HISTORICAL ARTICLE

Carl Reinhold August Wunderlich and the Evolution of Clinical Thermometry

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"But in science the credit goes to the man who convinces the world, not the man to whom the idea first occurs."
—Sir Francis Darwin

For >100 years, the thermometer has been used by physicians as a clinical divining rod for ferreting out true disease among the many aches and minor perturbutations of otherwise healthy existence. Over this period, clinical thermometry has become such an integral part of everyday life that its origins are shrouded in a misty general suspicion that the body temperature has probably always been monitored as a means of distinguishing health from disease. Few but the most devoted medical historians could give more than a rudimentary account of the origins of the thermometer or of clinical thermometry. Fewer still could identify the source or explain the pertinacity of the generally accepted notion that 98.6°F (37°C) is the normal temperature. Although most people believe that there is a specific temperature that defines the lower limits of the febrile range, there is not a consensus as to what this temperature is, in spite of the fact that the generally accepted definitive work on clinical thermometry clearly identified the limit as 100.4°F (38°C) [1].

One man casts a longer shadow than any other over the history of the clinical application of the thermometer. Carl Reinhold August Wunderlich (figure 1), who lived during a pivotal period in the evolution of clinical thermometry, published an opus magnus in 1868, which persists to this day as the definitive work on the subject. In the book *Das Verhalten der Eigenwärme in Krankheiten* (*The Course of Temperature in Diseases*) [1], Wunderlich gave 98.6°F (37°C) its special significance vis-à-vis the normal temperature [2]. He described diurnal variation of the body temperature and, in the process, alerted clinicians to the fact that the "normal temperature" is a temperature range rather than a specific temperature. In an analysis of temperature measurements obtained from a patient population whose size has never been equaled, he established 100.4°F (38°C) as the upper limit of the normal range and, in so doing, proffered the first quantitative definition for fever. He showed that women normally have slightly higher temperatures and exhibit greater thermal variability than do men. He also reported that old people tend to have lower normal temperatures than do young people.

In spite of the fact that Wunderlich's work was published over a century ago and was based primarily on axillary measurements, which were generally taken no more often than twice daily, it has survived almost verbatim in modern day concepts of clinical thermometry. More important, because of his work, Wunderlich is generally regarded as the father of clinical thermometry.

The Man

At the time of Wunderlich's birth at Sulz on the Neckar, Germany, on 15 August 1815, the guns of the great powers of Europe still littered the battlefield at Waterloo. Prince Otto Eduard Leopold von Bismarck, who would unify Germany and claim for it the mantle of power left vacant as a result of the collapse of Napoleon's empire, was 4 months old. Both Bismarck and Wunderlich would become instruments of the intellectual revolution that consumed the nineteenth century. However, unlike Bismarck and many of the great physicians of the epoch, Wunderlich would forgo direct participation in the simultaneously occurring social and political revolutions [3, 4].

Wunderlich's father worked in Ludwigsburg, Germany, as a government physician until his untimely death at the age of 51, thus leaving the education of his young son to the boy's French mother and maternal grandmother. Under their indulgent eyes, young Carl developed both a strong affinity for French culture and an aristocratic demeanor. The young "marquis," as he was known by his classmates, completed his premedical education in Stuttgart, Germany, before matriculating at the University of Tübingen (Tübingen, Germany), where he received a degree in medicine in 1838.

During his years as a student at the University of Tübingen, Wunderlich developed three critical relationships

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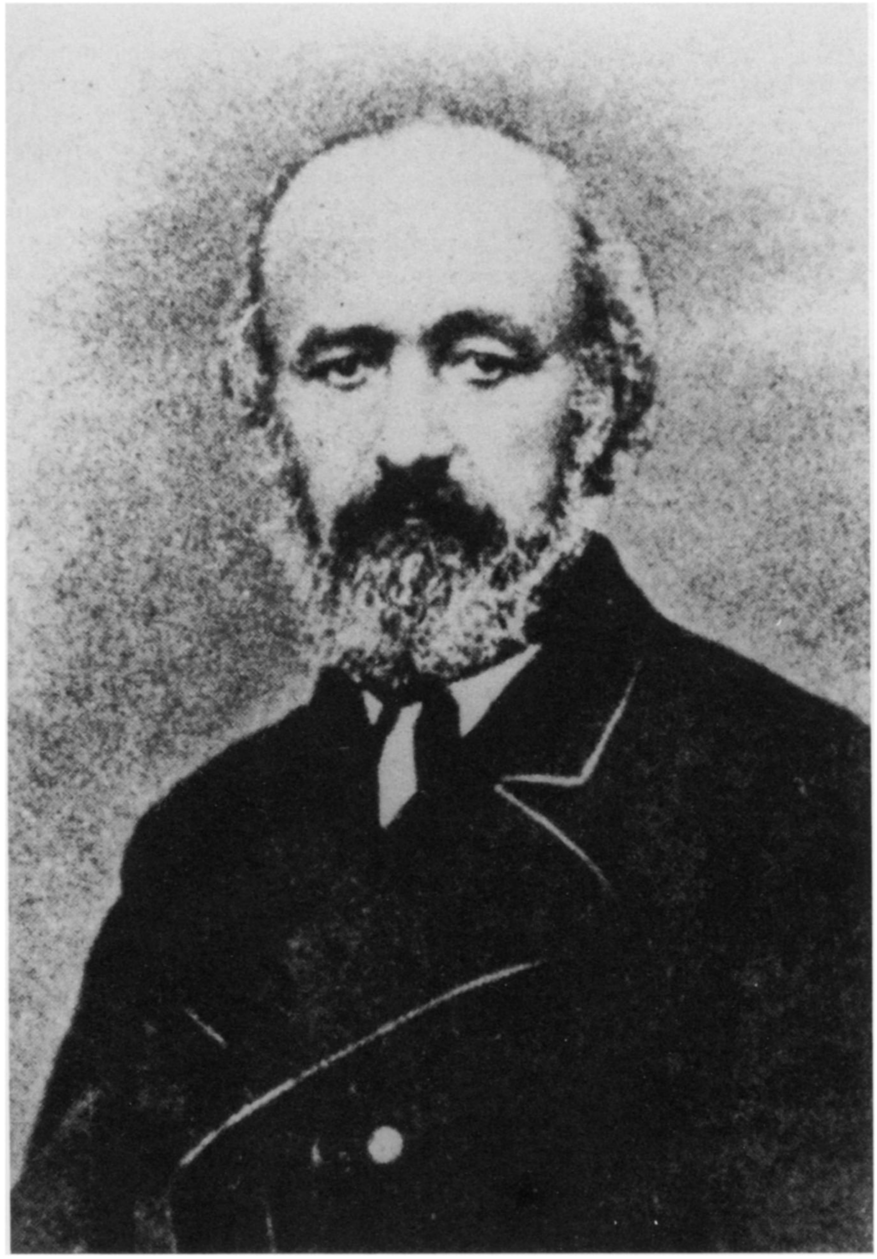

