Chapter 13
Henry M. Leicester and
Development of Biochemical Concepts from Ancient to Modern Times (1974)

Henry Leicester received his Ph.D. in Biochemistry from Stanford University in 1930. He pursued this subdiscipline of chemistry throughout his career. He also became a prolific historian of chemistry and was awarded the 1962 Dexter Prize for his work on the history of Russian Chemistry. His last major book combined his love of biochemistry and his love of history.

The Preface reveals that Leicester understood both chemistry and biology better than most biologists and chemists. He also understood what science history is. Rather than trying to narrow the field of discussion, he has chosen to follow the evolving concepts that were already evident in the work of Aristotle and Galen.

Leicester defines Biochemistry as:

> The study of the composition of living organisms and the mechanisms by which the various components interact to produce the changes in metabolism and function that make life as we know it.

One of the first issues for observing and thinking humanity was the distinction between living and nonliving matter. This led to a demarcation between “organic” and “inorganic” matter. This way of thinking is still present in 1974.

Other sets of distinctions arose: heat and cold, male and female, wet and dry, etc. The concept of “contraries” is found throughout the history of chemistry. Leicester attributes thinking of this kind to Mesopotamian culture: Sumerian and Babylonian civilizations. Extensive “pharmacopeia” have been discovered from this period.

Egyptian physicians and morticians engaged in dissection of animal bodies, including humans. They focused on the “input-output” nature of life. They also identified different kinds of “fluids” associated with living organisms. Strict “diets” were prescribed in order to maintain “balance.” (This form of medicine survives in Idaho and Hollywood.)

The greatest of the 2nd century physicians was Galen of Pergamon (129-199). He was a court physician and employed all the known "drugs" in his practice. One of his most famous potions was "theriac." He did not invent it, but he did concoct it as part of his imperial practice. The recipe contained 64 ingredients. The basic theriac started with wine, herbs and honey. It often included cinnamon. Flesh of vipers was a common ingredient. But the most important constituent was opium!

In the "Molecular World" (Jackson, 2023) of the 21st century it is easy to forget that for 30,000 years chemists thought in terms of macroscopic "substances." Galen was a keen observer of the biological world. He applied his knowledge to the health of his emperors and gladiators. Like Paracelsus, most of his patients lived, rather than died. He was a keen observed of blood, and recognized that there were "different" forms in the arteries and veins. He studied phlegm and used it to diagnose disease. He studied "bile" and divided this "world" into yellow and black. He observed both input substances, like air and water and wine, and output substances, like vomit, urine and excrement. (There are still Galenic physicians in Idaho.) Galen created a "coherent" world that persisted until the present.

Leicester chooses Theophrastus Bombast von Hohenheim (1493-1541) (Paracelsus) as the first practitioner of biochemistry. Like many of his predecessors, Paracelsus was a practitioner of "medicine." Unlike most of them, he treated the poor as well as the rich. He adopted a dynamic view of material reality and believed that substances could be changed from one sort into another. Paracelsus "personalized" his agent of change: the Archeus. He claimed that it was an Archeus that "dwelled" in the stomach that changed food into nutriment. He assigned a different Archeus to each human organ.

One of Paracelsus' insights was that material that "accumulated" in the body was not beneficial. Gout is caused by crystals of uric acid. Kidney stones are often due to crystals of calcium oxalate. He believed in "specific" medicines that cured actual diseases. He also understood that chemical remedies needed to be given at the right dosage. Too little may have no effect and too much may kill the patient.

While Paracelsus did not employ the common ploy of swirling urine in a flask to reveal the disease, he did chemically analyze urine. He understood that it was a mixture of substances. He precipitated "albumin" in the urine by adding acid.

Leicester quotes one of Paracelsus' biographers: H. M. Pachter (1907-1980) from *Paracelsus: Magic into Science* (1951).

