Diabetes Detectives

By Lee A. Witters, M.D., Marcus Luciano, Carla Williams, and Jessica Yang

Sometimes illumination comes from looking to the future—teasing out new knowledge at the lab bench or in a clinical trial. But sometimes it comes from delving into the past. A professor of endocrinology and three undergraduates perused 19th-century documents for clues to the changing understanding about one of today's most common chronic conditions.

Dartmouth medical students of the era represented here—except for the skinny guy holding the sign—were required to write a thesis before graduating. Students wrote on many subjects, from variola (smallpox) to diphtheria and fracture repair to diabetes mellitus. The latter was very uncommon then but is today a leading cause of death.

In handwriting embellished with the curlicues of a bygone era, James Goodwin recorded his professor's remarks about diabetes in the fall of 1813. Goodwin had entered Dartmouth College from South Berwick, Maine, in 1807; earned his undergraduate degree in 1811; and by the fall of 1813 was less than a year away from earning his M.D. He and his classmates were learning about diabetes from no less a luminary than Dartmouth Medical School's founder, Dr. Nathan Smith.

"Diabetes," Smith told the students—according to Goodwin's notebook, which today resides in the Dartmouth College archives—is a condition "in which the urine is discharged in great quantities and of a peculiar quality. The quantity depends upon the circumstances of the system. The quality depends upon hysteria."

This disease—now referred to by physicians as diabetes mellitus, to distinguish it from diabetes insipidus, which has similar symptoms but a different origin—was well represented in medical teaching as far back as the early 19th century. But it was as poorly understood then as it had been over the prior two millennia.

Hippocrates, in 400 B.C., recognized diabetes but termed it very rare. Six hundred years later, another famous Greek physician, Galen, admitted to seeing two cases during his lifetime.

Today, however, over 240 million individuals worldwide—more people than live in the United Kingdom and France combined—have diabetes mellitus. In the United States, nearly 25 million individuals—8% of the population—suffer from the disease, and almost 25% of those over the age of 60 have been diagnosed with it. Its incidence is disproportionately high among Native Americans, Hispanics, and African-Americans. It is the nation's seventh-leading cause of death; it rose to that rank over the course of the 20th century, in good measure due to the concurrent rise in the prevalence of obesity.

The disease's effects are serious. It is a major contributor to atherosclerosis, known popularly as "hardening of the arteries," which is the leading cause of death in the U.S. It is also the leading cause of blindness in individuals aged 20 to 74, of renal failure, and of nontraumatic lower-limb amputations. And it is a major risk factor among pregnant women for fetal death and for birth defects.

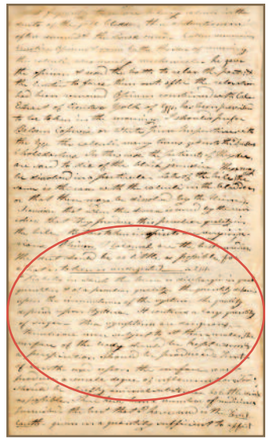
The earliest medical texts, and Smith's lectures, contained descriptions of the disease's symptoms. But the understanding of its pathology and pathophysiology required the emergence of the disciplines of chemistry, histology, and cellular pathology and physiology later in the 19th century. These spawned, in turn, the birth of endocrinology—the branch of medicine dealing with glands such as the thyroid and pituitary. This journey of understanding can be revealed by looking into the notebooks and theses of Dartmouth medical students through the course of the 19th century—the period during which the study of the disease became a fixture in medical school curriculums.

Another Dartmouth medical student, William Pratt, wrote in his 1825 thesis: "Perhaps future experiments may discover the real nature of the proximate cause of diabetes and establish a different mode of treatment from what has hitherto been tried. But until such a discovery is made, the physician must be guided by the symptoms that appear in the disease in the treatment of it."

Indeed, it was the symptoms and signs of diabetes that dominated its story from ancient times until the late 19th century. The Ebers Papyrus, a document that dates from 1500 B.C., tells of a disease in Egypt characterized by the "passing of too much urine" and even suggests a remedy: "Mix cakes, wheat grains, fresh grits, green lead, earth, and water. Let stand moist, then strain, then take for four days."

