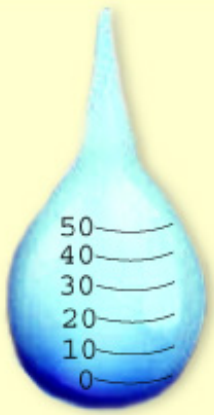
HMS BEAGLE

FEATURE 1

The Art of the Pipet

by Jay A. Martin



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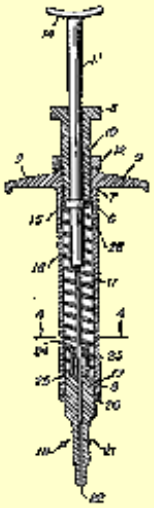
Abstract

In the last quarter century, the adjustable mechanical pipet has become an ergonomically correct and precise tool for researchers. A combination of artistry and innovation inspired its evolution.

People who spend most of their adult lives at the bench gain a lifelong friend - the adjustable mechanical pipet. Like the bricklayers and masons who built a great city with the "stones of Venice," we can admire the scientists and engineers who built better lab tools for us. "It is less the actual loveliness of the thing produced," says Ruskin, "than the choice and invention concerned in the production, which are to delight us."

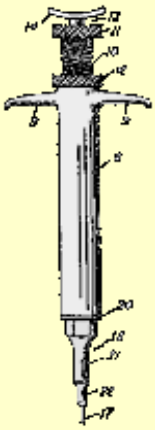
Because of its advanced design, today's air-displacement pipet dispenses liquids with high accuracy. (In an air-displacement pipet, an air pocket always lies between the liquid and a piston. In positive-displacement pipets, a piston makes direct contact with the drawn liquid.) Rainin's L-2 Pipet-Lite, for instance, can pick up 1.0 µL of liquid with 3 percent accuracy. Features like "Magnetic-Assist" and advanced pipet components like LTS tips reduce hand strain while depressing pipet plungers and ejecting tips. These improvements may, according to Rainin, reduce

repetitive stress injuries by as much as 65 percent. An ergonomically correct pipet feels as though the tool is doing most of the work for us. This was not so with the first Pipetmen that weighed in our younger hands.



In the history of science, "We want to know where new ideas come from," says Katherine Ott, curator of the Division of Science, Medicine and Society of the National Museum of American History at the Smithsonian Institution. "We want to understand the process." For more than two centuries people have been driven - by its imperfections and the needs of science - to improve incrementally the pipet so that the modern design is sufficiently economical to mass produce and as natural to use as our own hands. The pipet is now a tool arrayed to perform the work of millions of hands in fractions of seconds. Let us use our one free hand to turn the pages on a short exploration of how an indispensable lab tool improved, and how innovators turned invention into an art - the art of the pipet.

> *One of the most notable developments for us in the design and manufacture of instruments for biochemistry was the result of meeting Eric Marteau d'Autry in about 1959, while he was a visiting French student in the business school (at the University of Wisconsin at Madison). At age 22, he was an outstanding individual. I wanted to learn French, and he was ambitiously interested in manufacturing. He turned out to be a combination of Marco Polo, Napoleon, and Alexander the Great, with just a touch of Attila the Hun.*



On the body of the traditional P-series pipet it says, in relief, "Gilson." Warren Gilson, who earned his M.D. in 1940 at the University of Wisconsin, invented and patented the mechanical basis for the popular adjustable pipet (U.S. Patent 3827305, 1974). Nearly 30 years after its patent, the Pipetman continues to be manufactured in France in a factory started by Gilson's colleague and manufacturing mentor, Eugene Marteau D'Autry. Shortly before Gilson's patent was issued, Gilson sold the marketing and sales rights for the Pipetman to Ken Rainin, president of Rainin Instrument, because, Gilson says, "He was a good salesman."

Gilson has been inventing lab and medical devices his entire life. He founded Gilson Medical Electronics in 1945, and three years later introduced a modified Warburg respirometer, a device used to measure respiratory volumes. Crafted in "circular" format with a digital readout, it was a marked improvement over the original "rectangular" format Warburg respirator introduced at the turn of the twentieth century. Gilson combined the features of the digital readout from his respirometer and the engineering of a German-made pipet to invent a pipet featuring a digital readout with counter wheels. It was compact, cheap to make, sturdy, and dispensed accurate volumes of liquids. To this day, Gilson continues as chairman of the board at Gilson, Incorporated, in Madison, Wisconsin.