> "As a biochemist he asserted that man is made out of the same
> material as the rest of creation,
> feeds on the substances which make up the universe,
> and is subject to the laws which govern their growth and decay.
> At the same time, each living being is unique,
> individually constituted, and follows his own destiny."

Two 17th century physicians that adopted the "spirit" of Paracelsus were Santorio Santorio (1561-1636) (Sanctorius) who wrote *Medicina Statica* (1720, my English copy) and William Harvey (1578-1657) who wrote *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* (1628). While the microscopic level of chemistry was centuries away, these physicians adopted a coherent picture of observable physiology. They knew that biological fluids were complex. They traced the actual flow of these substances.

The 18th century was characterized by major advances in understanding Chemistry and by aggressive attempts to impose ancient ideas on modern chemistry. Hermann Boerhaave (1668-1738) was Professor of Medicine, Botany and Chemistry at the University of Leiden. He inherited a Physic Garden and eventually bought an estate to expand and curate the best such garden in the world. Many 18th century physicians were trained at Leiden. And his *Elementa Chemiae* (1732) is still worth reading!

Boerhaave was a consummate experimentalist. Rather than merely accepting ancient bad ideas, he tested actual biological samples in the laboratory. Fresh urine is neither acidic nor alkaline when tested. Over time changes can occur and he analyzed the substances that composed urine and blood.

Boerhaave clarified the processes of digestion and refuted many of the older speculations. He promoted the notion that internal chemical processes were involved and that no external fictive agents were involved.

The Netherlands was the home of great thermometers and microscopes. Boerhaave employed them in the service of biochemistry. He observed red blood cells and discovered the effect of pure water on these cells: hemolysis! He observed biological “fibers” with his microscope. The long march from naked observations to electron microscopy went through Leiden.

Boerhaave studied the products of fermentation of both plants and animals. Plants tended to produce acidic products, while animals yielded alkaline substances. (Leicester notes that a great history of agricultural chemistry was written by Charles A. Browne (1870-1947): “A Source Book in Agricultural Chemistry,” *Chronica Botanica* **8,** 103 (1944). Browne was a sugar chemist and Director of the US Bureau of Chemistry. He was also a founder of the Division of the History of Chemistry.) He distinguished between “carbohydrates” that dominated plant life and “proteins” that dominated animal life. Boerhaave isolated “gluten” from wheat and showed that it was a protein!

Boerhaave also isolated urea from urine. This chemical process took over a year of patient manipulation. (Boerhaave was the most patient chemist of all time: he distilled the same sample of mercury 511 times. Its mass density increased with time!) His biographer, G.A. Lindeboom (1905-1986) credits him with introducing real biochemistry into medical teaching.

Georg Ernst Stahl (1660-1734) was also a Professor of Medicine, but he set both medicine and chemistry back 100 years by his work. He retained a firm belief in animism: the belief that there was a non-material spirit that energized plants and animals. He is known today mostly for his theory of “phlogiston,” a throwback to Aristotle: bare matter became combustible by adding phlogiston. (One of the most amusing applications of this conceptual framework was the creation of laughter by adding “hilarity” to bare nitrous oxide!) In medicine he promoted the idea that an immaterial “anima sensitiva” acted “directly on all bodily processes.” He denied most of the currently accepted facts about human physiology.

One of Boerhaave’s most famous students was Albrecht von Haller (1708-1777). He was Professor of Medicine at the University of Gottingen and published the books: *Primae lineae physiologie* (1747) and *Elementa physiologiae corporis humani* (1757). He debunked many of the demonstrably false medical notions of his time by careful experimentation and lucid description. He isolated iron from blood. He also verified the work of Stephen Hales (1677-1761) that demonstrated that gas was dissolved in blood.

Haller carried out extensive studies of “bile.” He demonstrated that it served to “digest” “oily” food. The chyle became an “emulsion.” He added the class of “fats” to carbohydrates and proteins.