Figure 1. Carl Reinhold August Wunderlich (1815–1877) [4].

that would greatly influence his career. Albert Frederich Schill, a junior member of the faculty, taught the young medical student the importance of looking beyond the boundaries of his own country for a proper medical education. As a result of Schill's influence, Wunderlich studied the new art of percussion and auscultation in Paris and Vienna during three trips abroad between 1837 and 1839; he published an account of his experiences in 1840 in his first book entitled *Wien und Paris. Ein Beitrag zur Geschichte und Beurteilung der gegenwärtigen Heilkunde in Deutschland und Frankreich* (*Vienna and Paris. A Contribution on the History and Evaluation of Medicine in Germany and France*).

The two other important relationships established during the student years at the University of Tübingen were with Wilhelm Rosser and Wilhelm Greisinger, two fellow medical students with whom Wunderlich would found the *Archiv für Physiologische Heilkunde* (*Archives of Physiological Medicine*) in 1842. Through the Archives, the three joined their voices to a chorus of academic physicians clamoring throughout Germany for a new medicine based on scientific observation.

In 1841, Wunderlich accepted an appointment as an assistant at the Tübingen clinic and during the next 5 years published two additional books, one entitled *Versuch einer pathologischen Physiologie des Blutes* (*Examination of the Pathological Physiology of Blood*) (1845) and a three-volume work entitled *Handbuch der speziellen Pathologie* (*Handbook of Special Pathology*) (1846–1850). In 1846, at the age of 31, he was appointed Chief of Medicine at the Tübingen clinic. The promotion was initially opposed by the faculty of the Tübingen clinic, who resented the new chairman's aristocratic demeanor and his patent disregard for the traditional philosophic approach to medicine [3]. This early hostility was so intense, in fact, that the ministers of education of the kingdom of Württemberg, Germany, had to intercede on behalf of their young chairman. Wunderlich not only survived as chairman but also emerged as a leader among the new generation of German academic physicians. In 1850, he accepted the Chair in Medicine at the more prestigious University of Leipzig (Leipzig, Germany). He occupied the position for 25 years, during which time he published the highly regarded history of medicine *Geschichte der Medicin* (1858) and his masterpiece *Das Verhalten der Eigenwärme in Krankheiten* (1868).

Wunderlich completed the bulk of his work on clinical thermometry while at Leipzig. During the 18-year period before the publication of *Das Verhalten der Eigenwärme in Krankheiten*, he is believed to have supervised the examinations of some 25,000 patients in the University of Leipzig's medical clinic [2]. Several million temperature readings were reportedly obtained during these examinations. Wunderlich's analysis of these data produced 20 papers on clinical thermometry, in addition to his definitive book on the subject.

Wunderlich's later years were sad ones, owing to the loss of three of his children [5]. His youngest daughter's death in 1864 as a result of meningoencephalitis was perhaps his most painful loss. On 25 September 1877, at age 62, Wunderlich himself died of lymphosarcoma, leaving behind a legacy in clinical investigation that is the foundation of modern clinical thermometry.

Contributions in Perspective

"Discoveries and inventions," according to Bolton [6], "are sometimes the product of the genius or of the intelligent industry of a single person and leave his hand in a perfect state . . . . but more often the seed of the invention is planted by one, cultivated by others, and the fruit is gathered only after slow growth by someone who ignores the original sower." Such was the case with the thermometer.

The mercury thermometer used by Wunderlich to study patients in the clinic at Leipzig had been perfected in Holland in the early eighteenth century by Gabriel Daniel Fahrenheit [7, 8]. Fahrenheit's mentor, Herman Boerhaave (1668–1738), used the thermometer regularly in his clinical practice, as did two of Boerhaave's other pupils, van Sweeten and deHaen.

The seed of Fahrenheit's "invention" had many antecedent cultivators. In 1631, a French physician named Jean Rey produced the first liquid expansion (water) thermometer and, in the process, initiated a search that would eventually lead to the recognition of mercury's special properties as an ideal thermometric substance [9]. Ten years later, Grand Duke Ferdinand II of Tuscany developed the first hermetically sealed (alcohol) thermometer, thus eliminating the influence of fluctuations in barometric pressure on thermometric readings [10]. In 1665, Robert Boyle, Robert Hooke, and Christian Huygens suggested independently that thermometers could be calibrated effectively from a single fixed point [10]. Their work laid the foundation for the development of the first thermometric standard scale and ultimately enabled Fahrenheit to perfect his own scale based on the boiling point of water (212°), the freezing point of water (32°), and the temperature of the mouth of a healthy man (96°).

