CLIO MEDICA

NUTRITION

GRAHAM LUSK

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CLIO MEDICA

A SERIES OF PRIMERS ON THE HISTORY OF MEDICINE

EDITOR: E. B. KRUMBHAAR, M.D.

X

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BY

GRAHAM LUSK, SC.D., M.D., LL.D.

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CLIO MEDICA

NUTRITION

BY

GRAHAM LUSK, SC.D., M.D., LL.D.
Late Professor of Physiology, Cornell University Medical College, N. Y.;
Former Member, Royal Society; Corresponding Member,
Preussische Akademie der Wissenschaften

WITH 13 ILLUSTRATIONS

PAUL B · HOEBER · INC
NEW YORK · MCMXXXIII

PUBLISHED JUNE, 1933 ⸍ PRINTED IN THE
UNITED STATES OF AMERICA.

EDITOR'S PREFACE

This little volume is one of a series of handbooks which under the general title of "Clio Medica" aims at presenting in a concise and readable form a number of special phases of the long and complex history that underlies the great edifice of modern medical science.

Since the times of the Aldines and Elzevirs, small easily portable booklets have been popular with the intelligent reader. Today books that add no appreciable burden to the coat pocket are real helps to the busy worker or student in gaining ready access to considerable worth-while reading. Such booklets, too, seem peculiarly appropriate for a new line of approach to such a subject as the History of Medicine from a different point of view than has hitherto maintained. From the very nature of this subject, when treated in a general way, it has thus far appeared either in ponderous tomes or, if in smaller volumes, in such scanty garb that almost no details of the costume are depictable. Then, too, the strictly chronological method of approach, with emphasis on prominent individuals, becomes almost a necessary form of treatment in the comprehensive general histories. The searcher for knowledge of the history of some small branch of the subject—a specialty, let us say, or the progress of medicine in this or that country—is thus forced to hunt, often painfully with help of index and marker, through the pages of the larger book or books, to be rewarded with a necessarily disconnected and usually incomplete presentation.

Our hope is that the series "Clio Medica" will obviate these difficulties. Conveniently small and inexpensive, yet prepared by recognized authorities in their chosen field, each volume will aim to present the story of some individualized phase of the history of medicine in such compact, connected, convincing and reasonably complete form that the medical undergraduate, the specialist, the busy general practitioner and the "intelligent layman" will all be attracted to a few hours' reading, which in many cases may prove to be the introduction of an awakened interest to a more comprehensive study.

An increasing interest has recently become manifest in the history of medicine in the English speaking as well as in other countries, as is shown by the successful formation of new societies, journals and institutes for the study of the subject. The times, then, seem auspicious for this venture. Several volumes of the series have already appeared; as others materialize still more will be undertaken, with the possibility of a large number being attained. We bespeak the support of our colleagues and friends and pray that the Goddess whose name we have used to designate our series may deign to foster the undertaking!

E. B. Krumbhaar.

Philadelphia. Pa.

PREFACE

Graham Lusk finished the manuscript of this book a few weeks before the brief illness which terminated in his untimely death on July 18, 1932. The writer of this preface was asked by Dr. Lusk's family to correct the proof. In this small task he has received the invaluable assistance of one of Dr. Lusk's former pupils, Robert O. Loebel, and Dr. Lusk's secretary, Miss P. R. Schaub. We beg indulgence for mistakes.

I do not know of anything that gave Lusk more pleasure than the preparation of this brief history of nutrition. After forty-two years of teaching and the most fruitful type of brilliant research he devoted his spare hours to recording the deeds of his predecessors. No man in the field of metabolism possessed a greater knowledge of the literature, no man had a better appreciation of the old masters. The influence of such a background on Graham Lusk and on his students is beautifully illustrated by a quotation from a recent memorial address by one of his former pupils, William S. McCann:*

> Someone has said that if teaching consisted only of the imparting of factual knowledge then Universities might well have ceased to exist with the invention of printing. Graham Lusk's lectures provided superb examples of the reasons why the living voice has not given way to the printing press. There on the page before us were the facts tersely marshalled in logical sequence. Through our ears came interpolations of personal anecdotes which made

* The Influence of Graham Lusk upon his Students. Address at Memorial Meeting, New York Academy of Medicine, Dec. 10, 1932. Privately printed. Baltimore, 1933.

those facts into a sort of aura of the living beings who discovered them. Lavoisier was our daily companion, as were Carl Voit and Max Rubner, while Magendie and Claude Bernard appeared never less than once a week. . . .

The more usual anecdote raised its subject to the heroic proportions of a legendary figure. The mind of Graham Lusk was a special Valhalla to which were conveyed dead heroes of the test tube or stethoscope: in it places were reserved for living heroes, for no man was more generous in appreciation of his contemporaries than was Lusk. In this legendary world Carl Voit was Woden, von Mueller was Balder, and Jove himself was not mightier than Rubner.

So in these lectures the prosy pages of his book became alive, and peopled both with common men and heroes. Just as the youths of ancient Greece, or our Teutonic ancestors, were inspired by the epic performances of their heroes, so were we inspired.

With the completion of this volume the vital, great-hearted personality of Graham Lusk passes onward to join the company of those leaders whose lives and works furnished him constant joy and inspiration.

EUGENE F. DU BOIS.

NEW YORK CITY,
May, 1933

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CHAPTER I

THE ANCIENT WORLD

BEFORE the mythical Asklepios appeared in history a man called Imhotep[3] was born in Egypt about the year 2980 B.C. and he is known as the first physician. He built the step pyramid at Sakkhara near ancient Memphis, which is the oldest large structure extant. The Edwin Smith papyrus describing surgical operations dates from the seventeenth century B.C., but Breasted[1] believes that it is a copy of a work composed by a surgeon many centuries before and about the time of the building of the pyramids when many accidents must have happened. For the Great Pyramid was 755 feet square and, rising to a height of 481 feet, required 2,500,000 blocks of stone, each weighting 2½ tons. In the papyrus one reads of an "observation of the heart by means of the pulse." The Ebers papyrus[5] of later date (1552 B.C.) prescribes cakes, wheat, corn, and grits "to drive away the too much emptying of urine." This is believed to refer to diabetes and was written about the time of Abraham and a thousand years before Hippocrates.

Breasted[1] states that under the shadow of the Great Pyramid of Cheops there is a tomb on the walls of which are portrayed scenes representing the grinding of flour, mixing and baking of bread, brewing of beer, slaughtering of cattle and poultry and cooking them, making pottery, and making music with three harps and a drum while the master ate. It is recorded that this cemetery official owned 853 oxen, 220 cows and calves, 2235 goats, 760 asses, and 974 sheep.

Several centuries before the day of Abraham, Hekanakht, the ka-servant in charge of an endowed temple in ancient Thebes, journeyed into Lower Egypt to investigate some properties which were owned by this temple. He wrote letters on papyrus to his son Mersu, who had been left in charge of the temple at Thebes. Evidently there was famine in the land of Egypt, for he wrote:

> The whole land is dead with hunger. . . . I have obtained your victuals as well as possible. Is not the Nile very low? [Here are listed the provisions.] . . . You must not be angry about this. Half life is better than dying altogether. . . . You must give my victuals to my people while they are doing work; mind this. Make the most of all my land; . . . dig the ground with your noses in the work. . . . Be very active; remember you are eating my bread.