The later 18th century was christened “The Age of Air”: pneumatic chemistry. Joseph Black (1728-1799) showed the way when he examined metal carbonates and heated them to drive off a gas he called “fixed air.” (CO_2) Marble could be restored by bubbling carbon dioxide through “lime water” ($CaO(aq)$). Black proved that human “exhalation” contained CO_2 by directing it at this solution, Although chemists knew that ordinary air could be deprived of its ability to support combustion, the notion that “air” could not react chemically still persisted until the late 18th century!

New “gases” were now being discovered with regularity. While many people contributed to the discovery of oxygen, Leicester focuses on Joseph Priestley (1733-1804). He heated mercuric oxide and collected the gas given off. He knew that there was a relationship between combustion and respiration. Manchester was famous for its breweries! The vats produced vast quantities of “fixed air.” One product of his research was “soda water,” still being produced today. Priestley called his “oxygen” “dephlogisticated air.” He also discovered many other gases, such as nitric oxide (NO), hydrogen chloride (HCl) and nitrogen dioxide.

Leicester admired Antoine Laurent Lavoisier (1745-1794). (So do I.) He named the new gas “oxygen” (acid-maker). This concept confused chemists for a century. While many acids do contain oxygen, many more do not. It was claimed that HCl must contain oxygen because it was an acid!

Lavoisier did carry out extensive studies of animal respiration. He identified three gases: “eminently respiration air” (oxygen), fixed air and “mephitic air” (nitrogen). He also constructed a good calorimeter based on the ice/water system. He also teamed up with the genius Pierre Simon Laplace (1749-1827). They used an actual guinea pig and showed that the amount of heat produced correlated with the amount of fixed air produced.

Respiration is thus a combustion, very slow, it is true,
but perfectly similar to that of carbon;
it occurs in the interior of the lungs,
without disengagement of visible light
since the matter of fire which becomes free
is at once absorbed by the humidity of these organs.
The heat developed in this combustion communicates itself to the blood
which traverses the lungs and from there
it spreads over all the animal system.

While this model was not correct, it was consistent with previous speculations about the site of "combustion." Had Lavoisier lived, he would probably have realized that the role of the lungs was to absorb oxygen, transport it to the cells, absorb carbon dioxide, transport it to the lungs and repeat.

Animals are not the only biologically active entities on earth. Plants obtain their "energy" from the sun. Priestley examined aquaculture of plants like mint. As long as there was light, they could grow on pure fixed air. In addition, they produced oxygen. Similar experiments were carried out by Jan Ingen-Housz (1738-1799) and by Jean Senebier (1742-1809). The best studies of plant growth were done by Nicolas Theodore de Saussure (1767-1845). In addition to carbon dioxide, plants require water for growth and minerals from the soil.

One by one correct concepts were being adopted by the best biochemists. One of these conservation laws was the natural outcome of the "stoichiometry" of Jeremias Benjamin Richter (1762-1807). The mass of the products is equal to the mass of the reactants. Part of the "understanding" of any chemical process is the identification of the reactants and products.

While the chemistry of "fire" dominated metallic and mineral chemistry, organic materials were simply destroyed by fire. Antoine Francois de Foucroy (1755-1809) developed "extraction" procedures for plant chemicals. (Many of these recipes are in use today. Many "extracts" can be purchased in the "grocery store.") One technique involved "steam distillation" of the raw plant or a "minced" portion. Other extraction media included pure and salt water solutions, and pure ethanol or aqueous solutions. Another approach perfected by Scheele employed the low solubility of many calcium salts. The solid salts could then be purified and the pure acid recovered: tartaric, citric, malic and lactic acids. Pure animal bone could be solubilized and reprecipitated as calcium phosphate.

While animal tissue contains proteins, it was not obvious how the nitrogen was obtained chemically. Claude-Louis Berthollet (1748-1822) characterized ammonia (NH_3), but it was not until the 19th century that quantitative nitrogen analysis of organic compounds was achieved by Jean Baptiste Andre Dumas (1800-1884) and Justus von Liebig (1803-1873).