An alcohol forerunner of Fahrenheit's instrument was long believed to have been invented in 1608 by a Dutch peasant named Cornelius Drebbel [7]. However, Wohlwill and Burkhardt have pointed out that Casper Ens in his 1651 translation of Jean Leurechon's *La Récréation Mathématique* (1624) embellished a description of the thermometer contained therein by adding the adjective *Drebbelianum* to the word *instrumentum* [6]. Others copied the apocryphal phrase, thus incorporating it into the authorative literature. Drebbel, for his part, apparently never claimed the thermometer as his invention, nor is there convincing evidence that he ever used one [6].

It is reasonably certain that Galileo Galilei manufactured a primitive (air) thermometer at about the time he assumed the Chair in Mathematics at the University of Padua (Padua, Italy) (1592) [6]. The device, which Galileo called a *thermoscope*, consisted of "a glass vessel about the size of a hen's egg, fitted to a tube the width of a straw and about two spans long; . . . the bulb was heated and turned down so that the tube dipped in water held in another vessel; as soon as the bulb cooled, the water rose in the tube to the height of a span above the level in the vessel" [6, 11]. Since both atmospheric pressure and temperature affected the expansion and contraction of the thermometric substance (air) in Galileo's device, it was more appropriately termed a *barothermoscope* than a *thermoscope*, although its dependence on barometric fluctuations was not recognized until the invention of the barometer in 1643 [9].

Galileo's instrument was used by Santoria Santoria (Sanctorius, 1561–1636), a colleague at the University of Padua, in studies generally accepted as the first to incorporate quantitative measurement into medical investigation. Sanctorius recognized, and may well have been the first physician to do so, that the human body has a normal temperature, which can be monitored as an aid to diagnosis. The word *thermometer* surfaced in the literature during this period in Leurechon's *La Récréation Mathématique*, which mentioned use of the instrument to "test the intensity of fever."

Table 1. Examples of the great medical figures of Wunderlich's lifetime (1815–1877).

Jean Courvisart (1755–1821)	Joseph Skoda (1805–1881)
René Laennec (1781–1872)	Karl Rokitansky (1804–1878)
Pierre Louis (1787–1872)	Lucas Schoenlein (1793–1864)
Oliver Wendell Holmes (1809–1894)	Johan Meckel (1781–1833)
Armand Trousseau (1801–1867)	Theodor Schwann (1809–1885)
Guillaume Dupuytren (1777–1835)	Jacob Henle (1809–1885)
Robert Graves (1796–1853)	William Stokes (1804–1878)
Louis Pasteur (1822–1895)	D. J. Corrigan (1802–1880)
Paul Broca (1824–1880)	Richard Bright (1781–1858)
Carl Ludwig (1816–1895)	Thomas Addison (1783–1860)
Herman Helmholz (1821–1894)	Lord Lister (1827–1912)
Robert Koch (1843–1910)	Charles Brown-Séquard (1817–1894)

Devices for measuring the expansion property of air appear to have antedated even Galileo. In the second or first century B.C., Philon of Alexandria is believed to have invented several such devices [10]. Galileo's contribution, according to Abbe, was not to invent the instrument but simply to add a scale that could be used by Sanctorius to express the intensity of fevers [6].

Thus clinical thermometry, like the thermometer itself, evolved in staccato fashion over several centuries, with a host of investigators each adding his own small contribution to the concept. These efforts reached their climax in the nineteenth century. Most of what has been done since has consisted of little more than tinkering modifications of the great contributions of these earlier investigators.

The nineteenth century, particularly the years spanning Wunderlich's life, teemed with great medical minds (table 1) [12]. It was a time of global *Sturm und Drang*, in which the social, political, and intellectual dogma of centuries was battered into oblivion by a world newly awakened to the scientific method. It was a time of momentous events (table 2) [7].

Whereas, before the nineteenth century, medicine had been scientific in intention, by the time Wunderlich entered the University of Tübingen, it was fast becoming scientific in fact [12]. In contrast to the medicine of the Middle Ages and the Renaissance that had evolved, respectively, in libraries and at the individual sickbed, medicine of the nineteenth century flourished in hospitals necessitated by the urbanization that accompanied the industrial revolution. Clinical observation had become an obsession. Individual investigators actively observed massive patient populations using new techniques of physical diagnosis and quantitative measurement. Symptoms were no longer transmogrified intellectually to fit abstract precepts of romantic natural philosophy but were considered in light of lesions found at the autopsy table.

Germany embraced this new view of medicine reluctantly [12]. As a result, Teutonic revolutionaries like Wunderlich looked to France, Austria, England, and Ireland for early inspiration. Many, including Wunderlich, were able to study abroad because of modest stipends provided by the German government [3]. By the second half of the century, Germany became preeminent in medicine, largely as a result of its successful development and application of instruments involved in physiological experimentation and the advent of the full-time medical investigator.

Rudolph Virchow (figure 2) was prototypic of this new genre of investigator [12]. In contrast to Wunderlich, whose

Table 2. Some of the momentous events occurring during Wunderlich's lifetime (1815–1877).

