A smaller proportion, 3 of 8 (38%), had abnormalities affecting the forearm (1 of 8 had absent sweat volume; 2 of 8 had altered latency). TSTs were done on

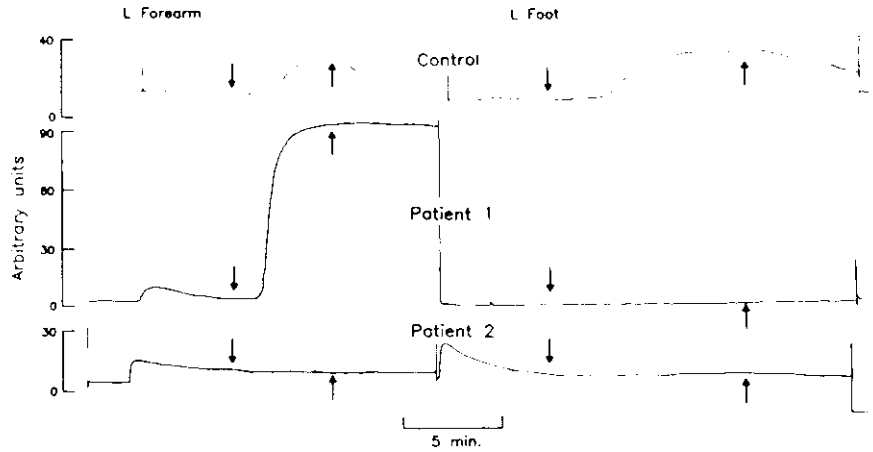

Table 2. Effect of Age on Latency and Volume Measures in Quantitative Sudomotor Axon Reflex Test in Female and Male Control Subjects

Measure	Sex of Subjects	Intercept	Regression Coefficient (*b*)	*r*
Latency (forearm)	F	1.80 min	−0.003	0.1
	M	2.69 min	−0.020[a]	0.4
Volume (forearm)	F	1.21 μl/cm²	−0.004	0.1
	M	2.14 μl/cm²	0.008	0.1
Latency (foot)	F	2.90 min	−0.006	0.1
	M	3.27 min	−0.024[b]	0.6
Volume (foot)	F	2.33 μl/cm²	−0.022	0.3
	M	4.54 μl/cm²	−0.196	0.2

Statistical significance: [a]$p < 0.025$; [b]$p < 0.005$.

F = female; M = male.

2 patients in category B. Both TST and Q-SART were normal in these subjects. A TST was done on the patient with a thoracic sympathectomy and showed a hypohidrotic right upper extremity. The sweat volume was normal, but the latency was shortened; the sweat output in response to intradermal injection of 0.1 cc 10% ACh was almost identical to the Q-SART response. The Q-SART response was thought to be compatible with a preganglionic lesion. Both the TST and Q-SART studies indicated anhidrosis in the relevant limb in the 3 patients with lumbar sympathectomies.

Discussion

When a focal area of skin is stimulated electrically [2, 34] (faradic sweat response) or with a parasympathomimetic agent [5–8, 17, 18] (such as ACh), there is a brief latent period followed by an outbreak of sweating occupying an area 3 to 5 cm in diameter surrounding the point of stimulation [5–8, 17–19, 22]. This is the axon reflex sweat response. When the stimulus is ACh, this response, often designated the nicotinic response, can be differentiated from the muscarinic response [18], which is caused by the direct stimulation of sweat glands [6]. Pressure from a fine rubber band (which has been shown to block diffusion but not nerve transmission [32]) will limit the muscarinic but not affect the nicotinic response [32]. In contrast, if a local anesthetic such as procaine is infiltrated to one side of the stimulus, it will block the reflex sweat response on the relevant side but spare the muscarinic response [8, 32]. The reflex is local, because it persists immediately following sympathectomy [8] or proximal nerve trunk lesioning [8]; the reflex is also preserved in the freshly excised toe pad of the cat [8]. The reflex appears to be mediated entirely by sympathetic postganglionic fibers and is lost days to weeks following postganglionic sympathectomy [18, 32]. The somatic sensory neuron does not appear to participate in the reflex, because electrical stimulation of dorsal root in the cat will not activate this reflex, whereas stimulation of ventral spinal root will cause sweating in its area of supply [6]. Although the axon reflex sweat response provides an excellent test of postganglionic sympathetic function, many of its neuroanatomical and physiological characteristics are assumed rather than demonstrated. There appears to be an afferent and efferent limb, the latter being cholinergic and blocked by atropine. Impulses are thought to travel centripetally along postganglionic axons, arrive at branch points, and then travel centrifugally down the efferent limb [6, 8]. The pharmacological characteristics of the afferent limb are less clearly delineated. The receptor has not been defined. It is not known if it is the nerve terminal, axon, sweat gland, or some other receptor. It is also not known why tetraethylammonium and related ganglion blockers will block the afferent limb [6, 17, 18].