One of the greatest chemists of the 19th century was Jons Jacob Berzelius (1770-1848). While he was a great analytical chemist, he reminded the "Animal Chemists" that their job was not done until they incorporated the full chemical network of biochemicals. Isolated substances were not the full story.

There are many classes of animal compounds. Michel Eugene Chevreul (1786-1889) devoted his research to “fats.” These compounds are composed of glycerol and are esters of organic acids. They can be “saponified” with lye. Vegetable oils are also “triglycerides”.

Chapter 13 focuses on the concept of “vitalism.” Leicester presents a quotation from Berzelius: “Vitalism is a word to which we can fix no idea!” It served as an “explanation” when there was no actual understanding. One form of the question was the demarcation between inorganic and “organic” substances. Vitalism insisted that only living organisms could produce organic molecules. Another demarcation was between living and nonliving systems. Living systems contained a ”vital force” that both initiated and sustained life. No chemist could create a living system. Claude Bernard (1813-1878) expressed it this way: “Life cannot be characterized exclusively by either a vitalist or a mechanist conception.” (Vitalism still pervades rural American culture in places like Idaho.)

Understanding living systems required a central physiological concept: “cells.” Both plants and animals contain cells with a defined boundary and a complex interior structure. The contents of cells were called “protoplasm.” (small unknowns!)

> In 1868 Thomas Henry Huxley (1825-1895) delivered a lecture
> In which he called protoplasm “the physical basis of life.”

Pure “physiologists” tended to treat protoplasm as a pure substance in its own right. While this appealed to them as a simple solution, it could not account for the myriad properties of cells. Chemists thought about cells as “vessels” with a solution inside. (The classic form of a cow: a sphere with uniformly distributed milk.) Real cells are highly specialized and are extremely complex inside.

As the 19th century progressed, chemists such as Marcellin Berthelot (1827-1907) synthesized many “organic” molecules directly from the elements. (One of my favorite 19th century books is *Chimie organique fondee sur la synthese* (1860).) While the mechanism employed by cells to synthesize the required molecules was not yet known, the laboratory versions were often shown to be identical to the “natural” ones. Biochemical philosophy in the 19th century was complicated and much of it has not persisted, except in Idaho.

Chapter 14 revisits the physiological issue of digestion and “assimilation.” The “alimentary canal” is continuous with substantial tortuosity and a few valves. It is also an “open” system that communicates with many other physiological systems, including the arterial blood. One of the most important 19th century chemists and physiologists was Dr. William Prout (1785-1850). His Bridgewater Treatise was on *Chemistry, Meteorology, and the Function of Digestion* (1855, Fourth Edition, my copy). While religiously he was “very devout,” he insisted that chemical processes were just that, and the understanding of digestion should focus on the chemical substances involved. Prout carried out experiments on animals after eating; he extracted their stomachs with cold, distilled water. He found a very acid solution, but no sulfuric or phosphoric acid. He stated:

> The results then seem to demonstrate that
> free or at least unsaturated muriatic acid
> in no small quantity exists in the stomachs of these
> animals during the digestive process.

One of the most remarkable studies of human “gastric juice” was carried out by the North Americans William Beaumont (1785-1853), Robley Dunglison (1796-1869) and Benjamin Silliman of Yale. They were able to drain gastric juice from a fistula in the stomach of an injured man. Dunglison reports:

> We have found it to contain free muriatic and acetic acid,
> phosphates and muriates of potassa, soda, magnesia and lime,
> and an animal matter soluble in cold water but not in hot.

Aqueous hydrochloric acid does in fact react with many foods *in vitro*. But real gastric juice contains other active substances. One of the best French chemists of the mid-19th century, Anselme Payen (1795-1871), discovered “diastase” which converted starch, a carbohydrate studied by Payen, to simple sugar. Later it was shown that “saliva” also contains diastase. (Today a whole group of enzymes are called diastases: they break down carbohydrates.) (The cellulose division gives an annual award in honor of Payen.)

