Scientists have a lot of tools to choose from but generally rely on the same handful to complete the day-to-day tasks involved in their research. Few, if any, labs could function without pipets, centrifuges, and freezers. However, one type of instrument stands alone as arguably the most important technology for contemporary endocrinology: mass spectrometers.

Detailed Analysis

Kevin Yarasheski, PhD, professor and assistant director of the Biomedical Mass Spectrometry Research Facility at Washington University in St. Louis, sees spectrometry as the primary analytical platform for any endocrinology laboratory. “Gas chromatography-mass spectrometry and liquid chromatography-mass spectrometry are the most critical assets for my research,” he explains.

By providing the greatest sensitivity for identifying, characterizing, and quantifying the broad range of organic molecules involved in disease pathogenesis — including proteins, carbohydrates, lipids, nucleotides, and chemically modified forms of these biomolecules — mass spectrometers allow for a high level of accuracy in diagnosis and treatment monitoring.

For Yarasheski, this exactitude makes his work possible. His research focuses on identifying the pathogenesis and potential treatments for metabolic-endocrine complications in HIV/AIDS, Alzheimer’s disease, obesity, diabetes, and advanced age.

He uses other state-of-the-art biotechnologies as well, such as magnetic resonance spectroscopy and positron emission-computed tomography. But mass spectrometry offers specific quantitation of the various hormones, signaling molecules, and metabolites that cannot be beat.

Origins of Discovery

Among the many inventions born from the Second Industrial Revolution came the mass spectrograph, an amalgamation of imaginative devices that began its evolution at the tail end of the 19th century with British physicist J.J. Thomson.

By directing ionized neon through both electric and magnetic fields and analyzing how far the particles were deflected, Thomson found that the particles behaved varyingly. He thus concluded that they must have differing masses.

It would be Thomson’s assistant, though, to bring to life the mass spectrograph 20 years later. Francis W. Aston experimented with updates and improvements to Thomson’s instrument until finally devising a tool that would allow him to confirm the existence of isotopes — a discovery that ultimately won him the Nobel Prize in Chemistry in 1922.
As World War II neared, the mass spectrometer took on a new role. Only this device could answer questions about nuclear fission, and so it became a tool of the scientists in the Manhattan Project, which developed the first atomic bombs. Although the results of this research would lead to wartime devastation, the mass spectrometer gained greater recognition in the scientific community for its other potential uses, from testing petroleum samples for oil companies to drug discovery.

The latter half of the 20th century saw many refinements to mass spectrometer technology that expanded its applications for a wide range of scientific endeavors, especially medical research. In 2002, Koichi Tanaka and John Bennett Fenn each received one-quarter of the Nobel Prize in Chemistry for developing a new way to analyze biological macromolecules using mass spectrometry — demonstrating the enormous advantages of the new generations of the instrument.

Spectrum of Findings

Today, the mass spectrometer is ubiquitous in healthcare laboratories. It sequences oligonucleotides for genomic tests, finds disease biomarkers for clinical diagnoses, monitors enzyme reactions for proteomic analysis, and outlines the structures of metabolites and drugs. In the complex field of endocrinology, such activities have proven invaluable.

The advances that have occurred in medicine with the help of mass spectrometry are so far-reaching that the entirety would take ages to list. Endocrine researchers are coming to depend on this technology more and more to pursue growing areas of interest.

According to an article in the *American Journal of Clinical Pathology* titled “Current and Future Applications of Mass Spectrometry to the Clinical Laboratory,” one of these major areas is vitamin D.

“The increase in testing for vitamin D has resulted in a dramatic amplification in interest and implementation of clinical mass spectrometry,” it states. Immunoassays cannot accomplish some of the tasks that mass spectrometry can, such as separating out vitamin D2 from vitamin D3. The authors go on to describe how “a lack of specificity and accuracy at low concentrations in many steroid immunoassays has contributed to mounting frustration in the diagnosis of endocrine disorders and has led several medical groups to recommend mass spectrometry as the preferred method of analysis.”

The growing demand for mass spectrometry in endocrine research does not come without certain obstacles, however. “The application of mass spectrometry to steroid analysis has not been free of challenges and requires a high degree of technical competence, skill, and experience to provide the needed improvement for measures of endocrine function,” the authors explain.

The Next Generation

Mass spectrometry includes increasingly complicated machinery that requires more and more training for experts to operate. The equipment has come a long way from the rudimentary mass spectrograph that Aston created nearly a century ago.

Today, scientists like Yarasheski rely on newer renditions like gas chromatography mass spectrometers and liquid chromatography mass spectrometers to analyze complex gas and liquid samples. Stanford University, for example, has 11 varying types of mass spectrometers in its laboratories, each capable of different tests.

Thanks to these devices, diagnoses of endocrine disorders in newborns have greatly advanced, and future therapies for diseases like Alzheimer’s seem to be on the horizon. Although the knowledge and skill required to use modern spectrometers may intimidate some, the accuracy they provide has rocketed them to the forefront of medicine. Yarasheski anticipates that research publications will soon cease to accept certain types of research that excludes the technology.

“In the near future, peer-reviewed endocrine journals will demand that manuscripts report protein/peptide hormone and biomolecule concentrations quantified using mass spectrometry platforms,” he says. “Manuscripts will be rejected if they don’t adhere to this analytical demand.”

As a result, according to Yarasheski, mass spectrometrists are scrambling to develop and validate quantitative mass spectrometry-based assays for all protein/peptide hormones and biomolecules of interest so that they can duly serve their endocrine clients.

If this prediction comes to fruition, soon endocrinologists worldwide will rely on mass spectrometers in their laboratories more than ever before.

— Mapes is a Washington, D.C.–based freelance writer and a frequent contributor to Endocrine News. She wrote about the “Plan B” pill and overweight women in the August issue.