Year	Event
1815	Battle of Waterloo
	Birth of the German Federation
	Laennec discovers mediate osculation
1818	Courvisart describes cardiac insufficiency
1819	Steamship crosses the Atlantic
1823	Lancet founded
1827	Merck starts wholesale manufacture of morphine
1828	Robert Brown describes Brownian movement
	Ohm's law stated
1829	Louis Braille introduces printing for the blind
	Daguerre introduces photography
1832	Faraday describes galvanic and magnetic induction
1835	Malcolmson describes beri beri
1836	Quelelet founds social statistics
	Registration of Birth and Deaths Act (England)
	Child labor act (Massachusetts)
1837	Morse establishes telegraphic system
1839	Schwann publishes treatise on the cell theory
	Rowland Hill introduces postage stamps
1840	First dental school and society founded at University of Maryland
1842	Long operates with ether anesthetic
1846	Smithsonian Institution founded
1846–1849	Irish potato famine
1847	Semmelweis discovers the pathogenesis of puerperal fever
1848	Claude Bernard discovers glycogenic function of the liver
1849	John Snow publishes views on water-borne cholera
1852	Remark shows that growth of tissues is due to cell division
1853–1856	Crimean War: Florence Nightingale
1854–1856	Belgrand constructs sewers of Paris
1855	Bessemer steel process and Bunsen burner invented
1859	Darwin's *Origin of Species* published
	Florence Nightingale publishes *Notes on Nursing*
1860	Pasteur demonstrates presence of bacteria in air
1861–1865	American Civil War
1865	Gregor Mendel publishes memoir on plant hybridity
1867	Lister introduces antiseptic surgery
	Opening of the Suez Canal and Pacific Railway
1869	Massachusetts State Board of Health created
1870–1871	Franco-Prussian War (test of vaccination)
1876	Johns Hopkins University founded
	Kolbe isolates salicylic acid
	Bell telephone introduced
1877	Stricker treats articular rheumatism with salicylic acid

NOTE. Table is adapted from [7].

Figure 2. Rudolph Virchow (*top left*) as he looked in 1850 at the time of his editorial imbroglio with Wunderlich over the theory of cellular pathology [4].

career closely paralleled that of today's clinical investigator, Virchow embodied today's basic medical scientist. Wunderlich had little regard for Virchow's theories of cellular pathology and repeatedly attacked them and their originator in the *Archives of Pathological Medicine*. In the end, however, Virchow's accomplishments eclipsed Wunderlich's polemics. Although the two were never professional collaborators, it is reasonable to assume that such competition had a salutary effect on the productivity of both investigators.

There can be little doubt that had Wunderlich not lived, someone else would have performed the analysis that launched clinical thermometry. Both Wunderlich and clinical thermometry embodied the zeitgeist of nineteenth-century medicine that extolled careful, repetitive, analytical observation. In fact, others performed analyses contemporary with Wunderlich's [13, 14], which while not of the scale or the eloquence of his publications might have sufficed as the seeds from which clinical thermometry would blossom.

A Critical Analysis of Wunderlich's Dictums

Das Verhalten der Eigenwärme in Krankheiten is remarkable for its content, its clarity, and, perhaps most particularly, its longevity. The size of the data set reportedly analyzed by Wunderlich in reaching conclusions articulated therein has never been equaled. The sheer volume of Wunderlich's data, in fact, has had a daunting effect on subsequent investigators who might have wished to critically appraise the validity of his observations and conclusions. As a result, concepts promulgated by Wunderlich in *Das Verhalten der Eigenwärme in Krankheiten* >120 years ago have survived largely intact in lay thinking and medical writing. Nevertheless, data from several sources suggest that at least some of Wunderlich's cherished dictums on clinical thermometry are in error.

Wunderlich wrote that ". . . when the organism [man] is in a normal condition, the general temperature of the body maintains itself at the physiologic point: 37°C = 98.6°F" [2]. Although Becquerel and Breschet [15] preempted Wunderlich by 33 years in concluding that the mean temperature in healthy people is 98.6°F (37°C), Wunderlich is generally credited with giving 98.6°F (37°C) its special significance vis-à-vis the normal temperature. Thanks to his work, for over a century, 98.6°F has been the reflex response of most people to the question "what is the normal temperature?".

In fact, considerable data indicate that 98.6°F (37°C) has no special significance for the normal temperature, if such temperature is monitored orally using modern thermometers. In a study of 54 young adults (average age, 23 years) monitored for several months, Horvath et al. [16] observed a mean morning oral temperature of 97.8°F (36.5°C) and a mean evening temperature of 98.2°F (36.8°C). A similar evaluation of nine healthy young adults (average age, 22 years) identified a mean daily temperature of 97.9°F (36.6°C) [17]. In a recent analysis of 700 oral temperature readings from 148 healthy young volunteers (age range, 18–40 years) conducted at the University of Maryland's Center for Vaccine Development [18], 98.6°F (37°C) accounted for only 8% of the observations recorded (figure 3). In this population, 98.6°F (37°C) was not the overall mean temperature, the mean temperature of any particular time of day, the median temperature, or the single most frequently recorded tem-