Sushruta—in 500 B.C. India, an early exponent of Ayurvedic medicine—observed that the urine of such patients tasted like honey, was sticky to the touch, and attracted ants. He even described two forms of the disease—one occurring in older, obese individuals and the other in young individuals who did not live long after the diagnosis. This exactly parallels the modern conception of, respectively, type 2 and type 1 diabetes mellitus. Ancient Arabic texts—such as those of the great Islamic physician Avicenna, who practiced and wrote about medicine 1,000 years ago—also referred to a disease characterized by excessive urination (known as "polyuria") and sweet-tasting urine.

The disease bore many names over the centuries—Galen called it "dropsy of the chamber pot." It eventually came to be known as "diabetes mellitus"—the first word of the name thanks to early descriptions of the disease by Greek physicians, and the second word thanks to an exclamation by

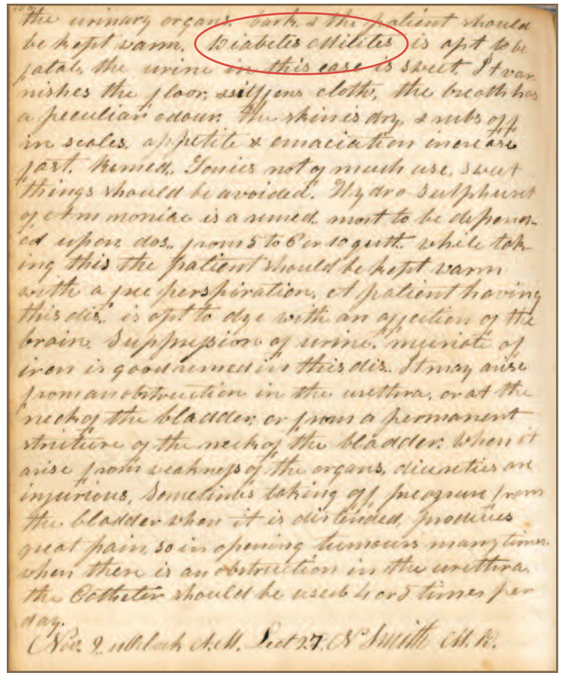


In these notes from an 1813 lecture at DMS, James Goodwin recorded Dr. Nathan Smith's description of diabetes. To research this article, the authors—three of them undergraduates—deciphered hundreds of handwritten pages like this one.

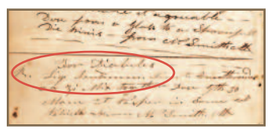
Avicenna, who wrote about medicine 1,000 years ago, referred to a disease characterized by excessive and sweet-tasting urine. Diabetes bore many names over the centuries—Galen called it "dropsy of the chamber pot."

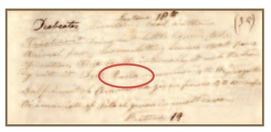
For a WEB EXTRA video of Lee Witters, one of the authors of this feature, talking in more detail about the history of diabetes, see dartmed.dartmouth.edu/winter08/html/diabetes_we.php.

Witters is the Eugene W. Leonard Professor of Medicine and Biochemistry at Dartmouth Medical School and also holds an appointment as a professor of biological sciences at Dartmouth College. Luciano and Williams, both '09s, and Yang, a '10, are Dartmouth undergraduates; all have an interest in both medicine and history. *All the images illustrating the article are courtesy of the Dartmouth Libraries. The authors are indebted for assistance in researching this article to the archivists in Dartmouth's Rauner Special Collections Library—especially Barbara Krieger and Jay Satterfield—as well as to the staff of Dartmouth's Dana Biomedical Library.* *Some of the punctuation in the historical quotations has been standardized for ease of comprehension, but the words are rendered exactly as they appear in the source documents.*



Above, Ezekiel Allen's notes from an 1816 lecture on diabetes. Below left, James Tracy's 1814 notes about an opiate-based remedy for the disease. Below right, Calvin Gorham's mention of Rollo's treatise (whose frontispiece is on page 39).