Here is authentic corroboration of the biblical maxim, "By the sweat of thy brow shalt thou eat bread." In another letter he orders Mersu to have Heti cultivate land on lease and to "take its rental from cloth that has been woven here." These letters are among the oldest in the world, having been written in the year 2001 B.C. In an elementary way they tell the story of the relation between food and manual labor, as well as the relation between the industries of agriculture and manufacture.

The development of a system of credit began with the Babylonians five thousand years ago. And today the life of Britain measurably depends on her ability to exchange manufactured cloth in payment of an annual bill for imported food amounting to $2,500,000,000.

There are relics in the Nile valley of men who lived there in the Stone age. Breasted[1] estimates that it required several hundred thousand years for them to emerge from savagery. Then they developed agriculture, cattle breeding, the manufactures of cloth and metal. Their medicine was founded on the idea that disease was due to evil spirits or demons. They built the pyramids five thousand years ago and then, Breasted tells us, began to reflect upon the utter futility of material conquest, and thus they became the first discoverers of human character in which sweetness and light counted for more than brute force. Before 2000 B.C. the god most worshipped was the god of fertility, who granted good crops, but after this came the conception that there were other things than material satisfaction by food.

The Greek traveler Herodotus (484–424 B.C.) tells us that the ancient Egyptians made beer and that its discovery was attributed to Osiris, the god of good things. The discovery of wine also belongs to the age of mythology. Diodorus[8] writes as follows:

> The Egyptians boasted that they were the healthiest o all mortals. They probably knew that the majority o diseases proceed from indigestion and excess of eating and these evils they combatted, by emetics, gentle aperients, and other means of relieving the system. The whole manner of life was so ordered that it would appear that it had been arranged according to the rules of health by a learned physician rather than by a law-giver.

Egyptian medicine was filled with the magic number four; there were four columns necessary to support the roof of a temple, the pyramids stood four square, and medicine was taken four times a day. This mystical number the Egyptians passed on to the Greeks. The word "chemistry" is derived from *Khemi*, the native name of Egypt, and means literally "black earth" because of the rich alluvial deposits made annually by the swollen waters of the Nile, inundating the level valley bordering on the river. On account of its derivation chemistry came to be known as the "black art." Indeed, Diocletian is said to have burned the books of the Egyptians concerning the transmutation of silver into gold. At the time of Homer the Egyptians knew far more about chemical processes, as shown in metallurgy, dyeing, making soaps, glass, alloys, and amalgams, than did the Greeks (Garrison[2]). They also knew more then about medicine. Later, however, the Greek mind developed conceptions which were to maintain their hold upon the intellect of mankind through the ages.

Empedocles (504–432 B.C.) was a physician who introduced the idea of four elements into the philosophy of his day. These were fire, air, earth and water. There were also four qualities: dry, cold, hot and wet.

Hot and dry made fire
Cold and dry made earth
Cold and wet made water
Hot and wet made air.

Thus, if by heat one drove the cold out of water, it was converted into air, and this air, if condensed on a cold plate, was reconverted into water again through the expulsion of heat by cold. Empedocles[19] is represented as saying to his followers:

> But unto ye I walk
> As god immortal now, no more as man
> On all sides honored fittingly and well,
> Crowned both with fillets and with flowering wreaths.

And indeed his conception of the elements was well-nigh immortal, for it held sway for over two thousand years.

About this same era, using the same mystic number four, it was concluded that there were four humors: blood, yellow bile, phlegm, and black bile. These humors were compounded as follows: Hot and dry made yellow bile; hot and wet made blood; cold and wet made phlegm; cold and dry made black bile.

These were the accepted doctrines of Plato and Aristotle. Hippocrates[7] (b. 460 B.C.), who was thirty-two years old when Empedocles died, was somewhat sceptical about the scientific application of these elements to the human being, for he writes:

> Whoever having undertaken to speak or write on Medicine, have first laid down for themselves some hypothesis to their argument, such as hot or cold or moist or dry, or whatever else they choose (thus reducing their subject within a narrow compass and supposing only one or two original causes of disease and death among mankind) are all clearly mistaken in much that they say.

Here are the words of the sceptical observer of facts, and Hippocrates goes on to prove his contention. For he says if hot or cold or moist or dry be injurious to a man, then to treat a patient properly one must apply cold to the hot, hot to the cold, moist to the dry, and dry to the moist. Let a man eat raw wheat taken from the threshing floor together with raw meat and water. From such a diet he will suffer much and severely, his bowels will be disarranged, and he will not live long. But if, instead of raw wheat, you give bread; instead of raw meat you boil it, and give a drink of wine in addition to these, then it is certain that the patient will improve, "unless completely disorganized by time and diet." Is the improvement due to the application of heat or cold? Did he who prepared the bread out of the wheat remove from it the hot, the cold, the moist or the dry principle in it? "I should think this question must be a puzzler to whomsoever it is put, for bread is consigned both to fire and to water, and is wrought with many things, each of which has its peculiar property and nature."

The problem of whole wheat bread and the various methods of bread making are touched upon by Hippocrates, who comments as follows:

> Whoever pays no attention to these things, or paying attention does not comprehend them, how can he understand the diseases that befall a man? For by every one of these things a man is affected and changed this way or that, and the whole of his life is subjected to them, whether in health, convalescence or disease. Nothing else can be more important or more necessary to know than these things. . . . For the first inventor of bread did not suppose that the dry or the moist or the hot or the cold, or any of these, are either injurious to man, or that man stands in need of them; but whatever in each was strong and more than a match for a man's constitution, whatever he could not manage, they held to be hurtful and sought to remove.

His scepticism of the universal health giving qualities of bran and whole wheat bread was convincingly justified by the experiments of Rubner during the World War.

Hippocrates attributes the development of medical knowledge to the problems of nutrition, for he writes:

> Let us inquire therefore what is admitted to be medicine. . . . To me it appears . . . that nobody would have sought for medicine at all, provided the same kinds of diet had suited with men in sickness as in good health.

The tolerant spirit of Hippocrates is marked in the following paragraph:

> For cheese does not prove equally injurious to all men, for there are some who can take it to satiety without being hurt by it in the least, but on the contrary it is wonderful what strength it imparts to those with whom it agrees; but there are some who do not bear it well, their constitutions are different, and they differ in this respect, that what in their body is incompatible with cheese is aroused and put in commotion by such a thing; and those in whose bodies such a humor happens to prevail in greater quantity and intensity, are likely to suffer the more from it. But if cheese had been pernicious to the whole nature of man, it would have hurt all. Whoever knows these things will not suffer from it.

This represents an ancient conception of the disturbance of bodily humors by external means.

Of the celebrated Aphorisms of Hippocrates the first reads:

"Life is short and the art long; the opportunity fleeting; experiment dangerous, and judgment difficult."

Goethe, in "Faust" reincarnates these ideas in the lines:

> Ach Gott! die Kunst ist lang
> Und kurz ist unser Leben
> Mir wird bei meinem kritischen Bestreben
> Doch oft um Kopf und Busen bang.

One of the famous aphorisms reads:

> Growing bodies have the most innate heat; they therefore require the most food for otherwise their bodies are wasted. In old people the heat is feeble and they require little fuel, as it were, to the flame, for it would be extinguished by much.

