Academic genealogy and direct calorimetry: a personal account

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Jackson DC. Academic genealogy and direct calorimetry: a personal account. Adv Physiol Educ 35: 120–127, 2011; doi:10.1152/advan.00121.2010.—Each of us as a scientist has an academic legacy that consists of our mentors and their mentors continuing back for many generations. Here, I describe two genealogies of my own: one through my PhD advisor, H. T. (Ted) Hammel, and the other through my postdoctoral mentor, Knut Schmidt-Nielsen. Each of these pathways includes distinguished scientists who were all major figures in their day. The striking aspect, however, is that of the 14 individuals discussed, including myself, 10 individuals used the technique of direct calorimetry to study metabolic heat production in humans or other animals. Indeed, the patriarchs of my PhD genealogy, Antoine Lavoisier and Pierre Simon Laplace, were the inventors of this technique and the first to use it in animal studies. Brief summaries of the major accomplishments of each of my scientific ancestors are given followed by a discussion of the variety of calorimeters and the scientific studies in which they were used. Finally, readers are encouraged to explore their own academic legacies as a way of honoring those who prepared the way for us.

family tree; heat production; legacy; metabolic rate

EVERY PERSON has a family history that dates back, depending on one’s perspective, to the Garden of Eden or the primordial soup. Few family trees attempt to trace the generational path that far back, but identifying as many forebears as possible has long been a popular pursuit, aided in recent years by internet sites dedicated to the task. I possess two family tree books, both on my mother’s side, that reach back to Ireland in the mid-18th century, when patriarchs named, respectively, William and Faris came to the New World seeking a better life. Their descendants included many farmers and ministers, but careful reading discovered an abolitionist professor who left South Carolina for Bloomington, IN, in the 1840s, a member of General Grant’s personal guard during the Vicksburg Campaign, and a link to the abstract expressionist painter Jackson Pollock through his wife, Lee Krasner, also a noted painter. Even within this relatively short time frame, numerous other pathways could be traced back to different patriarchs or matriarchs.

As members of a research and scholarly community, though, we each have another type of family tree that we can explore. Through our training and education we occupy one or more links in complex networks of mentor-student relationships that may trace back many generations into the past. The common way to define a family tree is to start from a particular individual and trace all that person’s descendants. In my field of comparative physiology, a particularly well-described scientific family tree of this sort is that stemming (rooting?) from George Bartholomew (1919–2006), a rather prolific founding father whose scientific descendants at last count numbered 1,175 in 6 generations. This means that each member of this tree trained, on average, between three and four students. Bartholomew’s newest progeny are his academic great-great-great-grandchildren. Interested readers can consult http://bartgen.bio.ucl.ac/tree/.

A somewhat simpler academic genealogy can be constructed by starting at the end of the line and tracing back through the generations as far as possible. Academic genealogies of this sort are not always as complex as biological genealogies because each academic offspring does not necessarily have two parents, each with their own antecedents. Often, however, we or our forebears have trained with more than one mentor, and this gives us the possibility of multiple pathways. I personally can trace two distinct ancestries: one through my PhD advisor (Fig. 1) and one through my postdoctoral mentor (Fig. 2). In each case, I follow a single line, although many other pathways are possible due to multiple mentors. In each case, I am deeply humbled by the esteem of my predecessors.

I learned of the line leading from my PhD advisor, H. T. (Ted) Hammel, when a certificate containing the genealogy was presented to Ted on the occasion of his retirement from the Scripps Institution of Oceanography in 1988, although I have discovered that an earlier, and by necessity, shorter version was published in a memoir written by an earlier member of the genealogy, Eugene F. DuBois, about his mentor, Graham Lusk (14). This pathway leads back, beginning with me, for 10 generations to Antoine Lavoisier in the 18th century. The line leading from my postdoctoral mentor, Knut Schmidt-Nielsen, is a very clear succession leading back five generations to Carl Ludwig. All of these predecessors of mine were distinguished scientists, but a particular theme can also be found here. Fully 8 of the 10 members of my PhD genealogy, including myself, used the technique of direct calorimetry to measure metabolic heat production. Furthermore, the first members of this line, Lavoisier and Laplace, invented this technique and were the first to use it. In addition, three of the five members of my postdoctoral genealogy, including myself, also used direct calorimetry in their research.