Another biochemically active gland is the pancreas. It is connected to the alimentary system by a “duct.” (It is part of the “exocrine” system.) Three major digestive enzymes are produced by the pancreas: amylase (diastase), lipase (breaks down fats) and protease (trypsin breaks down proteins).

Leicester discusses the growing awareness that many biochemical processes were “catalyzed” by active chemical agents in bodily fluids.   Claude Bernard devoted his life to tracing the biochemical pathways of sugars. He discovered the role of the liver in sugar metabolism. (Humans cannot metabolize sucrose. It must be broken down to glucose.) Remarkably, the liver can synthesize glucose without the need for starch. (Blood enters the liver by the “portal vein” without the presence of sugar; it leaves through the hepatic vein with sugar present.) The source of the sugar is the carbohydrate “glycogen.” (Glycogen in muscles produces lactic acid.)

Chapter 15 continues the discussion of “ferments.” Dealing with higher animals and plants was complicated. Charles Cagniard de Latour (1777-1859) realized that yeast was the key factor in alcoholic fermentation. Louis Pasteur (1822-1895) established the field of chemical microbiology. Some fermentations required the full living cell to be effective. One of the phenomena documented by Pasteur is the role of oxygen in the life-cycle of yeast. When it is freely available, the yeast uses it to metabolize whatever it can and gain the needed energy. When oxygen is only sparingly available, the yeast obtains its oxygen from oxygen-containing molecules like sugar. He also discovered truly anaerobic cells.

Another chemical process is the inversion of sucrose by the soluble enzyme invertase. In 1876 Willy Kuhne (1837-1900) proposed the name “enzyme” for the now numerous soluble ferments. Leicester summarizes this period with:

> All fermentations produced by living organisms
> were due to ferments **secreted** by the cells.
> The distinction between “organized” and “unorganized” ferments
> no longer existed, and all could be called enzymes.

In 1897 Gabriel Bertrand (1867-1962) demonstrated that additional substances were often needed to activate soluble enzymes. (These are now called coenzymes.)

The chemical nature of enzymes was still obscure until in 1926 James B. Sumner (1887-1955) isolated a pure crystalline enzyme, urease. It was a protein! The race to crystallize enzymes was on and Nobel Prizes were awarded in 1946. His co-recipients were John Northrup (1891-1987) and Wendell Stanley (1904-1971). Once biological enzymes were recognized as “catalysts,” Leonor Michaelis (1875-1949) constructed an actual chemical mechanism for their action.

While groups of substances could be identified, their chemical microstructure needed to wait until difficult analytical and synthetic methods were developed. Emil Fischer (1852-1919) (Nobel 1902) brought order out of chaos for both carbohydrates and proteins. A conclusion was reached by Franz Hofmeister (1850-1922):

> On the basis of the facts given,
> we can regard the proteins chiefly as
> condensations of α-amino acids
> in which the group CO-NH-CH
> is regularly repeated.

(This macromolecular insight was strongly resisted by the biochemical community and proteins were viewed as colloidal aggregates throughout the 20th century.)

The discovery of "nucleic acids" is attributed to Friedrich Miescher (1844-1895) and Felix Hoppe-Seyler (1825-1895). The "smoking gun" was the presence of phosphorus. Progress in understanding the nucleic acids was slow, but Phoebus A. Levene (1869-1940) gradually identified a set of nucleotides composed of a carbohydrate, a phosphate linker and a group of attached bases: adenine, thymine, guanine and cytosine. In 1930 Levene finally identified the carbohydrate as 2-deoxypentose. Another of Levene's major discoveries was the apparent molecular weight of the intact DNA macromolecule (1-2 million).

Chapter 16 focuses on "Energy Production and Biological Oxidation."