This is a forecast of modern calorimetry.

Another aphorism of Hippocrates reads, "Persons who are naturally very fat are apt to die earlier than those who are slender." This sounds like the circulars of modern life insurance companies.

The term *calidum innatum* or "innate heat" endured many centuries, for we find Harvey agreeing with Aristotle that innate heat is not fire nor derived from fire, but rather sharing the nature of another, a more divine, body or substance. So we have to go back to Hippocrates to find animal heat derived from fuel and likened to a flame.

There was a beautiful temple to Aesculapius[19] at Cos in which the father of Hippocrates was a priest and in which Hippocrates himself learned the art of medicine. A similar temple was erected to Aesculapius at Epidauros. Here was also a great concourse for games and an open air theater set in a hillside which seated 14,000 spectators. The treatment of patients consisted in dieting, exposure to sunshine, exercise, psychic diversion. The same treatment is administered today to our well-to-do citizens.

Hippocrates was a contemporary of Pericles, the statesman, of Phidias, who built the Parthenon, of the poets Sophocles and Aristophanes, of the immortal philosopher Socrates, with his pupils Plato and Xenophon, and of the historian Herodotus. It was an age of supreme intellectual and cultural magnificence.

If one turns to Goethe on the subject of national culture one may read these words:

> If a talent is to be speedily and happily developed, the great point is that a great deal of intellect and sound culture should be current in a nation.
>
> We admire the tragedies of the ancient Greeks. But, to take a correct view of the case, we ought rather to admire the period and the nation in which their production was possible, than the individual authors; for though these pieces differ a little from each other, and though one of these poets appears somewhat greater and more finished than another, still, taking all together, only one decided character runs through the whole: grandeur, fitness, soundness, human perfection, elevated wisdom, sublime thought, pure strong intuition, etc. But when we find all these qualities, not only in the dramatic works that have come down to us, but also in lyrical and epic works—in the philosophers, the orators, and the historians, and in an equally high degree in the works of plastic art . . . —we must feel convinced that such qualities did not merely belong to individuals, but were the current property of the nation and the whole period.

We might close our eyes and repeat with the British poet as he stood on the Acropolis at Athens.

> The past return'd, the present seemed to cease,
> And Glory knew no clime beyond her Greece.

Among the contemporaries of Hippocrates were Leucippus and Democritus, who conceived of a true atomic theory of matter which, however, was rejected by Aristotle (384–322 B.C.) and through his great influence the theory of Empedocles was confirmed in the mind of man.

Aristotle,[14] whom Harvey revered, has this to say:

> The life of animals may be divided into two acts,—procreation and feeding; for on these two acts all their interests and life concentrate. Their food consists chiefly of the substance of which they are severally constituted; for the source of their growth in all cases will be this substance. And whatever is in conformity with nature is pleasant, and all animals pursue pleasure in keeping with their nature.

Erasistratus (310–250 B.C.), according to Garrison,[10] was the first experimental physiologist. He believed that *pneuma* in the atmosphere was transformed into spirit in the body. He devised the first respiration apparatus. For he put fowls into a jar, weighed them and their excreta both before and after food. He antedated Sanctorius by nearly two thousand years.

The traditions of Greek medicine were presented to the Romans by Celsus[14] (53 B.C.–7 A.D.) in a Latin handbook which may have been a translation. This book was printed at Florence in 1478 before the works of Hippocrates or Galen were printed. Celsus tells us that the life giving principle is *pneuma* or air, renewed through breathing and transmitted by the blood through the veins and arteries, the arteries containing more pneuma; and that sickness arises from disorder of the pneuma due to irregularities in the hot, cold, moist, and dry factors, which induces a pathological excess of one of the humors (H. O. Osborne). Celsus[8] stated that in diabetes the water of the urine was greater in amount than the quantity of water drunk, an error which persisted for centuries.

Celsus confirms Hippocrates in the idea that medicine had its origin in nutritive disturbances, for if in the first days of illness a patient's appetite is good, he may take food, whereas if he has nausea and takes none, "the disorder of those who had abstained was the more alleviated." The same was true of fever. When remedies were found, men began to ask the reasons why the results were obtained.

After Hippocrates the greatest medical character of ancient times was Galen (130–200 A.D.). Galen[16] was born at Pergamum and was the son of an architect who was both intellectual and wealthy. Galen tells us that the temple of Aesculapius at Pergamum was as illustrious as any other existing in his time. Here he received his education in medicine. His father owned a farm in the vicinity and the slaughtering of cattle gave Galen his interest in experimental physiology. To complete his education he repaired to Alexandria where one was allowed to dissect the bodies of executed criminals. He lived in Alexandria five years, working at the Egyptian Museum or Temple of the Muses in company with many of the most famous men of his day. For eleven years he studied medicine before returning home to practice the art. A year after his return at the age of twenty-nine he was appointed surgeon to the gladiators. He was also the medical director in the training school for gladiators. He always insisted that gymnastics should be regulated by medical knowledge.

Galen[17] maintained that no one could understand physiology without a knowledge of Euclid. He placed Euclid on the same plane as Hippocrates. As regards the action of the four humors, he felt that he could offer nothing which was wiser than Hippocrates and Aristotle. Galen[14] writes, "When the matter which flows to each part of the body in the form of nutriment is being worked up into it, this activity is nutrition, and its cause is the nutritive faculty." He fed hogs and concluded that the stomach was a place in which food could be resolved into particles sufficiently small to be absorbed. He[15] remarks, "The blood is like the oil [of a lamp], the heart is like the wick, and the breathing lungs an instrument which conveys external motion." It was thought that respiration cooled the heart which was the source of the innate heat.

Before the time of Galen the idea was prevalent that mental activity took place in the chest and probably in the heart, for since we speak with the larynx the impulse to speak must arise in the lungs. Galen,[16] however, showed that a pig stopped squealing and a dog stopped barking if the recurrent laryngeal nerve were cut. Hence Galen placed the intellectual faculty in the brain, which had previously been considered a device for cooling the blood. Galen's[18] interpretation was not accepted in Rome, one writer refuting him as follows:

> Urine is passed through the urethra by the compression of the bladder wall; words are passed through the larynx by the compression of the lungs; it would be as logical to say that urine comes from the brain as to say that speech does.

Galen defines diabetes as "a weakness of the kidneys which cannot hold back water."

"Chance favors only the prepared mind," said Pasteur. Galen[12] coming from the sick chamber of Glauco, a Roman, "who had never before had a physician of consummate ability," puts the matter thus: "Fortune often presents us with the means of acquiring fame, which, through ignorance, many are not able to turn to good account."

The writings of Galen have been handed down through Arabic translations. Burr[9] concludes: "It was not his fault that the world for centuries accepted his hypotheses and his therapeutics as final, but neglected to learn and to use the greatest lesson he taught, the importance of experimental research."

Aretaeus,[11] the Cappadocian, lived in Rome about the time of Galen and gave diabetes its name. His diet for it is similar to that of Hippocrates: milk, cereals, starch, groats, and gruels. He feels that it may be cured by finding a drug to control thirst. He writes:

> The affection called diabetes is a rather wonderful but fortunately rather rare disease. It consists of a liquifaction of the flesh and bones into urine. As with hydrops the cause is of wet and cold nature. The kidneys and bladder, the usual passage ways of fluid, do not cease emitting urine, and the outpouring is profuse and without limit. It is just as though the aqueducts were open wide. . . . And when the disease is at its height they urinate constantly. From this fact the disease has derived the name *diabetes*, meaning "siphon." Life lasts only for a time, but not very long.