I will first give a short synopsis of the life and accomplishments of my forebears in each of the two pathways and then will discuss how members of these pathways used direct calorimetry in their research.

Genealogy Stemming From My PhD Mentor

I studied for my PhD from 1961 to 1963 under H. T. (Ted) Hammel (1921–2005), a scientist of impressive breadth. My thesis project was on temperature regulation in exercising dogs (26). Hammel initially trained as a physicist and worked as a young man on the Manhattan Project at Los Alamos during World War II. His interests turned to biophysics, and he earned his PhD at Cornell University with Donald Griffin, who is famous for his work on bat sonar, although Hammel’s thesis...
topic concerned the thermal properties of fur. Griffin could therefore lead to a distinct ancestral path, but one I will not follow here. Hammel’s best known work in physiology was in temperature regulation, and a set of papers leading to his theory of an adjustable set point temperature are included in the American Physiological Society’s series on classic papers (38). He participated in and often led a large number of field studies, frequently in collaboration with Per (Pete) Scholander, who was also an important mentor for Hammel. These field studies were on a wide range of topics including sap pressure in vascular plants, freeze tolerances of arctic fish and insects, thermal relations of various indigenous cultures, and thermal relations of penguins and reindeer. Hammel’s passion late in his life when he retired to his home state of Indiana was to promote his theory on the physical mechanism for osmotic pressure (18), an interest that grew out of his earlier work on sap pressures with Scholander. Hammel’s mentor in the line being followed was James D. Hardy (1904–1985), also a physicist who became a physiologist (11). Hammel joined Hardy’s group at the University of Pennsylvania and then followed him to the John B. Pierce Laboratory in New Haven, CT, when Hardy was appointed director. Hardy grew up in Mississippi and went to university there. His transition from physics to physiology occurred at the Russell Sage Institute of Pathology at Cornell University in New York City, where his research on the measurement and effect of thermal radiation on human skin was the foundation for his interest in temperature regulation and also for his extensive studies of thermal pain (22). Later, as Professor of Physiology at the University of Pennsylvania and then director of the John B. Pierce Laboratory in New Haven, his focus was fully on human temperature regulation (21). A member of the National Academy of Sciences, Hardy was also a World War II naval veteran who later rose to the rank of Rear Admiral in
DuBois trained at the Russell Sage Institute with Graham Lusk (1866–1932), who was the founder and Director of the institute. Lusk was a member of an old Connecticut family. His father was a prominent physician and physiologist who had himself published a paper on the metabolic aspects of diabetes, a subject that would occupy his son for much of his career. After his undergraduate studies at Columbia, Lusk spent 4 yr studying and working in Munich, where his lifetime interest in metabolism and nutrition began. Lusk published extensively on these subjects, although his scientific contributions were noted more for clarifying and correcting current understanding rather than breaking new ground (14). His best known publication was his monumental The Elements of the Science of Nutrition (36), first published in 1906, which had four editions and was the standard book on the subject even long after his death. Lusk was a prominent leader in his field, and his residence in New York City was a meeting place for physiologists from around the world. It was here that the Society for Experimental Biology and Medicine and the Harvey Society were both founded in the early 20th century. He served as the Chair of Physiology at Bellevue Hospital Medical College and then at Cornell Medical School.

Lusk’s teacher in Munich was Carl von Voit (1831–1908), who has been referred to as the founder of metabolic research (40). Voit was born in Munich and lived there his whole life except for relatively brief training sojourns in Würzburg and Göttingen. Notable among his scientific accomplishments was the discovery that the urinary excretion of nitrogen, mainly as urea, bears a consistent relationship to the rate of protein metabolism. This measurement, together with the respiratory exchange ratio, made it possible to quantitatively determine the contributions of fat, carbohydrate, and protein to whole body metabolism. Voit also disproved the theory that the fuel for muscle metabolism was the muscle. He further showed that the level of metabolism determines the oxygen consumption, rather than the oxygen supply as the prime mover, as was the prevailing idea. His use of input/output balance as a basic experimental approach in metabolism research was the foundation for the enormous progress that his work inspired.