The sweat response has been recorded by a color change [1, 20, 29], a change in skin resistance [28], or a sweat print (imprinted on a soft medium [11, 25]). More accurate quantitation of sweat volume has been made by sudorometry based on recording the humidity change of an airstream of defined flow using sensitive humidity sensors [4, 13, 14, 27]. These recordings were performed at room temperature, and the temperature of the inflowing stream was not controlled [4, 14, 27]. In the Mayo sudorometer dehumidified nitrogen of controlled temperature and flow rate was used, and the studies were done under standard conditions of room temperature and humidity. Limb temperature was also controlled. A further improvement is the direct calibration of the time integral of the recorded output against known volumes of calibrating solution. The most important innovation is the simultaneous recording and axon reflex stimulation using ACh electrophoresis, providing a dynamic recording of the sweat response with the indices of latency, volume, and amplitude. Through axon reflex stimulation we avoid potential problems inherent in direct sweat gland stimulation [26]: false positive responses resulting from skin hydration (by the electrophoresed test solution) or direct chemical stimulation of sweat glands, which may be transiently supersensitive following denervation [6, 21].

The dimensions and geometry of the sweat cell were designed to optimize the recording of axon reflex sweat response. The 1 cm diameter of the recording compartment is much smaller than the typical diameter of approximately 5 cm in axon reflex sweat responses [5, 8]. The air gap provides added security against fluid leak. The recording chamber is surrounded by two circumferentially arranged ridges 1 mm wide, which, like the rubber band used in early work [32], permit axon reflex responses while preventing diffusion of chemicals from the stimulation well to the recording compartment.

The median sweat volume in males was 2.7 and 3.0 times that of females in the forearm and foot, respectively. Such large sex differences in axon reflex sweat response have been reported previously [12, 14, 17, 18, 31]. Kahn and Rothman [18] found a slight or absent response in 90% of the 41 females they studied. With our sensitive method, we did not record any absent responses, although minimal responses were often found in females. The latency of the Q-SART was not different in the two sexes, so that the threshold was not different. Previous workers have not found a statistically significant difference in threshold between sexes [5, 26].

The correlation between the TST and the Q-SART is good. Patients who have a peripheral pattern of anhidrosis (suggesting postganglionic denervation) have reduced or absent Q-SART responses. The measurable response in many of these patients is important in that it offers the potential to monitor improvement or deterioration in sudomotor innervation. The short latency and sometimes exaggerated output seen in some partially denervated areas (see Fig 5) is of interest. The sweat response is evoked by a smaller charge (current-time) and indicates a reduction in Q-SART threshold. The mechanism of this pattern of response remains to be explored. Electrophoresed ACh must (1) traverse sweat gland epithelium and (2) stimulate the axon reflex receptor(s). The nerve impulse must then (3) conduct along axonal pathways and (4) traverse a neuroglandular junction to (5) stimulate a second set of exocrine sweat glands at a distant site. The time required for steps 3 through 5 is brief (less than 1 second) [10, 30, 33]. Steps 1 and 2 are much slower, and the abnormalities are likely to be found here. With increasing age, males undergo a significant shortening of latency, a finding not seen in females.

Presumably demyelinating neuropathies with little axonal degeneration (on nerve biopsy; absent positive symptoms, lack of fibrillation on electromyogram) have largely normal Q-SART responses. In contrast, patients with presumably prominent, active axonal degeneration have abnormal Q-SART responses. This relationship needs further substantiation but suggests that the test has potential value in predicting the course of a neuropathy, because those neuropathies with much axonal degeneration recover more slowly and less completely. Another potential value of this sudorometer is in apportioning preganglionic and postganglionic involvement in certain neuropathies. We have been able to do this in a few patients by performing a Q-SART study and then a TST and recording the sweat output from the identical area using the sudorometer. In normal subjects the sweat volume evoked by TST exceeds that produced by ACh. When there is involvement of both preganglionic and postganglionic fibers (as in some cases of amyloid neuropathy), the TST evoked sweat volume is much smaller than the Q-SART volume. The reproducibility of Q-SART responses within subjects is quite good, so this test also provides a tool to diagnose autonomic postganglionic involvement and to monitor the course of an autonomic neuropathy and its response to treatment.

Supported in part by Mayo Funds. The authors acknowledge the statistical advice of Peter O'Brien, PhD, Department of Medical Statistics and Epidemiology, and the technical assistance of Carolene Neumann and Marceil Blexrud, Autonomic Reflex Laboratory.