Dr. Thomas Willis, a noted 17th-century English physician, anatomist, and physiologist (more about this part of the name later).

Accounts differ as to who first used the term diabetes. Some say it was Demetrius of Apamea, who in about 200 B.C. likened polyuria to the siphoning of wine between pots—a practice now called "racking," which has long been used during fermentation to remove the sediment of dead yeast and promote proper aging. Noting the excessive flow of urine in some individuals, Demetrius is said to have referred to the condition as *diabetes*—a Latin word whose origin was a Greek term meaning "a passer-through, a siphon."

Others ascribe the medical appropriation of the word to Areteaus of Cappadocia, a second-century Greek physician who was the first to write extensively about the disease. He provided in one of his surviving texts a stark description of the consequences of the disorder—then still uncommon: "Diabetes is a wonderful affection, not very frequent among men, being a melting down of the flesh and limbs into urine. . . . The patients never stop making water, but the flow is incessant, as if from the opening of aqueducts. The nature of the disease then is chronic, and it takes a long period to form; but the patient is short-lived if the constitution of the disease be completely established, for the melting is rapid, the death speedy. . . . They pass urine with pain, and the emaciation is dreadful; nor does any great portion of the drink get into the system, and many parts of the flesh pass out along with the urine."

The "mellitus" part of the disease's name derives from the Latin word for "honey" and appears to have sprung from an exclamation by Thomas Willis, who called the disease the "pissing evil." Upon tasting the urine of a patient, he said it was "*quasi melle aut saccharo imbutam, mire dulcescere*" ("as if made from honey or sugar, to taste marvelously sweet"). Willis's rediscovery of the observations of Sushruta and Avicenna, among others, led to the distinction between diabetes mellitus and diabetes insipidus ("insipidus" meaning "tasteless"). The latter is now recognized as a totally distinct disease, arising from a failure of the pituitary gland to secrete a hormone called arginine vasopressin (also called antidiuretic hormone, or ADH).

The saccharine nature of the urine of people with diabetes mellitus appears to have first been probed experimentally by Dr. Matthew Dobson, an English physician of the late 18th century who was also the first to document hyperglycemia (an elevation of glucose, or sugar, in the blood), as well as glycosuria (an elevation of glucose in the urine). In his 1776 text *Medical Observations and Inquiries*, Dobson—evidently relying at least in part on gustatory analysis—wrote: "It appears . . . that a considerable quantity of saccharine matter [is] passed off by the kidneys, in this case of diabetes, and probably does so in every imbalance of this disease, where the urine has a sweet taste. . . . It further appears that this saccharine matter is not formed in the secretory organ but previously existed in the serum of the blood." Dobson's observation proved to be an important turning point in the understanding of diabetes mellitus.

The next significant discovery, about 20 years later, was the work of Dr. John Rollo, a surgeon in the British Royal Artillery. With Dr. William Cruickshank—an artillery surgeon, chemist, and apothecary—Rollo undertook a longitudinal study of one Captain Meredith, who weighed 232 pounds and suffered from intense polyuria and dehydration. While adjusting Captain Meredith's diet, the two doctors recorded the quantity and nature of the sugar in his urine and blood, relying in part on taste and in part on the degree of effervescence caused by the addition of yeast to his urine. Rollo showed that a diet rich in protein and fat (largely from animal sources) and low in carbohydrates—together with the administration of several medications, which are noted below—resulted in a substantial weight loss, the elimination of Meredith's symptoms, and the reversal of both his glycosuria and hyperglycemia.

Rollo's recognition of the role of obesity in the development of type 2 diabetes, and of dietary therapy in treating it, were key to the eventual unraveling of the mystery of the disease. He reported his observations on Captain Meredith (and one other officer) in a book titled *An Account of Two Cases of the Diabetes Mellitus*; it was published in 1797—the same year Dartmouth's medical school was founded by Nathan Smith. It appears, based on student notes from Smith's lectures between 1806 and 1816, that he drew heavily on Rollo's conclusions in his own teachings about the disease.