Barach[8] states that about this time (229 A.D.) a Chinese wrote that the urine of a diabetic was very large in amount and so sweet that it attracted dogs to drink it. By the sixth century the Hindus spoke of "honey urine," induced by gluttonous over-indulgence in carbohydrate food (rice, flour, and sugar).

Charles Singer[13] closes an essay upon "Greek Medicine" with the words:

> It would be a bad day indeed for medicine if this debt to the Greeks were forgotten, and the loss would be as much ethical as intellectual. But there is happily no fear of this for the figure and spirit of Hippocrates are more real and living today than they have been since the great collapse of the Greek scientific intellect in the third and fourth centuries of the Christian era.

Even though the doctrines of Hippocrates no longer form the basis of our medical teaching, we may well ask ourselves whether the subject of nutrition which he declares originated medicine has today a sufficient place in the curriculum of the average medical school.

CHAPTER II

THE MIDDLE AGES

We may drop the curtain on a period of nearly a thousand years after the death of Galen. Carl Voit[20] thus portrays the happenings during the Dark Ages:

One usually regards this period of the world as intellectually barren, during which only a blind imitation of the old and senseless scholasticism prevailed. However, one makes a great mistake to condemn the human race as having been incapable for a thousand years. We should rather understand why a rapid development was impossible. The conditions for a continued expansion of scientific knowledge were about as unfavorable as imaginable. The Age of Antiquity reached the highest standard of cultivation possible from the knowledge of the time and it needed entirely new ideas in order to move forward, for the cultivation of mankind is not accomplished like a constantly growing branch, but rather like one which is stimulated anew after having been formerly ripe. I doubt whether the ancient Greeks and Romans with their peculiar mental temperament had the power further to extend knowledge. The Empires in which the old cultivation had flourished went down, and younger races reigned in their stead. These rough victors eagerly acquired the intellectual treasures which the conquered people had accumulated in the days of their glory; they regarded themselves as pupils and fell for a time into intellectual dependence as they devoutly entered into this great heritage. The education of peoples is like that of an individual. It is some time after education in the schools has taught one to think that one is capable of independent action, and usually one seeks first the wrong way before one finds the right. Even so, the change from the olden to the modern could take place only after prolonged struggle. The spirit was gradually sharpened but there were not enough new facts to create new ideas. Satisfaction was sought in acute dialectics. This was only an indication that the old methods brought no one forward. Finally the tremendous events which took place in the fifteenth century changed dutiful scholars into critics and independent investigators who, through the revelation of heretofore unknown methods of the mind, were able to open up new pathways.

The curtain rises upon Salerno, the first great Italian medical school. Here Benedictine monks had founded a hospital. Here during the eleventh century Constantinus Africanus had his abode. He had traveled in Egypt and in India and introduced Arabic medicine into Italy. The Arabs had translated the original Greek manuscripts into Arabic, and these formed the basis of their knowledge. The celebrated "Regimen Sanitatis Salernitatum,"[22] which was written in Latin about the year 1100 and was translated into English by Sir John Harington five hundred years later, served for several hundred years as a text for medical instruction. One of its verses reads:

Good dyet is a perfect way of curing:
And worthy much regard and health assuring:
A King that cannot rule him by his dyet,
Will hardly rule his Realme in peace and quiet.

And the effect of the Greek intellect, transmitted through centuries of time, reappears in the following pronouncement:

Four humors reigne within our bodies wholly,
And these compared to foure elements,
The *Sanguine*, *Choller*, *Flegme* and *Melancholy*,
The latter two are heavie, dull of fence,
The other two are more Jovial, quick and Jolly,
And may be likened thus without offence,
Like ayre both warm and moist is *Sanguine* cleare,
Like fire doth *Choler* hot and dry appeare,
Like water cold and moist is *Flegmatique*,
And *Melancholy* cold, dry earth is like.

There came in Italy an interval of passionate search for the works of the old classical authors. Thus Petrarch (b. 1304), who was a contemporary of Dante, Boccaccio, and Giotto, made long and fatiguing journeys to discover the earliest editions of Varro, Pliny, Livy; he found the letters of Cicero and two of his orations; he discovered the earliest version of Homer, and several of the writings of Plato. This was a time when Italy was turning from the Middle Ages and awakening to the realization of the glory of a forgotten past.[24]

Leonardo da Vinci lived between 1452 and 1519. He was educated in Florence at a time when the Medici ruled in their glory. He received instruction in mathematics from the famous Toscanelli, who taught Columbus and Amerigo Vespucci and enabled them to sail to America. Leonardo was a pupil in Verrocchio's studio together with Botticelli, Perugino and Lorenzo di Credi. Through the Guild of Apothecaries there was a close association between artists and physicians, for the apothecaries furnished paints to the artists and drugs to the physicians. Leonardo's anatomical drawings are unsurpassed. He dissected nearly one hundred bodies. He was the forerunner of Vesalius. George Sarton says of him, "This father of modern sciences was still in many respects a child of the Middle Ages." He believed in the elements of Empedocles and drew pores in the septum of the heart to correspond with the doctrines of Galen, although he said they were invisible. But the intellectual flame of Hippocrates had its re-birth in the mind of Leonardo when he wrote, "Those who study only the ancients and not the works of nature are step-sons, but not sons of nature, the mother of all good authors."

Leonardo left many memoranda[23] for an unwritten book, among which may be found one entitled "How the body of animals continually dies and is born again." This reads as follows:

> Hast thou marked Nature's diligence? The body of everything that takes nourishment constantly dies and is constantly reborn; because nourishment can only enter into places where that past nourishment has expired, and if it has expired it has no more life; and if you do not supply nourishment equal to the nourishment departed life will fail in vigor; and if you take away this nourishment life is utterly destroyed. But if you restore as much as is consumed day by day, just so much of life is reborn as is consumed; as the flame of the candle is fed by the nourishment given by the liquor of the candle, which flame continually with rapid succor restores from below what above is consumed in dying; and from a brilliant light is converted into dark smoke; which death is continuous as the smoke is continuous; and the continuance of the smoke equals the continued nutriment; and at the same moment all the flame is dead and regenerated with the movement of its nutriment. And its life receives from it also its ebb and flow, as the flicker of its point seems to show us.

Life, therefore, like the flicker of a candle, is dependent on nutrition! And Leonardo goes farther. He says, "Where there is life there is heat, and where there is vital heat there is movement of the humors." Again, "Where flame cannot live no animal can sustain its existence." And finally the great statement "Motion is the cause of all life."

In one paragraph Leonardo writes, "Man and the animals are merely a passage and channel for food, a tomb of other animals, a haven for the dead, giving life by the death of others, a coffer full of corruption." One wonders if these words inspired Pope (b. 1688) in his "Imitations of Horace" to write of gastric indigestion:

> A tomb of boiled and roast and flesh and fish
> Where bile and wind and phlegm and acid jar
> And all the man is one intestine war.