Leicester begins his story with Julius Robert Mayer (1814-1878), a ship's physician. In 1842 he published the now classic paper: "Observations on the Forces of Inanimate Nature." It connected the appearance of "heat" with changes in the energy of the system. Further progress was made by Max Joseph von Pettenkofer (1818-1901): "As coal, burned under a boiler, moves a steam engine, so do fats and carbohydrates by their oxidation in the body to carbon dioxide and water yield the power for our mechanical performance." This perspective was firmly established by the great physiologist and physicist Hermann Helmholtz (1821-1894).

Once the basic thermodynamics of energy production in living organisms was established, it was up to the chemists to "find the fuel" and construct the series of chemical reactions that liberated the heat. Justus Liebig and his student Carl Voit (1831-1908) conscripted a group of soldiers to be the guinea pigs for his chemical balance studies. Voit concluded:

> Liebig was the first to establish the importance of chemical transformations
> in the body. He investigated the chemical processes of life
> and followed them step by step to their excretion products.

Voit himself established the role of gases in human metabolism. Atmospheric nitrogen plays no role in this process. He also constructed a calorimeter large enough to accommodate a man! He showed that fats and carbohydrates are the dominant sources of human energy.

The issue of the site of oxidation raged throughout the 19th century, but the German physiologist, Eduard Pfluger (1829-1910), showed that true "respiration" takes place in the "peripheral tissue." He carried out extensive studies of glycogen.

Once it became clear that blood was primarily a transport entity, Hoppe-Seyler discovered oxyhemoglobin by its optical absorption spectrum. He finally isolated a crystalline compound now called hemoglobin. Further understanding was obtained by Gabriel Stokes (1819-1903):

> We may infer that the coloring matter of blood, like indigo, is capable of existing
> in two states of oxidation, distinguished by a difference of colors.
> It may be made to pass from the more to the less oxidized state
> by the action of suitable reducing agents,
> and recovers its oxygen by absorption from the air.

(Sir Gabriel Stokes was perhaps the greatest Irish mathematician of the 19th century!)

The active element in hemoglobin, the porphyrin ring, was elucidated by Hans Fischer (1881-1945) in 1927. Once the oxygen left the hemoglobin, it underwent a series of transformations resulting in cytochrome. The story is beautifully told in the book by Albert Szent-Gyorgyi (1893-1986) (Nobel 1937): *On Oxidation, Fermentation, Vitamins, Health and Disease* (1939).

Chapter 17 addresses what Leicester calls "Intermediary Metabolism." It is one thing to know the initial "reactants" and the final "products," but biochemistry is all about the actual reaction mechanism from start to finish. Many new molecules and new reactions were discovered in the 20th century. One of the leading biochemists of the 1920s was Sir Frederick Gowland Hopkins (1861-1947) (Nobel 1929) of Cambridge University. In 1921 he stated the fundamental fact about life:

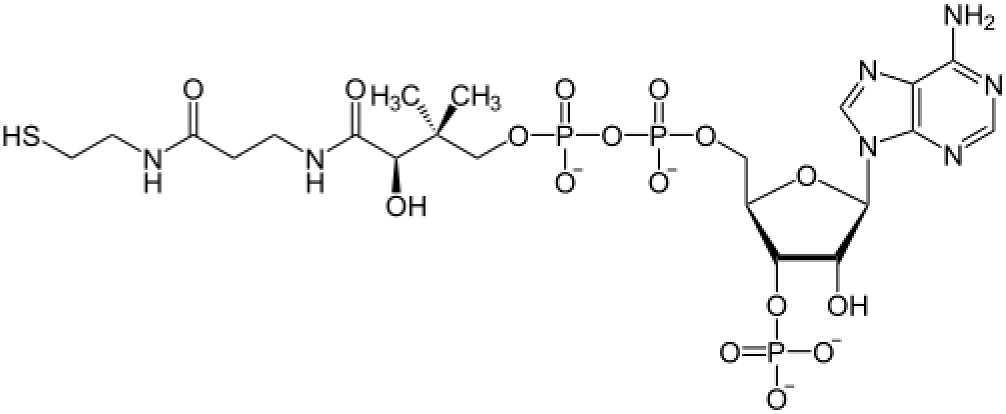
> The living cell is itself the unit.
> The manifestations of life viewed from this standpoint
> depend upon changes undergone by diverse molecules
> of a kind which need not elude ordinary chemical studies.
> On this view, the essence of what is peculiar to the cell
> as a chemical system lies not in the nature,
> but in the organization of its processes.