The earliest account of Smith lecturing on diabetes is found in medical student William Ellsworth's 1806 notes, which include an apothecary recipe for one of the medications prescribed by Rollo—"hepatised ammonia," a mixture of hydrogen sulfide (a chemical with a rotten-egg smell) and ammonium hydrosulfide (a salt).

"Diabeates" [sic] was the subject of Nathan Smith's "Lecture 18" during 1811-12, according to Calvin Gorham's student notebook. Gorham wrote that Smith, citing Rollo by name, recommended several of his therapies: low liquid intake, warm clothing, a diet heavy in meat, and several medications—including "tincture of cantharides" and "hydrogenated sulfuret of ammonia" (another name for "hepatised ammonia").

Ninety-two years elapsed between the publication of Rollo's account and the next turning point in understanding the disease. In 1889, a pair of German scientists, Drs. Oscar Minkowski and Joseph von Mering, associated diabetes mellitus with a malfunction of the pancreas when they noticed that a dog whose pancreas had been removed acquired the disease. The observation set in motion events that led to the first isolation and administration of insulin—in Toronto, Canada, in 1921-22. That seminal discovery was the result of a collaboration between a surgeon, Dr. Frederick Banting; a medical student, Charles Best; a physiologist, Dr. J.J.R. Macleod, who with Banting received the Nobel Prize in 1923; and a biochemist, Dr. J.B. Collip. (A compelling version of this oft-told story—including a still-raging debate over whose work was more central to the finding—can be found in Michael Bliss's classic 1982 book, *The Discovery of Insulin*.)

During this 90-year period, as the ancient disease grudgingly gave up its secrets, successive findings made their way into the classroom at Dartmouth. There was an early emphasis on therapies, especially the use of medications, even though Rollo had put greater stress on diet. Smith felt, according to notes by an anonymous student, that the best medication was "tinct. canth. given in a quantity sufficient to affect the urethra." This abbreviation for "tincture of cantharides" refers to an alcoholic extract of the blister beetle, sometimes referred to as the "Spanish fly." Cantharidin, a terpenoid, is its active ingredient; when ingested, it irritates the genitourinary tract during excretion, which may reduce minute-to-minute urine flow.

Smith also advised the use of opiates, James Tracy wrote in his 1814 notebook: "For Diabetes. Rx Liq. Laudanum. Tinct. Cantharides of each 1 ounce. Mix together. Dose 30 drops *none et vespres* in some vehicle." This, too, probably came from Rollo, for he prescribed opium-based medications, such as laudanum, to relieve the pain of diabetes. "*None et vespres*" is Latin for "the ninth hour and evening"—a common way then to indicate twice-daily administration of a drug.

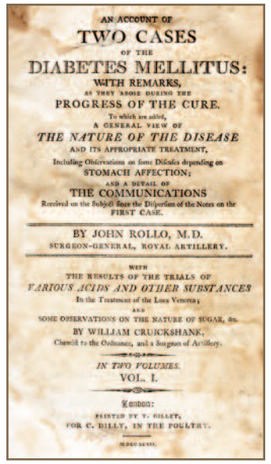
In an 1810 lecture, Smith mentioned that "the sympathy between the kidneys and the skin is very great." He apparently held the mistaken belief that increased demand on the kidneys to excrete water was the cause of glycosuria—the excess water purportedly having been absorbed through the lungs. As a result of this belief, both Rollo and Smith prescribed topical ointments, warm flannel garb, and drugs that induced sweating (including extracts of a tropical plant called *Pilocarpus*)—all to open up another route of water excretion.

From 1816 on, Smith and his fellow faculty members made increasing mention of the disease's pathophysiology. Smith had actually left Dartmouth in the winter of 1814 but was invited back to teach in the fall of 1816. Ezekiel Allen chronicled a lecture he delivered at 8:00 a.m. on November 7 of that year, covering diseases of the liver, pancreas, and kidneys. Little could Smith have known, given the understanding of that day, but his grouping included three of the organs most important in diabetes mellitus.