Among Voit’s mentors in Munich was Justus von Liebig (1803–1873). Liebig is widely credited with establishing chemistry as a distinct scientific discipline, and he pioneered the laboratory-based teaching of chemistry. He and his students identified numerous organic chemicals, and he emphasized the application of organic chemistry to clinical medicine, although the appreciation of its importance by physicians was delayed until a more detailed understanding of organic reactions was available (42). Liebig was not an animal experimentalist, so many of his physiological ideas proved to be incorrect, including the muscle fuel theory disproved, as noted above, by his student Voit. Liebig is also known as the founder of the fertilizer industry because of his discovery of the importance of nitrogen as a plant nutrient. He founded the journal Annalen der Chemie, which was the leading chemistry journal of its day, and he trained many of the chemists who founded new laboratories of chemistry throughout Germany and around the world. Although the final years of his career were in Munich, his major accomplishments were in Giessen,

**Fig. 2. Genealogy stemming from my postdoctoral mentor. [Permission for reproducing the Schmidt-Nielsen photo was granted by Duke University. Other photos are in the public domain.]**

the naval reserves and served as the Director of the Aviation Medical Acceleration Laboratory at Johnsville, PA, where he trained the original Mercury astronauts in the human centrifuge.

Hardy’s mentor at the Russell Sage Institute was Eugene F. DuBois (1882–1959). DuBois (2) grew up in what was then rural Staten Island and studied at Harvard University and the Columbia College of Physicians and Surgeons, where he received his MD. Like many aspiring American scientists of his day, he sought advanced training in Europe, in Berlin in this case, where he began his lifelong interest in metabolism. Returning home, he took a position at the Russell Sage Institute of Pathology of Cornell Medical School, and he remained at Cornell and its affiliated hospitals thereafter. During his career, he carried out extensive measurements of human metabolic rate and temperature regulation during health and disease. DuBois developed a formula for calculating body surface area using a subject’s height and weight (12) that led to the establishment of basal metabolic rates related to body surface area as a universal standard. His book, *Basal Metabolism in Health and Disease* (13), published first in 1925, was a classic that had several subsequent editions.

DuBois trained at the Russell Sage Institute with Graham Lusk (1866–1932), who was the founder and Director of the institute. Lusk was a member of an old Connecticut family. His father was a prominent physician and physiologist who had himself published a paper on the metabolic aspects of diabetes, a subject that would occupy his son for much of his career. After his undergraduate studies at Columbia, Lusk spent 4 yr studying and working in Munich, where his lifetime interest in metabolism and nutrition began. Lusk published extensively on these subjects, although his scientific contributions were noted more for clarifying and correcting current understanding rather than breaking new ground (14). His best known publication was his monumental The Elements of the Science of Nutrition (36), first published in 1906, which had four editions and was the standard book on the subject even long after his death. Lusk was a prominent leader in his field, and his residence in New York City was a meeting place for physiologists from around the world. It was here that the Society for Experimental Biology and Medicine and the Harvey Society were both founded in the early 20th century. He served as the Chair of Physiology at Bellevue Hospital Medical College and then at Cornell Medical School.

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where today the institution where he worked is called the Justus Liebig-Universität Giessen.

When Liebig was a student, France was the center for the study of chemistry, so he went to Paris, where he studied with Joseph Louis Gay-Lussac (1778–1850), who taught him advanced methods of chemical analysis. Gay-Lussac spent his career in Paris, having left his childhood home in central France when his father was arrested during the French Revolution. Among his many contributions (8) are the following: he independently and more accurately than Jacques Charles discovered the relationship between gas volume and temperature; he published the “Law of Combining Volumes,” which stated that gases react in small, whole number ratios, such as two hydrogens and one oxygen to form water; he devised a method for producing sulfuric acid that continued to be used long after his death; and he was involved in the discovery of the elements boron and iodine. Gay-Lussac was a chemist and not a biologist, but he did make an important observation of importance to high-altitude physiology and medicine. In 1804, he made a record-setting solo balloon flight to 23,000 ft (≈7,000 m) and confirmed that the composition of air was the same at high altitude as at sea level. He also reported experiencing increased breathing and heart rate during that flight.