Leonardo propounds these rules:

> Thou must first have a theory, afterwards practical work.
>
> Science is the captain, practical work the soldiers.
>
> Practical work without science is like a pilot of a ship without compass or rudder. Practical work must be based on a good theory.
>
> There is no certainty where mathematics is not involved, or which cannot be considered mathematically.
>
> An experiment is the repetition of a natural process designed to discover the laws of relations presented by science.
>
> An experiment is never fallacious, only our interpretation of it may be wrong.
>
> No action in nature is without a cause. If you understand the cause you need no experiment.
>
> People who recite other peoples' knowledge amount to nothing; only discoverers and investigators amount to something.
>
> He who disputes and quotes authorities uses his memory but not his brains.
>
> Nature never breaks its laws.
>
> Poor is the pupil who does not surpass his master.

These scientific sayings four hundred years old, a hundred years before Harvey, seem fully modern to us. And yet they came from a man who was at once artist, biologist and engineer, the greatest humanist ever produced. For in 1503 Florence sent him to the camp when she was fighting against Pisa with orders to divert the waters of the River Arno, so that it should not flow through her hated rival. And in 1505 we find him painting in Florence the "Mona Lisa." Living there at that time were Botticelli, sixty-one years old; Perugino, fifty-nine; Leonardo, fifty-three; Fra Bartholomea, forty-three; Michael Angelo, thirty; and Raphael, twenty-two. It is said that Raphael painted Leonardo as Plato. And remember that in these years Leonardo's old friend Amerigo Vespucci told him about his voyage to America.

Cosimo di Medici (1389–1464) had founded the Florentine Academy where philosophy could be discussed after the manner of Athens, and his successor Lorenzo (1449–1492) established the Medici Gardens in which classic Greek sculpture could be studied. But above all Lorenzo di Medici had an acutely perceptive sympathy for the talents and accomplishments of other men, and this gave direct individual encouragement such as no other rich man has since been able to communicate to those beholden to him. In Machiavelli's "History of Florence," published in 1513, the historian writes of his friend and patron Lorenzo il Magnifico:

> He was the greatest patron of Literature and Art that any prince has ever been, and he won the people by his liberality and other qualities. By his political talents he made Florence the leading state in Italy and by his other qualities he made her the intellectual, artistic and fashionable center of Italy.

And it was Giovanni Rucellai who thanked God that he "was a native of Florence, the greatest city in the world, and lived in the days of the magnificent Medici."

The year 1500 in ancient Florence seems a long time ago, far away in the distant past, and yet it is only the length of ten lives with active adult service of forty years for each individual. The eleventh person would be alive today. This length of individual service in years represents one per cent of the time since man acquired the moral sense. One hundred and twenty such lives would take us back to the time of the building of the pyramids.

Paracelsus[26] (1493–1541), a turbulent character, was very different from the courtly and distinguished Leonardo da Vinci. Born in Switzerland a year after the discovery of America, the son of a respected physician, Paracelsus participated in the mental turmoil of his time. His intellectual heritage descended from the classical scholar Reuchlin,[21] a German who in 1482 visited the Academy at Florence, one who inspired Trithemius, a chemist and an abbot of a Benedictine monastery, and Trithemius in turn taught Paracelsus. Paracelsus as a young man worked in the mines and laboratories of the wealthy Függer family in the Tyrol. He was army surgeon in Denmark and Sweden and visited England, France, Belgium and Italy, taking care to acquaint himself with the universities in those lands. At Strassburg in 1526 he set up as an M.D., though there is no record of his ever having obtained the degree. Concerning his training he writes:

> The wanderings I have thus far accomplished have proved of advantage to me. . . . All kinds of knowledge are not confined to the Fatherland, but are scattered throughout the whole world. They are not in one man or in one place. . . . If one would know many diseases, he must wander also. . . . Does not travel give more knowledge than sitting behind the stove? . . . Those that sit

behind the stove eat partridges and those that follow after knowledge eat milk-broth.

Paracelsus[26] had the good fortune to cure Froben, the celebrated bookseller of Basel, and this brought him a call to Basel to be professor at the university. Froben and Erasmus lived in the same house together and were good friends of Paracelsus. But Paracelsus aroused the enmity of his colleagues and was forced to flee the town.

Medical opinion of the day was based upon Hippocrates and Galen, as corrupted by Arab scribes. Two hundred years earlier Petrarch had detested the Arabs and had felt that they had added nothing to Greek culture. A corrupted edition of ancient Greek medicine, which was hugely popular in the Middle Ages, was the "Canon of Avicenna." Avicenna (980–1037), the so-called "Prince of Physicians," was physician-in-chief to the hospital at Bagdad. Paracelsus gave the greatest offence to the good people of Basel by throwing the Canon into a students' bonfire. Stillman[26] points out that in its way this offence was quite as awful as that of Luther, a contemporary of Paracelsus, when he burned the papal bull issued against him.

Paracelsus taught in the university from his own experience and would not rely on the books of the ancients. He says, "The business of the physician is to give to nature what she needs for her battle. . . . Nature is the physician." However, when he could not understand disease he explained it by other means, as for example, "The first cause of disease is the fall of the first man, with which came sin and death into the world. The second cause is the influence of the stars."

Paracelsus would have nothing to do with the four Greek properties of matter. For these he substituted three: mercury, the liquid principle; sulphur, the combustion principle; and salt, the fire-resisting principle. These were in air, fire, earth, or water. He did not believe that the humors existed. Thus he writes:

> In wounds, nature is the real physician. All that is necessary is to prevent infection in wound diseases. The humors and complexions, diet and the stars have no influence. Only the proper treatment, that which lets nature act in peace, determines the result.

In a book concerning "tartaric diseases," the fourth edition of which was published in 1537, Paracelsus attributes pathological deposits to abnormal acid formation and to its effect upon the tissues. Deposits of all sorts, calcifications and concretions, such as one finds in gout, rheumatism, etc., are all explained by chemical pathology, for he had observed the precipitation of colloids by acids. This was an early explanation of these diseases of metabolism (Sudhoff[27]).

Paracelsus first used the Greek word "chaos" for air. He believed in the existence of a spirit, an *archaeus*, which had its abode in the stomach, which determined the processes of digestion and nutrition. But he turned to chemistry for the preparation of medicine for the sick, deeming that more worthy than the seeking for the transmutation of base metals into gold. He therefore was the first biological chemist, establishing the school of Iatro-chemists, *iatros* being the Greek word for "physician."

> But I praise the chemical physicians for they do not consort with loafers or go about in gorgeous satins, silks, and

velvets, gold rings on their fingers and silver daggers hanging at their sides and white gloves on their hands, but they tend their work at the fire patiently day and night.

And again in the furious anger of a tormented spirit he cries out, "I may well rejoice that rascals are my enemies; for the truth has no enemies but liars."

After having been driven out of Basel he wandered through various cities, appearing as a beggar in rags at Innsbrück, and died an unhappy death.

CHAPTER III

THE SEVENTEENTH CENTURY

The influence of Paracelsus lived after him. Twenty-six years after his death van Helmont (1577–1644) was born, and he found the doctrines of Paracelsus the most suitable to his tastes. He believed in the doctrine of an archaeus. He coined the name "gas" from the Greek *chaos* meaning "air," but he questioned the theory of the principles of mercury, sulphur and salt, believing rather in the importance of water as the fundamental basis of all things.