Allen wrote: "Diabetes militis [this misspelling of "mellitus" marks the first documentation of Smith using the disease's full name] is apt to be fatal; the urine in this case is sweet. It varnishes the floor, stiffens cloth, the breath has a peculiar odor." Taken together, this appears to be Smith's first reference to diabetic ketoacidosis—a life-threatening stage in the disease marked by extreme polyuria and glycosuria, as well as ketosis (an increase in the production of acetone compounds, acetone being the odor referred to in Allen's notes).

Lecturing on a Saturday in November of 1822, according to the notes of student Amory Gale, Dr. Daniel Oliver, a member of the Dartmouth faculty, offered up an early theory about the cause of diabetes. Smith thought the kidneys were the primary organ affected, but Oliver emphasized the "morbid condition of the stomach of forming or evolving the aliment into saccharine matter." He acknowledged that postmortem examination of diabetics showed they often had enlarged kidneys. But Oliver focused, as did Rollo and others, on the gastrointestinal tract as the primary seat of the disease's pathology—though admitting that "the theory, it must be confessed, is in a great deal of obscurity."

Oliver also observed that diabetes "is difficult to cure . . . particularly when it arises in broken constitutions and intemperate habits." But he nonetheless suggested a laundry list of possible therapies—



AN ACCOUNT OF
TWO CASES
OF THE
DIABETES MELLITUS:
WITH REMARKS,
AS THEY AROSE DURING THE
PROGRESS OF THE CURE.
To which are added,
A GENERAL VIEW OF
THE NATURE OF THE DISEASE
AND ITS APPROPRIATE TREATMENT,
Including Observations on some Diseases depending on
STOMACH AFFECTION;
AND A DETAIL OF
THE COMMUNICATIONS
Received on the Subject since the Dispersion of the Notes on the
FIRST CASE.

BY JOHN ROLLO, M.D.
SURGEON-GENERAL, ROYAL ARTILLERY.

WITH
THE RESULTS OF THE TRIALS OF
VARIOUS ACIDS AND OTHER SUBSTANCES
In the Treatment of the Lues Venerea;
AND
SOME OBSERVATIONS ON THE NATURE OF SUGAR, &c.
BY WILLIAM CRUICKSHANK,
Chemist to the Ordnance, and a Surgeon of Artillery.

IN TWO VOLUMES.
VOL. I.

London:
PRINTED BY T. GILLET,
FOR C. DILLY, IN THE POULTRY.

DMS founder Nathan Smith clearly relied heavily in his teachings about diabetes on this early clinical study of the disease by British surgeon John Rollo. It was published in 1797, the same year that Smith founded DMS.

Dartmouth medical student Ezekiel Allen chronicled a lecture that Nathan Smith delivered at 8:00 a.m. on November 7, 1816. Smith said diabetes "is apt to be fatal; the urine in this case is sweet. It varnishes the floor, stiffens cloth, the breath has a peculiar odor."

Artistic flourishes and marginal digressions

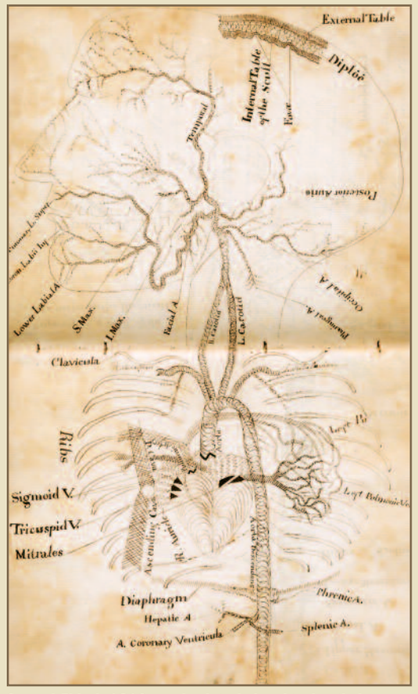
By Marcus Luciano, Carla Williams, and Jessica Yang

Much like today's Dartmouth medical students, those of the 1800s did not *always* have their noses to the grindstone. While their elegantly handwritten notes do cover subjects as serious as the anatomy of the head and chest, some student notebooks digress into more frivolous territory—such as garden layouts or faculty caricatures.