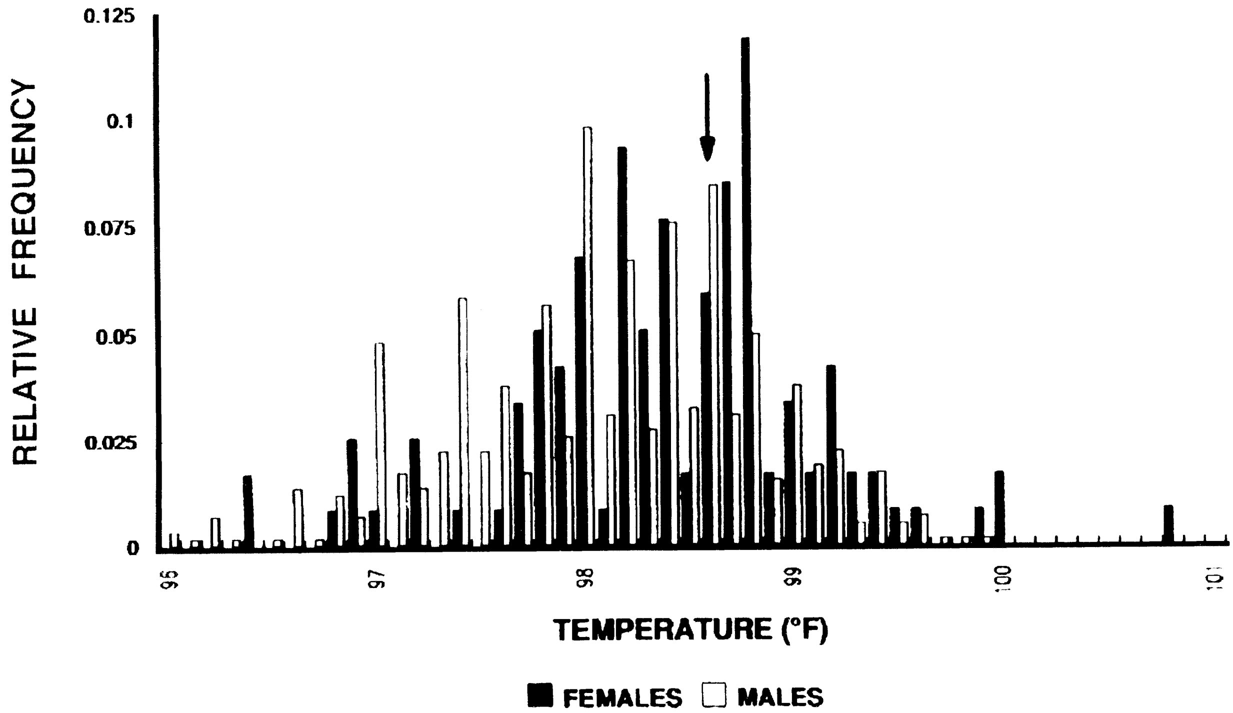

Figure 3. Frequency distribution of 700 baseline oral temperature observations obtained at various times during two consecutive days from 148 healthy volunteers. The arrow indicates location of 37°C (98.6°F). Reprinted with permission from the *Journal of the American Medical Association* **1992**;268:1578–80. ©1992, American Medical Association.

perature. Furthermore, 98.6°F (37°C) did not fall within the 99.9% confidence limits of the sample mean (98.06°F–98.24°F; 36.70°C–36.80°C).

Wunderlich regarded 100.4°F (38.0°C) as the upper limit of the normal body temperature and, by extrapolation, any temperature >100.4°F (38.0°C) as fever [2]. Modern medical textbooks differ in their definition of the upper limit of the normal oral temperature. Published values include 98.8°F (37.1°C) and 100.4°F (38.0°C) in textbooks of physiology [19, 20], 99.0°F (37.2°C) in *Harrison's Principles of Internal Medicine* [21], and 99.4°F (37.4°C) in a recently published monograph on fever [22]. A widely used medical dictionary defines this same upper limit as 98.6°F (37°C) [23].

The source of the confusion over what constitutes the upper limit of the normal body temperature most likely derives from the diurnal variability of the normal temperature [18] and the fact that the body temperature is actually a hodgepodge of temperatures, each representative of the various body parts. Thus, the body temperature varies normally not only with time of day but also according to the site at which the temperature reading is obtained. Because of such variability, no single temperature should be regarded as the upper limit of normal. In the series of the University of Maryland (*vide supra*) [18], 98.9°F (37.3°C) was the maximum oral temperature (i.e., the 99th percentile) recorded at 6:00 A.M., whereas at 4:00 P.M., the upper limit reached 99.9°F (37.8°C) (figure 4).

Wunderlich wrote that "[temperature] oscillates even in healthy persons according to time of day by 0.5°C–0.9°F" [2] and that "The lowest point is reached in the morning hours between two and eight, and the highest in the afternoon between four and nine" [24]. Modern authorities have generally concurred with Wunderlich's observation on such matters [21, 25]. However, Tauber [26] has suggested that the amplitude of diurnal variation might be as high as 1.8°F (1°C). Observations reported in the series of the University of Maryland [18] were more consistent with Wunderlich's view (table 3). Nevertheless, subjects in the Maryland series exhibited considerable individual variability, with some having daily oral temperature oscillations as wide as 2.4°F (1.3°C) and others as narrow as 0.1°F (0.1°C).

According to Wunderlich, women have slightly higher normal temperatures than men and often show greater and more sudden changes in temperature [2]. In a study of nine healthy young adults (six males and three females), Dinarello and Wolff [17] corroborated both observations. Data obtained from subjects participating in the investigation of the University of Maryland corroborated Wunderlich's former but not his latter observation (table 3) [18].