Leicester identifies this paradigm as the real start of Biochemistry as we know it today.

Two areas made major progress throughout the 1920s and 1930s: alcoholic fermentation and muscle metabolism. Sir Arthur Harden (1865-1940) (Nobel 1929) of the Lister Institute in Manchester deciphered the chemistry of “yeast juice” along with his assistant William John Young (1878-1942). They discovered that phosphate esters were required to break down the sugar to ethanol.

$$2C_6H_{12}O_6 + 2Na_2HPO_4 \rightarrow C_6H_{10}O_4(PO_4)Na_2 + 2H_2O + CO_2 + 2C_2H_6O$$

Hopkins and Walter Morley Fletcher (1873-1933) explored the inner details of muscle metabolism. Under anaerobic conditions lactic acid was produced. Otto Fritz Meyerhof (1884-1951) (Nobel 1922) discovered that there were common pathways in alcoholic fermentation and in muscle respiration. They involved phosphate esters. He published the book *Chemical Dynamics of Life Phenomena* (1924). Fritz Albert Lipmann (1899-1986) (Nobel 1953) continued this programme and formulated the role of adenosine triphosphate (ATP) and Coenzyme A:



The other Nobel Prize in Physiology and Medicine winner in 1953 was Hans Krebs (1900-1981). Krebs is most famous for elucidating the "citric acid cycle" and the "urea cycle." Biochemistry allowed chemists in the 20th century to obtain real gold!

Chapter 18 is devoted to the history of vitamins. A vitamin is an essential substance needed for life that is not synthesized by the organism itself. The first Nobel Prize for work on vitamins was awarded to Adolf Windaus (1876-1959) in 1928. In 1929 Christiaan Eijkman (1858-1930) and Sir Frederick Hopkins won for their extensive work on vitamins, including "growth stimulating B vitamins." In 1930 Paul Karrer (1889-1971) won for his work on beta-carotene (vitamin A). Many more Nobel Prizes have continued to be awarded for work on vitamins.

The final chapter is devoted to the signaling substances of life: hormones. One of the most important aspects of living organisms is their ability to "adjust" to their current state. Even in the 18th century, the French physician Theophile de Bordeu (1722-1776) identified "organs of secretion," such as the ovaries. In the 19th century A.A. Berthold (1803-1861) studied avian testes transplanted into other locations. They continued to secrete substances that promoted particular growth. The "endocrine system" is characterized by specific secretions from the adrenal glands. The thyroid gland also produces active control substances.

The research goal was to isolate and purify specific hormones. Adrenaline was crystallized in 1901 by Jokichi Takamine (1854-1922). Major progress in the understanding of hormones was made by William Maddock Bayliss (1860-1924) and Ernest Henry Starling (1866-1927) during their studies of the pancreas. In 1902 they found that:

> The contact of the [gastrointestinal] acid with the epithelial cells of the duodenum causes in them the production of a body (secretin) which is absorbed from the cells by the blood current, and is carried to the pancreas, where it acts as a specific stimulus to the pancreatic cells, exciting a secretion of pancreatic juice proportional to the amount of secretin present.

A Nobel Prize was awarded in 1923 to Frederick G. Banting (1891-1941) and John Macleod (1876-1935) at the University of Toronto for the discovery and purification of insulin. This story is thrilling and has recently been celebrated in Bologna, Italy with a statue at a park dedicated to Banting. (I was privileged to be the historian for this event.)

Henry Leicester was very pleased to be able to write the history of biochemistry as his last major contribution. HIST owes him many debts of gratitude for his many years of service and teaching.