Within the reams of 19th-century classroom notes and medical theses that are housed in the Dartmouth College archives, there are a number of artistic flourishes and marginal digressions.

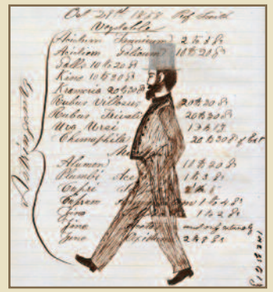
Depicted below are several of the more striking examples.

The authors are all Dartmouth undergraduates. They assisted DMS faculty member Lee Witters with the adjacent feature and, in the process, came across the engaging asides here.

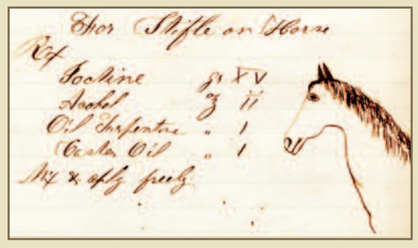


Samuel Elder's 1810 notebook includes this detailed anatomical drawing of the head and chest, with precise serif-style lettering identifying the major arteries and veins.

William Ellsworth's signature at the end of his 1806 notes from a chemistry lecture by Nathan Smith is a nearly perfect model of copperplate elegance. Note, however, that he appears to have gotten a little too carried away with his swashes and swirls—and as a result he ran out of space and was forced to insert the final two letters of his last name in the upper right-hand corner of the page.

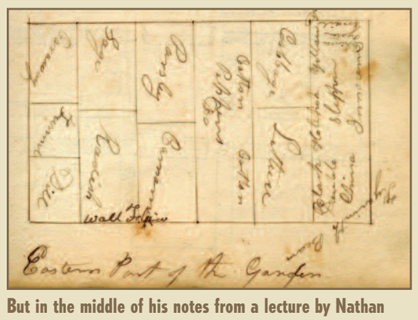


The art of doodling in class was apparently well developed, as indicated by these 1858 notes by George Gove.

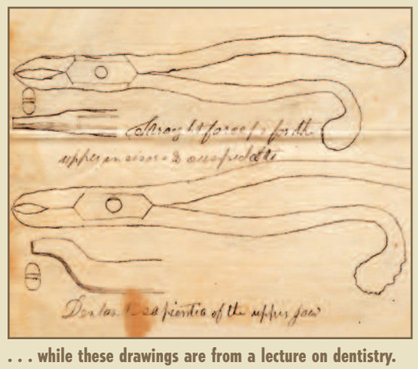


Dartmouth medical students of the 1800s benefited from a wide-ranging curriculum; the sketch above is contained in notes taken during a lecture on veterinary medicine . . .

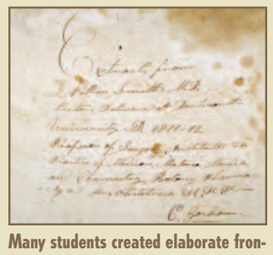
This cover sheet graces William Baldwin's 1880 thesis on gonorrhea.



But in the middle of his notes from a lecture by Nathan Smith and Cyrus Perkins, Elder plotted out his garden.



. . . while these drawings are from a lecture on dentistry.



Many students created elaborate frontispieces for their notebooks. Here, Calvin Gorham listed Nathan Smith's faculty appointments in 1811-12.

including Rollo's animal diet, "Peruvian bark" (a source of quinine), and "chalibeate [sic] tonics." Chalybeate waters (iron- and mineral-rich waters) were used widely at the time to promote health.

In addition, Oliver suggested bloodletting and inducing "blisters on the loins" as treatment options that "may always be tried unless there is a broken constitution." These two ancient practices were widely used for many maladies until the end of the 19th century. Oliver's advocacy for blistering implies a lingering suspicion that maybe diabetes was, after all, a disease of the kidneys—that blisters on the loins would allow what physicians of the time termed "bad humors" to exit from the kidneys.