"Old people," according to Wunderlich, "present a temperature 0.5°C = 0.9°F less than younger persons" [2]. In a study reported in the *Lancet* in 1948, Howell [27] confirmed this observation. Although there are considerable data suggesting that thermoregulation is impaired in the elderly due to various effects of aging on the autonomic system [28], more recent investigations have not shown lower average

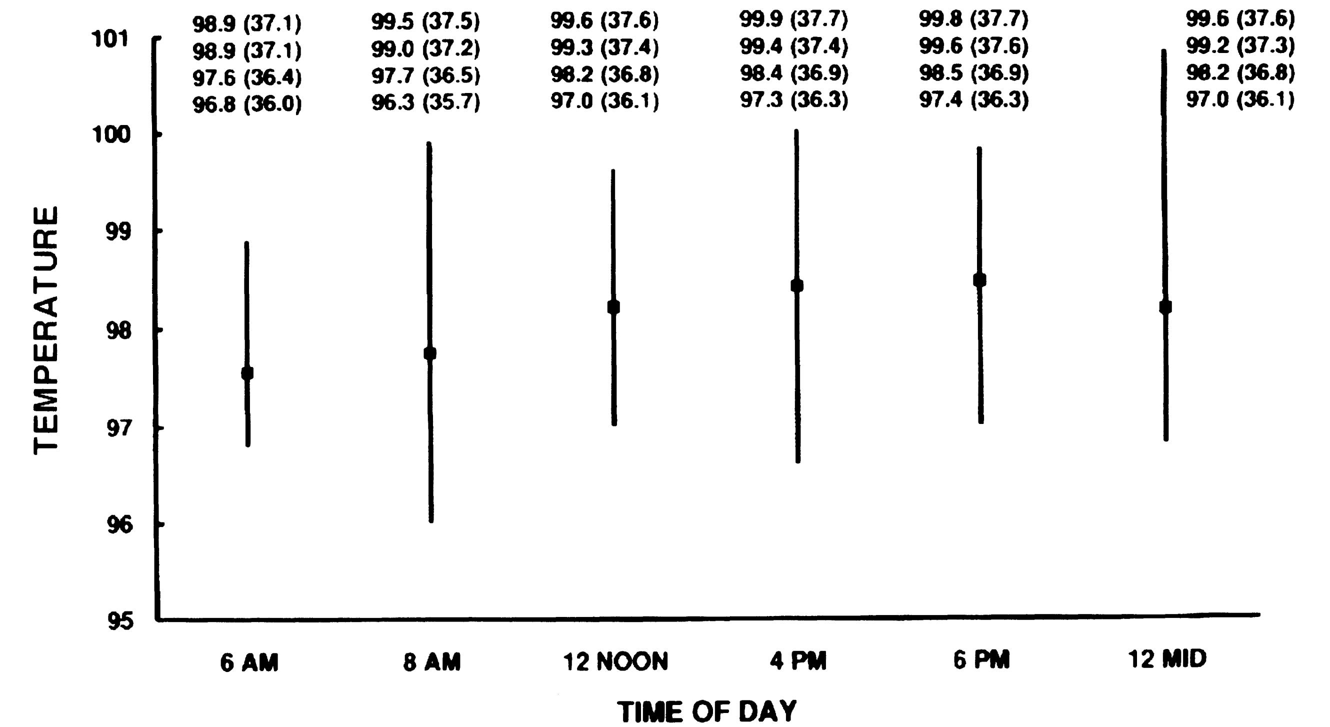

Figure 4. Mean oral temperatures and temperature ranges according to time of day for 148 healthy volunteers. The four temperatures (°F) shown at each sample time are the 99th percentile (*first*), 95th percentile (*second*), mean (*third*), and 5th percentile (*fourth*) for each sample set. Reprinted with permission from the *Journal of the American Medical Association* **1992**;268:1578–80. ©1992, American Medical Association.

core temperatures among healthy elderly people than among healthy young people [29]. Comparisons of simultaneously obtained oral, axillary, and rectal temperature recordings from groups of elderly and young subjects have shown lower average oral and axillary temperatures in elderly subjects but comparable average rectal temperatures in the two groups [29]. In view of these findings, Wunderlich's observations regarding the effects of aging on the normal temperature would appear to be applicable to axillary measurements (which Wunderlich used in his clinic) and oral measurements but not to rectal observations.

Wunderlich also wrote that mental exertion, constipation, and urinary retention raise body temperature [2]. To our knowledge, none of these assertions have been tested by modern investigators.

Finally, Wunderlich [2] wrote that "[fever] can give more certainly than anything else information as to the grade of the disease. If the departure of the temperature from the normal range is wide, the case is severe and *vice versa*." Many of today's clinicians subscribe to this concept, believing that the height of a fever correlates directly, albeit roughly, with the severity of an illness. However, to our knowledge, only a single recent investigation has examined this hypothesis experimentally [30]. This investigation studied the relationship between the oral temperature and other parameters of illness in 139 adult volunteers infected experimentally with *Shigella sonnei*. In individuals who developed clinical disease, peak temperature correlated positively with total number of signs and symptoms (other than fever), stool volume, and number of stools produced during the illness. Peak temperature also

Table 3. Relationship between race, sex, body temperature, and daily temperature oscillations in 148 healthy volunteers studied in the University of Maryland, Center for Vaccine Development.

		Body temperature in °F (°C)			Temperature oscillations in °F (°C)		
Subject	No. of subjects	Mean	95th percentile	5th percentile	Mean	95th percentile	5th percentile
White male	32	98.0 (36.6)	99.1 (37.3)	96.6 (35.9)	1.09 (0.6)	2.4 (1.3)	0.1 (0.1)
White female	9	98.3 (36.8)	99.2 (37.3)	96.7 (35.9)	1.11 (0.6)	2.3 (1.3)	0.2 (0.1)
Black male	88	98.1 (36.7)	99.2 (37.3)	97.0 (36.1)	0.92 (0.5)	1.9 (1.1)	0.2 (0.1)
Black female	17	98.5 (36.9)	99.9 (37.7)	97.2 (36.2)	0.95 (0.5)	2.3 (1.3)	0.3 (0.2)

correlated negatively with incubation period but exhibited no apparent correlation with duration of the illness. The average oral temperature during illness exhibited a positive correlation with a number of other signs and symptoms of infection but not with stool volume or stool number. Although Wunderlich also believed that convalescent-phase temperatures are more delicate and more readily influenced by external factors than are baseline temperatures [2], this was not the case in subjects convalescing from experimental shigellosis [30].