References

1. Barany FR, Cooper EH: Pilomotor and sudomotor innervation in diabetes. Clin Sci 15:533–540, 1956
2. Bickford RG: The mechanism of local sweating in response to faradism. Clin Sci 3:337–341, 1938
3. Buchthal F, Rosenfalck A, Behse F: Sensory potentials of normal and diseased nerves. In Dyck PJ, Thomas PK, Lambert EH (eds): Peripheral Neuropathy, Vol 1. Second edition. Philadelphia, Saunders, 1975, pp 442–464
4. Bullard RW: Continuous recording of sweating rate by resistance hygrometry. J Appl Physiol 17:735–737, 1962
5. Chalmers TM, Keele CA: The nervous and chemical control of sweating. Br J Dermatol 64:43–54, 1952
6. Collins KJ, Weiner JS: Axon reflex sweating. Clin Sci 21:333–344, 1961
7. Coon JM, Rothman S: Nature of a sweat response to drugs with nicotine-like action. Proc Soc Exp Biol Med 42:231–233, 1939
8. Coon JM, Rothman S: The sweat response to drugs with nicotine-like action. J Pharmacol 73:1–11, 1941
9. Cooper KE, Johnson RH, Spalding JMK: The effects of central body and trunk skin temperatures on reflex vasodilatation in the hand. J Physiol 174:45–54, 1964
10. Fagius J, Wallin BG: Sympathetic reflex latencies and conduction velocities in normal man. J Neurol Sci 47:433–448, 1980
11. Ferreira AJ, Winter WD: Age and sex differences in the palmar sweat print. Psychosom Med 27:207–211, 1965
12. Gibson TE, Shelley WB: Sexual and racial differences in the response of sweat glands to acetylcholine and pilocarpine. J Invest Dermatol 11:137–142, 1948
13. Gordon BI, Maibach HI: Effect of systemically administered epinephrine on palmar sweating. Arch Dermatol 92:192–194, 1965
14. Gordon BI, Maibach HI: Studies of acetylcholine- and methacholine-induced sweating. Arch Dermatol 94:778–781, 1966
15. Greene DA, Brown MJ, Braunstein SN, et al: Comparison of clinical course and sequential electrophysiological tests in diabetics with symptomatic polyneuropathy and its implications for clinical trials. Diabetes 30:139–147, 1981
16. Hreidarsson AB: Acute, reversible autonomic nervous system abnormalities in juvenile insulin-dependent diabetes. Diabetologia 20:475–481, 1981
17. Janowitz HD, Grossman MI: The response of the sweat glands to some locally acting agents in human subjects. J Invest Dermatol 14:453–458, 1950
18. Kahn D, Rothman S: Sweat response to acetylcholine. J Invest Dermatol 5:431–444, 1942
19. Kuno Y: Human Perspiration. Springfield, IL, Charles C Thomas, 1956
20. List CF, Peet M: Sweat secretion in man. I. Sweating responses in normal persons. Arch Neurol Psychiatry 39:1228–1237, 1938

21. List CF, Peet MM: Sweat secretion in man. III. Clinical observations on sweating produced by pilocarpine and mecholyl. Arch Neurol Psychiatry 40:269–290, 1938
22. Low PA: Quantitation of autonomic function. In Dyck PJ, Thomas PK, Lambert EH, Bunge R (eds): Peripheral Neuropathy, Vol 3. Second edition. Philadelphia, Saunders, 1983 (in press)
23. Low PA, Stevens JC: Peripheral and autonomic neuropathy. In Spittell JA (ed): Clinical Medicine. Hagerstown, MD, Harper & Row, 1981, pp 1–31
24. Low PA, Walsh JC, Huang CY, McLeod JG: The sympathetic nervous system in diabetic neuropathy: a clinical and pathological study. Brain 98:341–356, 1975
25. MacKinnon PCB: Variations with age in the number of active palmar digital sweat glands. J Neurol Neurosurg Psychiatry 17:124–126, 1954
26. MacMillan AL, Spalding JMK: Human sweating response to electrophoresed acetylcholine: a test of postganglionic sympathetic function. J Neurol Neurosurg Psychiatry 32:155–160, 1969
27. Neumann C, Cohn AE, Burch GE: A quantitative method for the measurement of the rate of water loss from small areas, with results for finger tip, toe tip and postero-superior portion of the pinna of normal resting adults. Am J Physiol 132:748–769, 1941
28. Richter CP: Instructions for using the cutaneous resistance recorder, or "dermometer," on peripheral nerve injuries, sympathectomies, and paravertebral blocks. J Neurosurg 3:181–191, 1946
29. Silverman JJ, Powell VE: A simple technique for outlining the sweat pattern. War Med 7:178, 1945
30. Sourek K: The Nervous Control of Skin Potentials in Man. Prague, Rozpravy Československé Akademie Věd, 1965
31. Stoughton RB: Physiological changes from maturity through senescence. JAMA 179:142–144, 1962
32. Wada M, Arai T, Takagaki T, Nakagawa T: Axon reflex mechanisms in sweat responses to nicotine, acetylcholine and sodium chloride. J Appl Physiol 4:745–752, 1952
33. Wang GH: The galvanic skin reflex: a review of old and recent works from a physiologic point of view. Am J Phys Med 37:35–57, 1958
34. Wilkins RW, Newman HW, Doupe J: The local sweat response to faradic stimulation. Brain 61:290–297, 1938
35. Winslow CEA, Herrington LP, Gagge AP: Physiological reactions of the human body to varying environmental temperatures. Am J Physiol 120:1–22, 1937
36. Young RR, Asbury AK, Corbett JL, Adams RD: Pure pandysautonomia with recovery: description and discussion of diagnostic criteria. Brain 98:613–636, 1975