Gay-Lussac had two important mentors: Claude Louis Berthollet (1748–1822) and Pierre-Simon Laplace (1749–1827). Lusk’s genealogy lists them both, but Hammel’s only mentions Laplace. Gay-Lussac, as a young man, worked with both of them at Berthollet’s exclusive laboratory at his home in Arcueil, near Paris. The chemist Berthollet probably had the greater influence, but Laplace will be discussed here, principally because of his contribution to the studies of animal heat and calorimetry. Laplace’s major contributions were in pure mathematics and in the applications of mathematics to celestial physics and probability theory. He is known by physiologists principally for the law of Laplace, which describes the relationship among transmural pressure, wall tension, and radius in a tube or sphere and has important applications in our understanding of the behavior of alveoli and blood vessels. Laplace was skillful both in science and in successfully negotiating the radical changes in the political climate that occurred during his lifetime. He has been called the “French Isaac Newton” because of his brilliance and range of expertise.

Laplace’s mentor in the genealogy is Antoine Lavoisier (1743–1794), with whom he collaborated on the study of combustion and animal heat. Lavoisier was not a student in the usual sense because he was already an accomplished and highly regarded mathematician when this collaboration began and younger by only 5 yr. However, at the time, he was less esteemed than his mentor, and their joint work concerned a field of study in which Lavoisier was already a major figure (16). Lavoisier has been called the “Father of Modern Chemistry” because of his fundamental contributions to this science. He disproved the phlogiston theory by proving the existence of oxygen as the agent of combustion. His careful quantitative approach to the study of chemical reactions led him to formulate the first version of the law of conservation of mass. He was a pioneer in recognizing that matter is made up of distinct elements, and he listed those identified at the time. Lavoisier supported himself and his scientific work by various government positions, including membership in the Ferme Générale, a tax-collecting organization. This proved to be his undoing when this organization was condemned during the French Revolution and many of its members were guillotined, including Lavoisier. Today, I can look back through this succession of outstanding scientists to Lavoisier as my academic great-, great-, great-, great-, great-, great-grandfather.

Genealogy Stemming From My Postdoctoral Mentor

My postdoctoral mentor, Knut Schmidt-Nielsen (1915–2007), was a premier comparative physiologist of the 20th century (44). He was Professor of Zoology at Duke University and a member of the National Academy of Sciences. I worked with him from 1961 to 1963 on heat exchange in the nasal passages of kangaroo rats (28) and on the metabolic rate of anoxic turtles (29). Schmidt-Nielsen’s classic studies on the desert adaptations of camels and kangaroo rats are perhaps his best known works, but he also made fundamental contributions to salt gland function, bird respiration, animal scaling, and many other topics. He also wrote lucid integrative reviews and monographs, and his textbook on comparative physiology (44) had five editions and is still used widely today.

Schmidt-Nielsen trained in Copenhagen with August Krogh (1874–1949) during the late 1930s. Krogh was a remarkable scientist who was awarded the Nobel Prize in Physiology and Medicine in 1920 for his research on the regulation of capillary blood flow in skeletal muscle. The comparative physiology community is very familiar with his statement that “for every physiological problem there will be some animal on which it can be most conveniently studied,” which is commonly known as the “Krogh principle.” Krogh made many other contributions to human and animal physiology and medicine, and of particular note was his confirmation, together with his wife, Marie Krogh, that oxygen moves from lung gas to pulmonary capillary blood by simple diffusion and not by active secretion, as was believed by many prominent workers at the time (31). The cited paper is one of seven papers on the subject (the “seven little devils”) that the Kroghs published together in the same issue of the journal Skandinavisches Archiv für Physiologie. The Kroghs were subjects of an excellent biography by their daughter, Bodil Schmidt-Nielsen (43).

August Krogh was introduced to animal physiology (zoo-physiology) in the laboratory of Christian Bohr (1855–1911) in Copenhagen. Bohr was a leading advocate of the oxygen secretion hypothesis and the fact that his own student proved him wrong caused him great pain and alienated him from Krogh. Bohr, however, was correct in most of his other physiological findings and is best known today for his description, together with Krogh, of the effect of hydrogen ions and carbon dioxide on the affinity of hemoglobin for oxygen, known, of course, as the Bohr effect, for his estimate of mean pulmonary capillary PO2 using what we now call the Bohr integration technique and for his characterization and calculation of pulmonary dead space using what we still call the Bohr equation. In a broader context, he is perhaps even better known as the father of Niels Bohr, a Nobel Laureate in Physics.