Wunderlich's Data

> *Materiem superabat opus* (the workmanship surpassed the material)
>
> —Ovid

Wunderlich wrote: "If the physician should sometimes suffer from injustice and misunderstanding, should his honest work be now and then ignored or even sneered at, he must bear in mind that in the majestic eye of Nature, the individual is nothing. And however depressed he may feel when intriguers and mountebanks blow about their ephemeral successes, he may be sure that these upstarts will be overtaken in the end by the Erinnyes of conscience. For natural science is a proud, silently advancing power, of whose might the spheres most threatened by it have hardly a notion. Just its singularity and its grandeur is that it showers its gifts upon friends and foes and scoffers alike, that it conquers and maintains its dominion by its blessings, as it noiselessly subdues and dissolves unreason" [7].

The ideas expressed in this passage did not originate with Wunderlich. Legions of investigators of the mid-nineteenth century were expressing similar views. Few, however, matched the almost sublime eloquence with which Wunderlich delivered his message. Such eloquence, in fact, more than his data, may have enabled Wunderlich to succeed as the first man to convince the world of the importance of clinical thermometry.

In view of the reverence for scientific truth expressed above and the prodigious volume of data Wunderlich collected and analyzed in reaching his conclusions about the human body temperature, it is difficult to explain the differences between his observations and those of more recent investigators. These differences might have been due, at least in part, to the fact that Wunderlich monitored axillary temperatures, whereas more contemporary investigators have generally studied oral temperatures. However, axillary temperatures are generally lower than simultaneously obtained oral readings [31], and Wunderlich's estimate of the average normal axillary temperature (98.6°F [37°C]) actually exceeded the average oral temperature (98.2°F [36.8°C]) obtained in more recent studies [18].

Although Wunderlich's data base was enormous (estimated to have included several million observations obtained from some 25,000 subjects), Wunderlich's lack of access to computer technology makes it inconceivable that he could have analyzed more than a small fraction of the total data set. In addition, although the principles of statistical analysis were known as early as the 1830s, these did not find their way into general use until the 1890s. There is no evidence that Wunderlich had knowledge of such principles. Because Wunderlich did not describe his process of data selection, nor did he present more than anecdotal glimpses of his raw data, one can only wonder as to the actual data chosen for analysis in arriving at conclusions published in *Das Verhalten der Eigenwärme in Krankheiten.*

Finally, Wunderlich's observations might have differed from those of more recent investigators because his thermometers were less reliable or were calibrated differently from later models. With regard to the first possibility, it is pertinent that Wunderlich did not insist on a high degree of precision in his instruments. In fact, he wrote that "Errors which do not exceed half a degree Centigrade (.9° Fahr. [sic]) are scarcely worth mention" [32]. To our knowledge, the second possibility—Wunderlich's thermometers might have been calibrated differently from today's instruments—has never been investigated. It is a possibility worthy of consideration because the first internationally accepted standard scale of temperature was not established until 10 years after Wunderlich's death (1887), following a meeting of the Comité International des Poids et Mesures in Paris [10].

It is fortunate that a thermometer from the nineteenth century, which is believed to be one of Wunderlich's, was recently discovered among the artifacts contained in the collection of the Mütter Museum in Philadelphia (figure 5). The instrument was donated to the museum in February of 1892 by Dr. Jacob Mendez DaCosta, who had obtained it from one of Wunderlich's students. Its design is typical of German thermometers of the period, in which the scale and mercury column are enclosed within an outer glass sheath. Most important, the features of the instrument are compatible with Wunderlich's enumeration in *Das Verhalten der Eigenwärme in Krankheiten* of "the desiderata in a thermometer which is to be used in medical practice" [32].

Table 4 gives the results of experiments comparing the Mütter Museum thermometer with a digital thermometer similar to the ones used in the series of the University of Maryland that was cited above, as well as with several other contemporary thermometers. In these experiments, sequential temperature readings were taken of water heated to various temperatures in a Precision H8 (GCA) circulating water bath. Readings obtained using the Mütter Museum thermometer were consistently higher than concomitant readings obtained with any of the contemporary thermometers. These were 1.6°C to 1.8°C (2.9°F to 3.2°F) higher than ones obtained with the digital thermometer and 1.9°C (3.4°F) higher than readings obtained with a National Bureau of Standards thermometer. The Mütter Museum ther-