Evidently he had visited the Grotta del Cane, near Naples, a place described by Pliny in his "Natural History." From this grotto, which at its exit takes the form of a long tube about 6 feet in height, a heavy invisible gas flows and spreads over the ground. A man can stand near the exit holding up a lighted torch, but if he lowers the torch, it is extinguished. If he is accompanied by a dog, the dog dies. Hence the name of the grotto. It may have been this fact that led Leonardo da Vinci to state that where a flame cannot live, no animal can sustain its existence. Van Helmont noted the similarity between this gas and that produced by burning charcoal, or by fermenting beer or wine, or by pouring vinegar upon chalk. He found it in the waters of Spa. He called it *gas sylvestre* or "wood gas." It would support neither life nor a flame. He discovered that intestinal gas or the gas obtained from the fermentation of dung was inflammable, and this he called *gas pingue*. It remained for Boyle, however, to invent the pneumatic trough by which gases could be collected. Van Helmont was the first to differentiate between air and water vapor. Since the phenomena of the energy metabolism are based on oxidations of foodstuffs in the body, it is obvious that a true knowledge of nutrition could be obtained only when a knowledge of gases was unfolded. How crude van Helmont's conceptions were may be understood from his experiment of planting a small willow tree in a weighed amount of earth, watering it diligently till it grew to large size, determining that the soil had not changed greatly in weight, and concluding that the willow tree must have been produced entirely from water.

John Quincy,[25] in his introduction to the "Aphorisms of Sanctorius" (London, 1712), questions whether "panaceas and I know not how many universal medicines" really please the Archaeus. He writes:

> That extraordinary Chymist van Helmont has carried this way of reasoning much farther; and to make the work short has placed but one general deity over the whole which he calls the Archaeus. . . . For let the distemper be what it will or seated in whatsoever part, yet it has its rise from some disturbance given to the Archaeus, so whatsoever can be found to quiet and appease this presiding Power will also bring about a cure, by restoring it to good temper and bringing it to govern and carry on all the several functions as before.

Sanctorius (1561–1636), a professor at Padua and a contemporary of van Helmont, invented the first thermometer. He spent most of his life weighing himself and determining the amount of "insensible perspiration" lost from his body, that is, the amount of weight lost during periods when

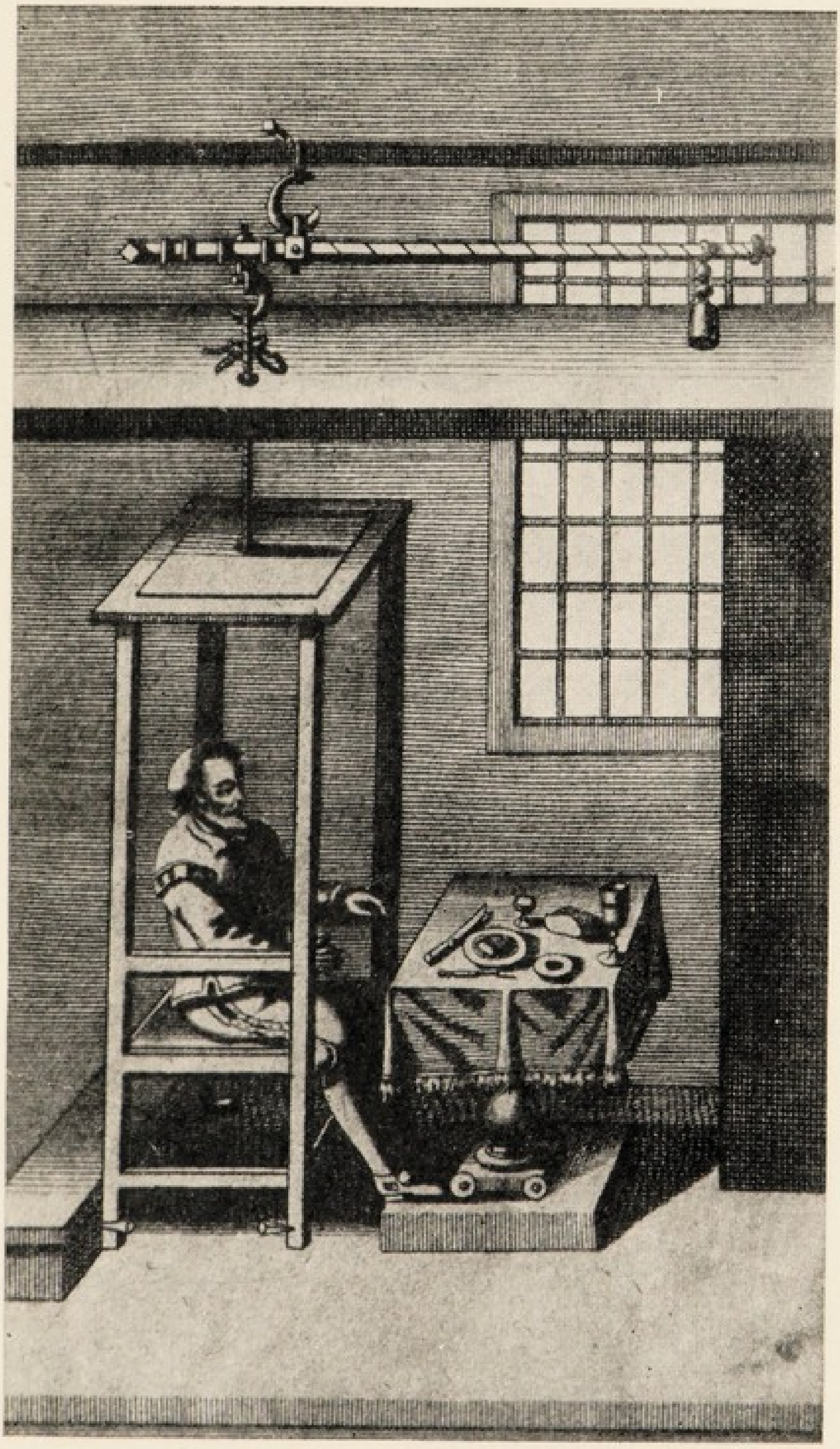

FIG. 1. Sanctorius balanced on a steelyard.

no additional food or drink was taken and no sensible evacuations from the body occurred. The essence of his doctrines is revealed in the following aphorisms taken from his celebrated "De medicina statica aphorisma," published at Padua in 1614:

> Sec. I, Aphorism V. Insensible perspiration is either made by the pores of the body, which is all over perspirable and covered with skin like a net; or it is performed by respiration through the mouth, which usually in the space of one day amounts to the quantity of half a pound, as may plainly be made to appear by breathing upon a glass.
>
> II. If a physician who has the care of another's health is acquainted only with the sensible supplies and evacuations and knows nothing of the waste that is daily made by insensible perspiration, he will only deceive his patient and never cure him.

Sanctorius practiced what he preached, as witnessed by the celebrated print showing him seated in a chair balanced on an immense steelyard. Having been weighed, the steelyard was adjusted to a proper increase in weight. He then partook of food and when the chair dipped he ended his repast. Physical measurements took the place of instinct, apparently to the satisfaction of the professor of Padua. Dodart, who died in Paris in 1707, spent thirty-three years of his life in doing similar experiments. A translation of the work of Sanctorius "with large explanation" was published in London in 1712 by John Quincy.