Christian Bohr, in turn studied in Leipzig with Carl Ludwig (1816–1895), who was one of the premier physiologists of the 19th century and who may have originated the lung oxygen secretion idea (15). Ludwig made outstanding contributions as an experimentalist, as an inventor of instruments, as a teacher, and as a proponent of physicochemical explanations for living
performed within a day during the winter of 1783, the first animal they used was a guinea pig, and two experiments were performed on the combustion of various elements and by a living animal. The Lavoisier and Laplace then turned to heat generated by the melting ice. Surrounding this inner ice compartment was a second compartment is always at 0°C and all the released heat is collected water and the heat of fusion of water, the amount of heat had on the result. The water that melted as a result of heat generated contributed to the demise of vitalism. Significantly, these discoveries depended critically on the technique of direct calorimetry. Direct calorimetry has been used in metabolic heat measurements ever since and has been an important tool for understanding metabolic heat and thermal physiology, but for the routine measurement of metabolic rate, it has been largely supplanted by the simpler method of indirect calorimetry. Direct calorimetry has been used in metabolic heat measurements ever since and has been an important tool for understanding metabolic heat and thermal physiology, but for the routine measurement of metabolic rate, it has been largely supplanted by the simpler method of indirect calorimetry. Direct calorimetry has been used in metabolic heat measurements ever since and has been an important tool for understanding metabolic heat and thermal physiology, but for the routine measurement of metabolic rate, it has been largely supplanted by the simpler method of indirect calorimetry. Direct calorimetry has been used in metabolic heat measurements ever since and has been an important tool for understanding metabolic heat and thermal physiology, but for the routine measurement of metabolic rate, it has been largely supplanted by the simpler method of indirect calorimetry.

Understanding the source and nature of animal heat was an ancient problem that occupied Plato, Aristotle, Hippocrates, and Galen, among others (47). Until the 18th century, it was generally believed that animal heat was an innate property of the living organism, the product of vital forces that could not be explained by the usual laws of chemistry and physics. The discoveries in the 18th century that animal heat was due to the slow combustion of carbon fuel and in the 19th century that an equivalency existed between the fuel consumed and the heat generated contributed to the demise of vitalism. Significantly, these discoveries depended critically on the technique of direct calorimetry. Direct calorimetry has been used in metabolic heat measurements ever since and has been an important tool for understanding metabolic heat and thermal physiology, but for the routine measurement of metabolic rate, it has been largely supplanted by the simpler method of indirect calorimetry. In the following paragraphs, key events in the history of animal calorimetry will be discussed with an emphasis on contributions by members of my academic genealogy. The history of direct calorimetry has been reviewed more thoroughly by Mclean and Tobin (39) and by Webb (47).

The **ice calorimeter of Lavoisier and Laplace**. Lavoisier and Laplace are generally credited with being the inventors of direct calorimetry and the first to use this method for the measurement of animal heat (32). Their calorimeter was called an ice calorimeter because the heat evolved was measured by the amount of ice that it caused to melt. The object or animal to be studied was placed in a central chamber surrounded by ice. Surrounding this inner ice compartment was a second ice-filled compartment that minimized the effect that external heat had on the result. The water that melted as a result of heat generated within the inner compartment was collected from a stopcock at the bottom, and by using the weight of the collected water and the heat of fusion of water, the amount of generated heat could be estimated. This represents a type of isothermal calorimeter because the temperature within the test compartment is always at 0°C and all the released heat is absorbed by the melting ice.

The initial experiments using the ice calorimeter were measurements of specific heat of various metals and solutions, but Lavoisier and Laplace then turned to heat generated by the slow combustion of charcoal (24). This represented a fundamental insight into animal energetics because it revealed that the living process was no different than the nonliving process. Lavoisier did not yet have a correct understanding of the site of heat production within the body. He thought it occurred within the lung and was due to the combustion of carbon (“the base of fixed air”) into carbon dioxide (“fixed air”) due to its combination with oxygen (“pure air”) (24).