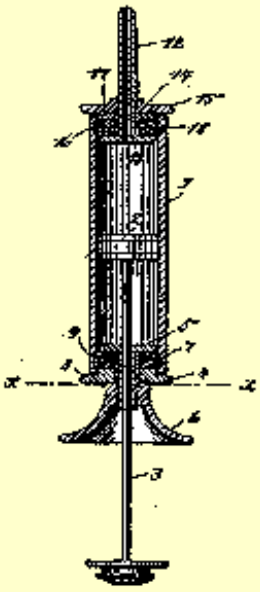
Marketing and scientific needs have driven the evolution of the modern pipet, design choices made by the original inventors, Gilson and Marteau D'autry. To be sure, Gilson's pipet of 1974 looks little like one of today's models. Marteau D'Autry elaborated on the Gilson design by introducing the stainless-steel tip ejector in 1991 (U.S. Patent 4141250, 1979). In tandem with his comrade, Marteau D'Autry, Gilson began the long, slow extinction of the original "volume adjustment assembly," or the turnable rings, once found on the handle of the pipet. In response to the AIDS epidemic of the 1980s, Gilson redesigned and patented a modified "rotary drive system" to make it easier to set the volume of the Pipetman with gloved hands (U.S. Patent 5018394, 1991). In 1995, Marteau D'Autry splined the "push rod" so we could adjust the volume setting by turning the top knob instead of turning the rings (U.S. Patent 5413006, 1995). Rainin's own engineered Pipet-Lite and Pipet-Plus do away with the rings completely. Gilson says he built better pipets "just for the fun of it."

Some of the technological leaps, however, toward an improved pipet were bigger.

> *We started a factory just north of Paris, and I can now speak a little French. The*

prototype, various parts, and crude sketches were taken by Eric to our factory in France. They developed and produced a suitably sturdy product, which could be dropped on the floor without harm.

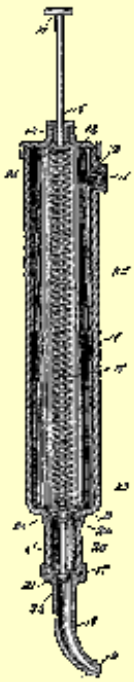
Scientists did not always handle small volumes with adjustable mechanical pipets. Even in the 20th century, when a mechanical pipet would have been handy, they used graduated glass tubes. The glass tubes had to be big enough to be visibly graduated, which forced scientists and inspectors in the field to dispense and transfer bigger volumes of liquids. The increasing volumetric demands of microanalysis and molecular biology over the past 50 years drove pipet innovation.



J.J. Rodriguez of Berkeley, California, for instance, introduced a patent (U.S. Patent 3013435, 1961) 13 years earlier than Gilson's for an "improved buret." Rodriguez designed the buret to dispense liquids like a buret, but he claimed his invention was providing "a novel and improved buret capable of use in pipetting." Gilson argued in his 1974 patent that Rodriguez's buret/pipet volume adjustment mechanism was too awkward and complex to adjust. "This device provides an indication useful for buretting, the indication does not correspond consistently with the actual volume setting when the device is used for pipetting." We owe Gilson's drive to perfect his own pipet to the so-called unreliability of the "continuously adjusted" volume mechanism of pipet precursors.

In the same 1974 patent, Gilson cited another ancestral liquid-handling tool. He recognized another conserved trait of the pipet besides volume adjustment: G.S. Riggs' pipet was "mechanical" (U.S. Patent 2530909, 1950). Riggs was, perhaps, a milk inspector when he patented his device. He observed that "it is a matter of common knowledge in the trade" that milk inspectors mouth-pipetted raw milk samples in a .018-inch-diameter glass tube and transferred the sample to a slide for view under a microscope. If inspectors used Riggs' invention, they would use the pipette, having a barrel with a "suitably bored intake tip." The barrel contained a piston, "provided with a spring returned manually depressed plunger which is such as to expedite the steps of first sucking the milk."

From Riggs to Gilson pipets, then, all were mechanical and they all had pistons or plungers, similar to the plungers found in syringes. These inventors found ways to automate the movement of pistons in mechanical pipets. The Riggs pipet, for example, had a plunger driven by a spring to suck in and push out milk, a spring-and-piston mechanism that perhaps is quite similar to George Wilson's bicycle oiler. It is no accident that Riggs, the putative milk inspector, cites in his mechanical pipet patent Wilson's patent of the oiler for bicycles (U.S. Patent 730065, 1903).



A rash of European and U.S. patents on bicycle ("velocipede") gears appeared between 1899 and 1906, so Wilson's 1903 patent for a bicycle oiler, "especially adapted for use in connection with the parts of bicycles," is consistent with the concurrent innovation of bicycle gears. For instance, Roxendorff's "Automatic Variable Driving Gear for Velocipedes" (U.S. patent 636184), and the "Sturmey-Archer" gear. Wilson's oiler featured a self-closing valve that opened by way of pushing on a piston that moved down a cylinder. Wilson provided "a means for automatically returning the piston when operated to a point at or near the bottom of the reservoir."