The French philosopher Descartes (1596–1650) believed that living things were machines, and he compared the body to a clock with counter weights and wheels. In 1637 he said that medical doctrines should be established on infallible experiments.

Jean Rey (d. 1645), a French physician who lived in the first half of the seventeenth century, noted that when tin or lead was calcined there was a gain in weight of each substance. It required the passage of a century and a half before this fact was understood.

The seventeenth century was the period of the founding of scientific societies. The Royal Society grew out of a club called the "Invisible Society" which met surreptitiously at an inn at Oxford as early as 1645 to discuss scientific matters. It received its royal charter in 1662. The older society is still perpetuated in the form of an inner circle called the "Royal Society Club" which dines periodically in London. The attention of members is attracted by an ivory mallet from an Egyptian tomb striking a bit of ancient oak which bears the date of the founding of the society. Three toasts are then drunk standing: "The King," "The Arts and Sciences," and "The Royal Society." Thus are preserved the traditions of the past.

The Académie des Sciences was founded in Paris about 1660 by Louis XIV, who, having vanquished his enemies, desired to decorate his kingdom with the graces of the arts and sciences, wisely taking his inspiration from the Italian Renaissance.

In Germany the first scientific society to be established was the Kaiserliche Leopoldina Deutsche Akademie der Naturforscher, founded at Halle in 1650. The Preussische Akademie der Wissenschaften was established in Berlin in 1700 by Leibnitz after his return from residence in London.

By far the most interesting developments in the seventeenth century took place in London where Harvey, as early as 1615, had begun to teach students the true doctrine of the circulation of the blood. Between 1621 and 1643, within a period of twenty-two years, Willis, Boyle, Lower, Hooke, and Mayow were born, all of whom were in their graves before the great men of the following century were born.

The discovery of the air pump by Otto von Guericke in 1641 was used by Boyle (1627–1691), one of the founders of the Royal Society, to demonstrate in 1660 that neither a flame nor an animal can live in a vacuum.[31] In his "Sceptical Chemist" he questions the validity of the theories of "chemists who assert that all mixed bodies are compounded of salt, sulphur, and mercury."

Willis[29] (1621–1675) was the first European to note the sweet taste of diabetic urine. Also he and his pupil Lower discovered that there was a change in the color of arterial blood, depending on whether air was admitted by the lungs or not. In 1665 Lower[30] transfused the blood of a large dog into the body of a small dog which latter simultaneously lost a volume of blood which nearly equalled its own volume. This experiment is described in the Diary of Samuel Pepys,[30] November 14, 1666:

> To the Pope's Nose, where all the Houblons were and Dr. Croone. Dr. Croone told me that at the meeting at Gresham College tonight, which it seems they now have every Wednesday again, there was a pretty experiment of the blood of one dog let out until he died, into the body of another dog, while all his own ran out on the other side.

The first died upon the place, and the other very well and likely to do well. This did give occasion to many pretty wishes as of the blood of a Quaker to be let into an archbishop, and such like.

Pepys was assured by Robert Hooke a short time afterward that the second dog remained well. Incidentally be it remarked, that though Pepys read Hooke's "Microscopical Observations," he felt that he was made well of an illness by having a fresh rabbit's foot in his pocket.

Robert Hooke (1635–1703) showed in 1667 that artificial respiration with a bellows could keep a dog alive when the thorax was open. "But upon ceasing this blast and allowing the lungs to lye still, the dog would immediately fall into dying convulsive fits; but he as soon revived again by renewing the fulness of his lungs with the constant blast of fresh air."

In 1669 Lower injected dark venous blood into insufflated lungs and saw that it became red and arterial and he concluded it had absorbed some of the air.

John Mayow[31] (1643–1679) wrote, "The lungs are placed in a recess so sacred and hidden" as to be "a sort of holy wonder."

In 1668, when twenty-five years old, he published his celebrated tracts on nitro-aerial spirit, on respiration, on the respiration of the fetus *in utero*, and on muscular movement. Mayow writes:

In the first place it must, I take it, be granted that something in the air, whatever it may be, is necessary for the burning of every flame. This Boyle's experiments have placed beyond doubt. For these show that a lighted candle goes out much more quickly in a glass flask empty of air than in the same vessel full of air, a clear proof that the flame, enclosed in the flask, goes out not because it is suffo-

FIG. 2. John Mayow (1643–1679).

cated by its own smoke, as some have thought, but because it is deprived of its aereal sustenance or food.

This food Mayow called "igneo-aereal particles," the same as were the nitro-aereal particles obtainable from niter. He writes:

> Respiration consists furthermore in the separation of the air by the lungs, and the intermixture with the blood mass of certain particles absolutely necessary to animal life, and the loss by the inspired air of some of its elasticity. The particles of the air absorbed during respiration are designed to convert the black or venous blood into the red or arterial.

Mayow likewise points out that fishes breathe nitro-aereal particles in water for they suffocate in boiled water, and that the child *in utero* gets its nitro-aereal particles from the placental circulation. He declares that the motion of the muscles "results from the chemical action in the muscle with the combustible matter contained therein." Surely this was a great vision!

Mayow died in 1669 at the age of thirty-six, a year after his election to the Royal Society, and these notable contributions to human knowledge appear to have been buried with him, only to be rediscovered a hundred years later. Thus within the seventh decade of the seventeenth century, as the result of the activity of a group of highly gifted men, oxygen had been discovered by Mayow as a separate constituent of the atmosphere, although it was handicapped by receiving the grotesque name of "nitro-aereal spirit."

Thomas Sydenham[33,34] (1624–1689) belongs to this period. He was at Oxford at a time when the Regius Professor of Medicine still read twice a week lectures from the works of Hippocrates and

Galen. Sydenham suffered personally from gout and in 1683 wrote an essay on the subject after thirty-four years of experience with it. He defined gout as "an effort of Nature striving with all her might to restore the patient by the elimination of morbific matter." He says that the disease is due to a faulty concoction of the juices of the body, that unlike any other disease, it kills more rich than poor, more wise than simple, that it rarely attacks fools, but that "those who choose must except the present writer." He states that water drinkers scarcely know what gout is, but he advises the gouty to drink London small beer which "does not sink to the weakness of water nor rise to the density of wine."

Francis Glisson (1597–1677) characterized rickets in 1650 in a volume which was described by a contemporary as "one of the glories of English medicine." Glisson was a Regius Professor of Physic at Oxford.

John Mayow had virtually discovered oxygen at the moment when George Ernest Stahl (1660–1734) was eight years old. Stahl subsequently became physician to the Duke of Weimar and later to the King of Prussia, positions which gave weight to his opinions. He invented the phlogiston theory. When anything burned it gave off phlogiston. No one had ever seen phlogiston. But carbon was rich in phlogiston, because calcined metals which had lost their phlogiston had it restored if they were heated with carbon. This theory flowered for a century, and the work of Jean Rey and John Mayow was completely forgotten.