The ice calorimeter was not without its problems, and it saw little use after the experiments described (35). One problem was the entry of heat from outside through the opening in the surrounding ice that meant that experiments had to be conducted in the winter when the ambient temperature was close to freezing. In addition, the temperature of the inner ice compartment had to be at the melting point, and an accurate determination of heat had to ensure collection of all the generated water. Finally, for the animal experiments, air had to circulate through the calorimeter to replenish the oxygen (pure air, as Lavoisier termed it) and eliminate the carbon dioxide (fixed air). The guinea pig was therefore studied in a cold, 0°C environment, and Lavoisier and Laplace acknowledged that this meant its metabolism was probably increased to maintain body temperature. Despite these difficulties, these French savants were skillful experimentalists, and they were able to obtain historic results that influenced the subsequent course of scientific investigations of heat and of animal heat production.

The next two scientists in the genealogy after Laplace were Gay-Lussac and Liebig, both of whom were chemists who did not engage in animal experimentation. They are the only members of this line who did not use direct calorimetry in their research.

The **Voit-Pettenkofer respirometer**. Carl von Voit is best known for his pioneering use of indirect calorimetry. He and his colleague, Max Joseph von Pettenkofer, also a student of Liebig, constructed the first quantitative open-circuit respirometer in 1862, although an earlier closed-circuit respirometer had been described by Regnault and Rieset in 1849 (47). Voit and Pettenkofer measured carbon dioxide production and estimated the heat production based on fuels consumed. This open-circuit method and the earlier closed-circuit respirometer of Regnault and Rieset were essential tools for understanding animal metabolism.

Voit never published results based on direct calorimetry, but, according to Lusk (37), Voit did construct a direct calorimeter in his laboratory in Munich. However, the findings he obtained using this calorimeter must not have been satisfactory. His efforts in this direction were not in vain, however. Several of his students went on to become pioneers in the use of direct calorimeters in their research, including Max Rubner, W. O. Atwater, and Graham Lusk, my academic great-, great-grandfather.
The contributions of Rubner and Atwater are of particular note because their work confirmed that the law of conservation of energy applied to living organisms. Rubner’s calorimeter used the thermal gradient between the isothermal animal chamber and an air space surrounding the chamber (39). The volume change produced by the small rise in air temperature was used to calculate heat loss. The whole system was surrounded by a constant-temperature water jacket. Rubner used this calorimeter to measure heat loss, including evaporative heat loss, in dogs while simultaneously determining the heat production by indirect calorimetry using an open-circuit Voit-Pettenkofer respirometer. Indirect calorimetry involved measuring oxygen consumption and carbon dioxide production to determine the respiratory quotient and urinary nitrogen excretion to estimate protein metabolism. These latter measurements permitted an accurate determination of the amounts of fat, carbohydrate, and protein oxidized. Using the known heat generated per gram of each fuel, animal heat production could be calculated. In a famous experiment of Rubner’s (6) in which a dog lived in a calorimeter for 45 days, heat production based on gas exchange and nitrogen excretion totalled 17,406 kcal and the heat loss measured by direct calorimetry was 17,349 kcal. The extraordinary agreement between these two values provided convincing evidence for Rubner’s “law of maintenance of energy in the animal body” as well as demonstrating the rigor of his experimental technique. His results proved that under steady-state conditions, the energy derived from the oxidation of food, measured by indirect calorimetry, was equal to the heat generated and lost to the environment, measured by direct calorimetry.

Atwater and his colleagues, in particular F. G. Benedict, verified the same principle on human subjects (47). Atwater’s calorimeter was an adiabatic or heat sink calorimeter in which the subject’s heat loss was captured by water flowing through copper tubes within the test chamber and no heat exchange occurred across the walls of the calorimeter (39). As in the Rubner calorimeter, heat production was also calculated by open-circuit indirect calorimetry, although in later modifications by Benedict a closed-circuit system was used.