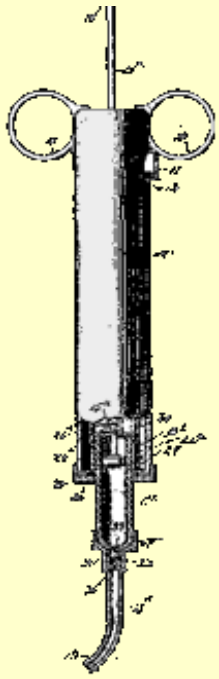
It was conceived in about ten milliseconds. I had a German-made fixed volume pipet in one hand, and in the other a volumometer used in our 1963 respirometer. It used a piston and counter with number wheels. With most of the existing parts in production, a prototype was made by a machinist in two days.

This first model was given to a local German laboratory technician, who was not favorably impressed. It sat on the corner of my desk for a month or three, until Eric saw it and realized its potential. He

somewhat excitedly commented that we could sell 3,000 of them a year! This turned out to be a considerable underestimation.

So, the cyclists, milk inspectors, and scientists of the early- to mid-twentieth century did not enjoy reliable and easy to use adjustable pipets. They relied on mechanical spring-loaded devices that acted on plungers or pistons that displaced air, created a vacuum, and sucked in liquids. In the drawings of Riggs's mechanical pipette and Wilson's oiler, a casual observer might say that the genesis of the modern pipet is the syringe. In fact, Riggs cites a patent by Martin Overlach, "resident at Frankfort-on-the-Main, Germany" (U.S. Patent 404105, 1889). Overlach recognized a need for a syringe to house a chamber that didn't leak.

According to Ott, a leading authority on the history of the syringe, history does not suggest that the syringe is a close relative of the pipet. The hypodermic syringe did not debut until the mid-19th century, about 50 years after Descroizilles, a French chemist and pharmacist, invented and first introduced the buret and pipet to science in 1795. He called his burette a "berrholli-metere": it was a graduated cylinder. He later described an "alcalimetre," to dispense small volumes of liquids. Not until 1824 did Gay-Lussac publish the names "burette" and "pipette" (French, "wine tester"; Ferenc Szabadvdry, *Instruments*). The syringe, on the other hand, was not graduated in its early stages. Early syringes were often made of metal rather than glass to avoid breakage when transported in saddlebags. Because of their mechanical nature, the syringe provided a "modernizing 'professionalization' tool," according to Ott, wielded by 19th-century doctors. Therefore, there is likely no direct lineage of the syringe, a medical device, to the pipet, a scientific tool.



But a technological relationship between the syringe and the pipet could have some validity. Wilson's oiler and Overlach's syringe contained pistons, and the piston remained a fundamental component of portable dispensing devices referenced in patents back to Overlach's late-19th century syringe. The syringe did not play a direct role in the development of the pipet, but the piston action, instrumental to the operation of many types of syringes, did find early success in shaping the modern pipet.

The principal and highly successful product of the French factory is the Pipetman, which I invented in Wisconsin in 1972.

- Warren E. Gilson, March 2001

Jay A. Martin is a full-time technical writer at Genentech. He also writes for several life-science and medical Web sites. *He "gratefully acknowledges the inventor of the Pipetman, Warren E. Gilson. Without his gracious willingness to tell his story of his invention and his patience to set me straight on Pipetman history and engineering, I could not have written this article. His story is as important to the article as the introduction of counter wheels was to the pipet. I am also very grateful and humbled by the valuable information provided by Katherine Ott, curator, Division of Science, Medicine and Society, National Museum of American History, the Smithsonian Institution, on the history of the syringe. Ghislaine Lawrence, curator at the Science Museum, and David Thomas, assistant curator at the same, provided invaluable leads on the syringe. Joanna Corden of the Royal Society, London, encouraged me to check the extensive resources of the Society's JSTOR database. Jim Petrek, vice president of engineering and manufacturing and Christine Hatch, service representative, both at Rainin, clarified many points for me on the engineering of the Pipetman. Thanks to Ms. Hatch for lending me the P-20."*

Cary Barnhard grew up in New Jersey, where his senior class voted him "most unique." He maintains that honor is a polite way of being voted "most likely to need therapy." After a few misadventures in the music industry, he started pretending to be a graphic artist. Eventually it became the truth.

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Early Bicycles - an *Encyclopedia Britannica* entry outlining features of the earliest bicycles.

Micropipet Practice - from the Fred Hutchinson Cancer Research Center, includes a virtual dialing exercise and pipetting instructions.

Epact: Scientific Instruments of Medieval and Renaissance Europe - one of many online exhibits accessible from the Museum of the History of Science.

Scientific Instrument Society - attracts members with an interest in both antique and modern research tools.

United States Patent and Trademark Office Web Patent Databases - provides quick access to the full text of U.S. patents issued since 1976 and images of patents issued since 1790. See also the Delphion Intellectual Property Network .

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