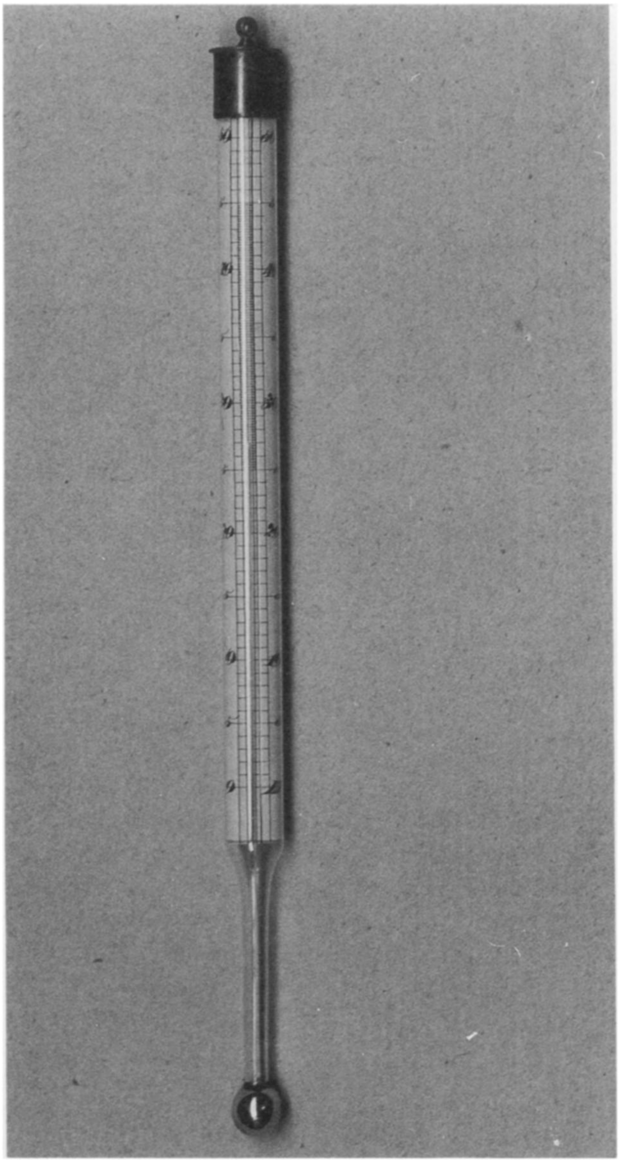

Figure 5. The Mütter Museum thermometer. The instrument was donated to the museum in 1892 by Dr. J. M. DaCosta who had acquired it from one of Wunderlich's students. Its length is 22.5 cm. The design is typical of German thermometers of the period and is consistent with Wunderlich's description of the ideal clinical thermometer in *Das Verhalten der Eigenwärme in Krankheiten*.

mometer also gave readings 1.4°C to 2.2°C (2.6°F to 4.0°F) higher than simultaneously obtained readings with four other nineteenth-century thermometers of similar design (data not shown). In contrast to the modern clinical instruments, the Mütter Museum thermometer was a nonregistering instrument, which had to be read in situ.

Axillary temperatures correlate poorly with oral temperatures. However, when simultaneous measurements are obtained, axillary readings are generally lower—in the extreme, as much as 4.2°F (2.3°C)—than oral readings [31]. Therefore, it is all the more surprising that Wunderlich, who relied primarily on axillary measurements in developing his concepts of the normal temperature, obtained higher values than those reported in more modern surveys in which oral temperatures have been studied. Wunderlich's higher readings and the results of the experiments with the Mütter Museum thermometer are consistent with the hypothesis that his thermometers were calibrated higher than those in use today. Nevertheless, it should be pointed out that with time, secular changes occur in glass thermometers that may result in a progressive and nonrecoverable decrease in the bulb volume, thus leading to a gradual increase in readings [33]. The huge discrepancy between the readings obtained with the Mütter Museum thermometer and the modern instruments, if related, would represent an extreme example of this phenomenon. Furthermore, the possibility that such a discrepancy might be due, in its entirety, to the effects of aging on the antique instrument seems unlikely in view of the finding that the Mütter Museum thermometer gave substantially higher readings than those obtained using other thermometers of comparable age.

Conclusion

Wunderlich did not create clinical thermometry, nor did he provide a completely accurate profile of the normal temperature of humans. Rather, he carried the concept one step further than others before had done. His specific contribution to clinical thermometry was to put it on a scientific basis. Because of his work, fever, which had previously been viewed as a disease, came to be recognized more appropriately as a clinical sign [7]. This, much more than a specific definition of the normal temperature range or characterizations of fever patterns, was Wunderlich's great contribution

Table 4. Comparison of the Mütter Museum thermometer with five contemporary thermometers.

	Thermometer readings of indicated water bath temperatures*				
Thermometer	33	35	37	39	41
Mütter Museum	35.2	37.2	39.2	41.0	43.1
Diatek 600 (clinical/digital)	33.4	35.4	37.4	39.4	41.3
ERTCO (laboratory/mercury)	33.8	35.8	37.8	39.6	41.7
BD K-OJL (clinical/mercury)†	...	35.2	37.2	39.2	...
VWR (laboratory/mercury)	33.2	35.4	37.3	39.2	41.4
NBS (standard/mercury)‡	...	...	37.33	...	...

NOTE. All temperatures (°C) represent the mean of six separate readings taken by two different observers.

* A Precision H8 (GCA) circulating water bath was used to heat water to the various temperatures studied in these experiments.

† This oral thermometer was calibrated in °F. Readings were converted to °C for purposes of comparison.

‡ National Bureau of Standards thermometer (no. 366 745).

to clinical medicine. The systematic study of the response of the body temperature to disease, which Wunderlich developed to an art form, was pathological physiology at its best.

One of the great ironies of Wunderlich's life is that in 1876, a year before his death, Kolbe isolated salicylic acid, thus ushering in the era of antipyretic therapy [12]. Wunderlich, who devoted his entire career to dismantling the ontology of philosophic medicine, ultimately created an ontology of his own through his theory of specific temperature patterns for specific diseases. As a result of Wunderlich's work and the availability of newly synthesized antipyretic agents, fever has since been suppressed with a determination reflecting a total disregard for Wunderlich's most important lesson —fever is a sign of disease and not the disease process itself.

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