The small animal water calorimeter of Lusk. This calorimeter, built by Lusk’s technical assistant Williams (48), was similar in design and principle to ones already in use by Atwater and Benedict. An animal or child rested in an air-filled copper box through which water circulated in a system of pipes to carry away the subject’s heat at the same rate it was produced. The copper box was surrounded by an outer zinc box, and water flowing through tubing in the space between this zinc box and a surrounding cork insulator held the zinc wall and the copper wall at the same temperature so that no heat could flow between them. By this means, all the heat produced by the subject was captured in the water flowing through the interior tubing system. The heat produced was then calculated based on the flow rate of the water and the temperature increase between inflow and outflow. Closed-circuit gas flow was used to measure oxygen consumption and carbon dioxide production. Evaporative heat loss was calculated from the amount of water vapor in the excurrent air absorbed by sulphuric acid. This apparatus was used in a series of studies, mostly on dogs, to determine the effect of various diets on metabolic heat production. This research was published between 1912 and 1932 in a series of 41 papers, the titles of which all begin with the words “Animal calorimetry,” primarily published in the Journal of Biological Chemistry.

The human water calorimeter of Lusk and DuBois. A second calorimeter was built at Lusk’s institute for the study of heat production in human subjects, both healthy and diseased. Its construction coincided with the arrival at the institute of Eugene DuBois, and he was the principal user of this equipment. Its principle of operation and design were similar to the previous one, and its description is given in papers by Lusk (37) and by Riche and Soderstrom (41). DuBois used this device to measure metabolic rates in subjects of different ages and sizes, consuming different diets, and with a variety of disease states, including typhoid fever, thyroid disease, pernicious anemia, diabetes, nephritis, and malaria. Similar to the reporting style of his mentor, Lusk, DuBois published this research between 1915 and 1941 in a series of 54 papers, the titles in this case all beginning with the words “Clinical calorimetry,” many in the Archives of Internal Medicine.

The Bohr-Hasselbalch calorimeter. Calorimetry was by no means a major aspect of the research of Christian Bohr, but he, in collaboration with Hasselbalch (4), conducted a study of the energetics of developing embryos of common fowl using both direct and indirect calorimetry. They used a quite different design from the calorimeters already described. Their method used two identical copper chambers: one contained a developing egg; the other, the reference chamber, contained an electrical resistance heater that was adjusted to keep the two chambers at the same temperature. The two copper chambers were bridged by a constantan wire soldered to each chamber that made each chamber one junction of a thermocouple. The known heat produced by the resistance heater was a measure of the heat production of the egg. Indirect calorimetry revealed that the eggs metabolized fat almost exclusively, and the calculated heat due to fat metabolism agreed well with the heat directly measured by the calorimeter.

This paper by Bohr and Hasselbalch (4) was discussed in a book published by August Krogh (30) in which he compared methods for measuring metabolism. Based on the close agreement that recent workers such as Rubner and Benedict had found between the heat directly measured by calorimetry and estimated indirectly by measuring gas exchange, Krogh favored the latter method because of its greater simplicity. Krogh himself apparently never used direct calorimetry in his research.

The gradient-layer calorimeters of Hardy and Hammel. Hardy initially worked with DuBois in the 1930s on the human calorimeter described above. This research was concerned with characterizing thermoregulatory responses to ambient temperature differences and to partitioning heat loss into its component parts. Later, while still at the Russell Sage Institute, Hardy and collaborators (33) constructed a small animal gradient-layer calorimeter to continue these studies of temperature regulation. The gradient principle they used differed from that used earlier by Rubner in that a large number of thermocouples connected in series and spanning the wall of the chamber directly measured the thermal gradient across the wall.

A early version of this type of gradient-layer calorimeter suitable for infants was described by Day and Hardy (10), but the method was greatly improved by Benzingier and Kitzinger (3), whose instrument was designed to study adult humans. The advantages of the gradient-layer calorimeter over earlier de-
Two separate calorimeters were constructed to measure the heat production of anoxic turtles at 24°C (25, 29). In the earlier calorimeter (29), designed by Schmidt-Nielsen, two identical insulated cylinders were used, one containing the experimental animals and the other serving as a control reference. Unlike the Bohr and Hasselbalch calorimeter, the reference chamber was not manipulated in any way but served to correct for any thermal changes not due to the experimental animals. Hourly temperature changes in the experimental chamber were used to calculate heat produced by the turtles.