In August of 1798, the Dartmouth Board of Trustees voted that every medical student "shall read and defend a dissertation on some medical subject . . . sixteen copies thereof to be delivered to the President for the use of the College and the Trustees." In 1812, the Trustees amended the requirement, calling for each dissertation's "principles [to be] defended by the author at a public examination in the University Chapel." Over the next 84 years—until the practice was discontinued following an 1882 vote by the faculty—Dartmouth medical students wrote more than 1,200 theses on a variety of subjects. All of them reside today in the Dartmouth archives; six are on the topic of diabetes. These six theses provide further insight into the evolution in what Dartmouth medical students were taught about the disease.

In his 1825 "Dissertation on Diabetes," William Pratt—while "confessing" that diabetes was a disease of "rare occurrence" and one he was not "personally acquainted" with—reviewed many of its aspects. He vacillated between attributing it to a "morbid state of the liver" and "a disordered state of the stomach." Seemingly unaware of Dobson's observations about elevated glucose in the blood, he rehabilitated a theory that had been proposed by a granduncle of the famous naturalist Charles Darwin, suggesting that chyle (a lymphatic fluid in the intestine) could pass directly to the kidneys by "retrograde action." The saccharine contents of the stomach could thus, Pratt proposed, make their way into the urine without appearing in the blood. Alternatively, he suggested that the kidneys may become "morbidly excited" and as a consequence "form the saccharine matter found in the urine of diabetic patients."

Jonathan Brown, in his 1828 thesis "On Diabetes," correctly predicted that sugar would always be found in the blood of diabetics "once sufficient testing techniques are developed." The ultimate "cure" for the disease, he wrote, lay in perfecting a regimen of "strict diet control"—an idea in line with modern thinking. He appears to be the only one of the six thesis-writers who had actually seen a case of diabetes. He lamented not having used a purgative—a drug that cleans out the bowels—to deal with this patient's "morbid irritation," as he put it. "My remarks in relation to purgatives in diabetes were suggested by a case which came under my inspection, where my neglect of the bowels was followed by a sudden increase in the quantity of urine. And were another case presented to me from the impression of this fact, I should be led to the efficiency of regular purging."

In 1835, William Brown titled his thesis simply "Diabetes." He made a conceptual leap, suggesting that the body itself produces the glucose present in diabetics' urine, presaging our current-day recognition of the impact of gluconeogenesis (the production of new glucose) in hyperglycemia. "The blood contains plenty of Carbon, Hydrogen, and Oxygen," he wrote, "and why may not they be combined in the proportions to form sugar in preference to the combination which constitutes the composition of urea?"

Story Goss wrote a thesis in 1856 on "Diabetes Mellitus." He drew in part on an important text in the Dartmouth library, William Prout's *Inquiry Into The Nature and Treatment of Diabetes, Calculus, and Other Affections of the Urinary Organs*, published in 1826. Goss's paper indicates that he had knowledge of two important developments in the emerging science of metabolism. First, he was clearly aware of the important observations of Dr. Claude Bernard, a French physiologist who in 1848 demonstrated that the liver could be a source of glucose and identified glycogen as its storage form. But rather than postulate that the liver was synthesizing and releasing excessive glucose, Goss claimed that the problem lay in the lungs. Glucose metabolism was known to generate carbon dioxide, and Goss assumed that process occurred exclusively in the lungs. He went on to suggest that hyperglycemia arises because the lungs are limited in the amount of glucose they can metabolize, so they dump unmetabolized glucose into the bloodstream.

The other scientific finding Goss mentioned was the identification of diastase—the first enzyme ever recognized and isolated (from a malt solution, by the French chemist Anselme Payen in 1833). Goss suggested that perhaps abnormal diastase action on starch in the stomach contributed to hyperglycemia. This was another prescient supposition, for the modern antidiabetic drug acarbose (which goes by the brand name Precose)

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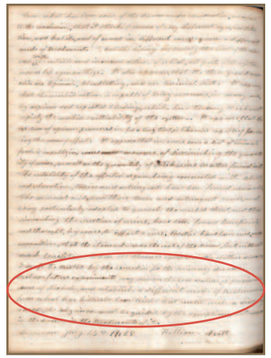

William Pratt's 1825 thesis was the first of five dissertations on diabetes written during the 19th century by Dartmouth medical students. On this page, he predicts that "future experiments" will eventually reveal the cause of the then-fatal disease.

The "cure" for diabetes, wrote a student in his 1828 thesis, lay in perfecting a regimen of "strict diet control"—an idea in line with modern thinking. He appears to be the only one of the six thesis-writers who had ever seen a case of diabetes.

Diabetes Detectives

continued from page 41

acts by inhibiting polysaccharide metabolism in the intestine.

But despite Goss's insightful leaps, and his comprehensive review of all the then-current therapies, he listed none beyond those posited by Rollo 60 years earlier.

The final two student theses on diabetes date from 1880—Fred Spafford's "History, Pathology and Treatment of Diabetes Mellitus" and Hoell Tyler's "Pathology of Diabetes Mellitus." Their papers present most of the then-known thoughts about diabetes and glucose metabolism.

Spafford leaned heavily on the French physiologist Bernard, citing his important observation that diabetes could be induced by making lesions in the floor of the brain's fourth ventricle, indicating a neural contribution. This understanding presaged observations by Dr. Bernardo Houssay about the role of pituitary hormones in the onset of diabetes—work that won him the 1947 Nobel Prize. Spafford even suggested a genetic role in the disease—despite the fact that human genetics did not yet exist as a discipline—in his mention of twin boys with diabetes mellitus and of a mother and her two children who died of the disease. This, too, presaged later knowledge: the modern recognition of an inherited form of the disease.

Tyler's 1880 thesis contained references to both the past and the future. He reached back to the first century in citing descriptions of diabetes by the Roman encyclopedist Celsus. But he also correctly theorized that a contributing factor in the development of hyperglycemia was "increased introduction [of glucose], decreased destruction, or both." This is consistent with modern understanding of the mechanisms involved in the elevation of blood glucose.

From William Ellsworth's 1806 notes to these two 1880 theses, the documents in Dartmouth's archives show an evolving comprehension about the nature of diabetes. Interestingly, however, the conceptual leaps that occurred during this period did not lead to a parallel evolution in treatments. As late as 1880, Spafford and Tyler still listed nearly the same remedies that Nathan Smith, borrowing from John Rollo, had taught in the first decade of the century. Furthermore, all these remedies were entirely empirical, reflecting the ignorance that then prevailed regarding the genesis of diabetes mellitus.

But less than a decade after Spafford and Tyler penned their theses, Minkowski and von Mering's 1889 observation regarding the role of the pancreas finally pierced the cloud of ignorance around the disease's metabolic derangements. And that led to the discovery of insulin just three decades later. Yet, as is the case with all advancements in medical science, the discovery of insulin was hardly due to the work and imagination of just a few investigators. Louis Pasteur once said, "If the fruit has appeared, there must have been some cultivation of the tree." This cultivation, in the case of diabetes mellitus, occurred over the course of many centuries—but especially during the period encompassed by the Dartmouth documents. These medical students of the 19th century bore witness to a dramatic unraveling of the mysteries of "dropsy of the chamber pot."

Jonathan Brown concluded his 1828 thesis with this qualification: "These desultory remarks, which be . . . called 'observations vented in mangled form,' possess perhaps more imperfections than would be ponderable even in a juvenile debut. . . . With truth I assert that nothing short of a law of this institution induced me to attempt the discussion of this medical subject which would come to the inspection of my elders in the sciences." (Let it be noted that though Brown deemed his thesis a "mangled" effort, he went on to a career of some distinction. He later studied with Dr. Walter Channing—Boston's leading obstetrician, the dean from 1826 to 1847 of Harvard Medical School, and a founding editor of the *New England Journal of Medicine*. Brown also—after living in Santo Domingo, now Haiti, in 1833-34—wrote one of the important early histories of that nation, from its French colonization to its independence.)

Brown went on to end with these words: "With a lively sense of gratitude, I express my acknowledgements to the learned professors of this school and wish them and the institution that prosperity and eminence which learning joined to virtue so much deserves."

Similarly, it is "with a lively sense of gratitude" that today's medical detectives acknowledge the clues left behind by Brown and others regarding that era's growing understanding of diabetes mellitus. ■