In the second study, using a calorimeter of my own design (25) although similar in principle to one used on the toad (Bufo bufo) by Leivestad (34), a single turtle was submerged in an insulated flask that was, in turn, submerged in a larger water bath. Careful temperature control maintained a constant temperature difference between the flask water and bath water so that all heat generated by the turtle was retained in the flask and measured with a sensitive thermistor. Because of the low metabolic rate of the turtle, the flask temperature rose by only a few 10ths of a degree during experiments lasting several hours. This instrument permitted small rapid changes in heat production to be observed.

Both of these studies on anoxic turtles yielded similar results. The heat production of the anoxic turtles fell dramatically to about 10–20% of the normoxic rate at the same temperature. The second study also revealed that this fall in metabolism did not occur until the internal oxygen stores of the turtle were exhausted. Decreased metabolism has proven to be one of the key adaptations that permit this animal to survive long periods without oxygen (26) and is now recognized as a common strategy for coping with stressful circumstances, such as anoxia (17).

Earlier studies using indirect calorimetry, such as a study by Harald Andersen (1) on alligators, had provided evidence for metabolic depression during diving in reptiles. Andersen measured oxygen consumption before and after forced diving and observed that the excess consumption after diving was often less than it would have been had the rate of metabolism remained unchanged during the dive. Indirect calorimetry, however, is not as reliable in this situation as direct calorimetry because it is necessary to assume that baseline oxygen consumption is the same after diving as before diving and that the excess oxygen consumed during recovery is an accurate measure of the diving metabolism. A slight excess oxygen consumption that continues long after the dive is complete is also difficult to detect. The repayment of the oxygen debt that is accrued during diving is also complex because it not only involves restoring normal oxygen stores but also returning ATP and creatine phosphate to their normal levels and metabolizing lactate produced during the dive. As discussed in studies of excess postexercise oxygen consumption in humans (e.g., Ref. 45), the oxidative costs of these separate events are not identical, so the energy yield per milliliter of oxygen consumed can vary. Direct calorimetry, therefore, is the best method for assessing anaerobic heat production. Its application may be challenging, however. For example, the ecological circumstance when submerged turtles most likely experience anoxia is during winter hibernation at low temperature. Because of the extraordinarily low rates of metabolism under these conditions (23), direct calorimetry is unfeasible and indirect methods involving the determination of total body lactate production are used.

Even though my use of direct calorimetry continued a long line of prior usage in my PhD academic ancestry, I applied it based on a project suggested by Knut Schmidt-Nielsen, my postdoctoral mentor, who was not part of the
main calorimetry legacy. He had never before used the technique himself but realized it was the best way to answer a scientific question that interested him. The question concerned the toadfish, *Opsanus tau*, a marine fish that prior research had suggested was an oxygen conformer, which means that its metabolic rate varies directly as a function of ambient oxygen levels. Schmidt-Nielsen wondered whether the fall in oxidative metabolism at low ambient PO2 might be accompanied by a balancing increase in anaerobic metabolism and realized that direct calorimetry would be the ideal way to test this hypothesis. To test this, he set up the calorimeter described above, but once it was operational I realized to my dismay that it was technically unfeasible to simultaneously measure oxygen consumption and heat production with this calorimeter. However, a recently published paper on anoxia tolerance in turtles suggested an alternative project for the instrument, and, with Schmidt-Nielsen’s blessing, I studied the turtle instead.

**Concluding Comments**

As noted earlier, I am humbled by the esteem of my predecessors and my respect for them as grown as I have reviewed their individual accomplishments. The fact that a direct link through a succession of mentor-student relationships connects them to me greatly enriches my appreciation of them and their work. It is gratifying as well to realize that my own history that continues through them. However, to date, none has as yet used direct calorimetry in their research.

I also hope that this effort will inspire others to more fully explore their own academic past history. The pressures of our profession force us to focus on the present and future, but we explore their own academic past history. The pressures of our history that continues through them. However, to date, none has as yet used direct calorimetry in their research.

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DISCLOSURES

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