CHAPTER IV

THE EIGHTEENTH CENTURY

The great Dutch physician Boerhaave[48] (1668–1738) had so wide a fame that a letter addressed "To the illustrious Boerhaave, physician in Europe," by a mandarin in China was delivered to him at Leyden without delay. He was educated in Greek, Latin, Hebrew and Chaldee. He studied mathematics and in his twenty-first year delivered an academic oration upon the subject, "The Doctrine of Epicurus concerning the Chief Good Was Well Understood by Cicero," for which he received a gold medal.

He published his "Elements of Chemistry" in 1724. He had attempted the transformation of mercury by admixture with lead, tin or gold, and accompanied the process with as many as 877 distillations, and yet in the end the same mercury was obtained unchanged.

Students from every nation flocked to his renowned clinic, and patients came from all over the world. The Czar Peter lay all night in his house-boat outside of Boerhaave's house to have the opportunity of talking with him in the morning.

Now Boerhaave, with his world wide acquaintance, a man who speaks of the "immortal Sydenham," may well have heard of the experiments of Mayow at Oxford, for he wrote in his renowned "Elements of Chemistry":

Who can say whether an air of special virtue for the maintenance of the lives of animals and plants does not exist; whether it may not become exhausted; whether its consumption is not the cause of the death of animals which can no longer possess it? Many chemists have announced the existence of a vital element in the air, but they have never told what it is or how it acts. Happy the man who discovers it!

Albrecht von Haller (1708–1777), the great Swiss physiologist of Bern, believed that the heat of the body was derived from the heart and from the friction of the blood on the blood vessels. His "First Lines of Physiology,"[39] translated from the Latin, was the only book used by American medical students between 1787 and 1815, and Oliver Wendell Holmes in 1833 listened to a few lectures on physiology and read Haller. Haller asks:

Does some subtle element from the air permeate the blood and cause its color, as light is required for the colors of plants? Is the use of the lungs to absorb nitre from the air? Is this the cause of the florid color observable on the surface of a cake of blood, while the bottom part is black? Does this preserve the animal from putrefaction? . . . The quantity of these salts which exists in the air is too small; and respiration is most salutary on the highest mountains, where they are most rare; nor have any marks of a nitrous salt ever been detected in our blood.

We may imagine from this that perverted tales about Mayow's nitro-aereal spirit had reached the great Haller half a century after Mayow's death.

The men who participated in the Chemical Revolution and who introduced facts which became the groundwork of modern knowledge of nutrition were born within fifteen years of one another between 1728 and 1743. Their names are Black, Spallanzani, Cavendish, Priestley, Scheele and Lavoisier.

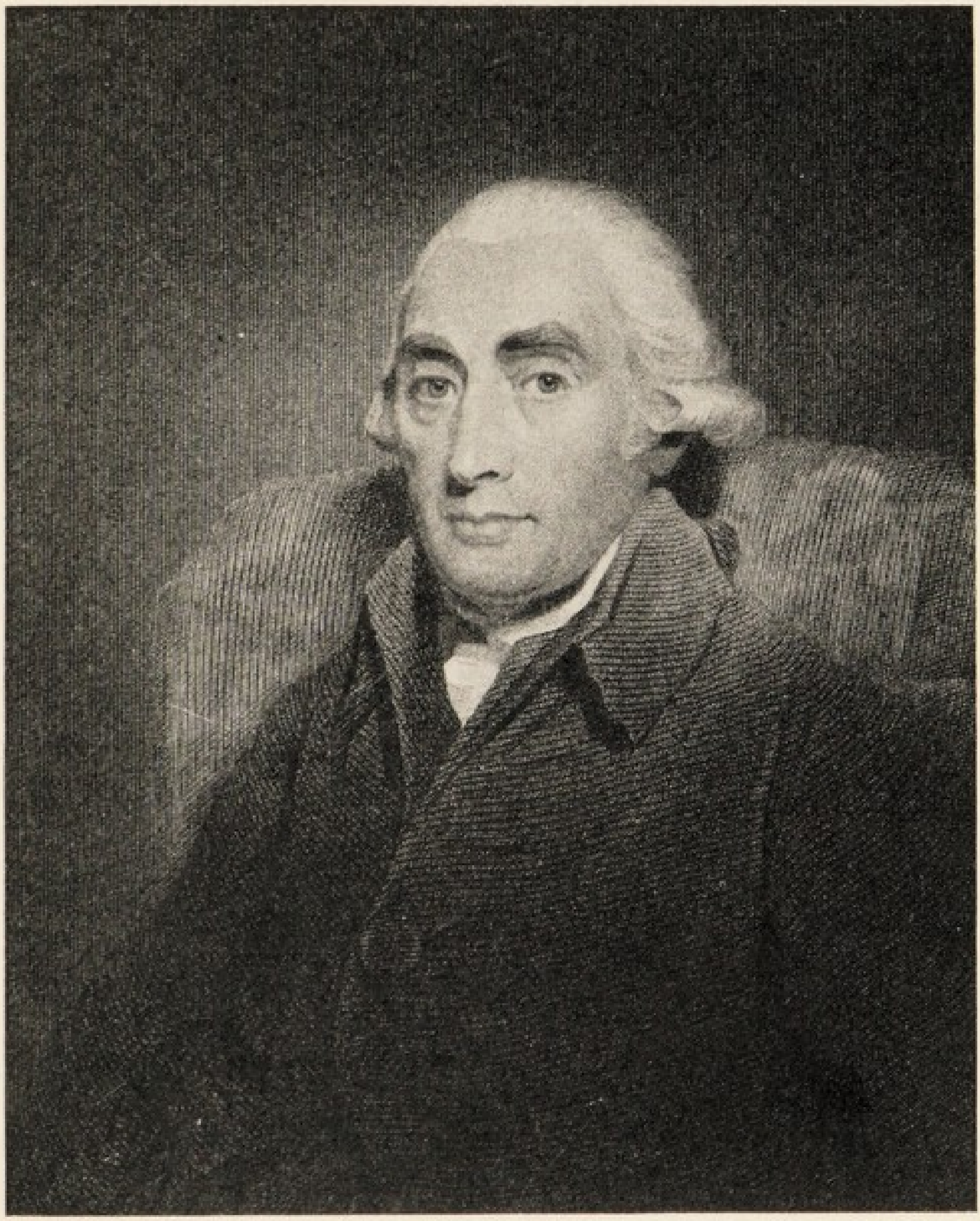

FIG. 3. Joseph Black (1728–1799).

Joseph Black (1728–1799) was early a pupil of William Cullen (1712–1790), Professor of Chemistry at Glasgow, and he afterward went to Edinburgh to complete his medical education under Dr. Monro, *primus*. In 1754 he received his medical degree and presented his graduation thesis "Dissertatio de Humore acido a Cibo orto et de Magnesia." This paper set forth how "mild lime," when burned, gave off "fixed air" and was converted into caustic lime. In 1757 Black found that if "fixed air" were passed into water mixed with caustic lime, a precipitate of "mild lime" was formed. He also found that magnesia alba lost half its weight when treated with acids and gave off "fixed air." Also all kinds of animals expired "fixed air" which gave the same reaction with lime water already described above and that it was produced in alcoholic fermentation. He recognized that he was dealing with the same gas which van Helmont had called "gas sylvestre." He found that the gas was deadly to all animals. He writes in his "Treatise on Chemistry" (1803):

> I found that by blowing through a pipe into lime water, or a solution of caustic alkali, the lime was precipitated and the alkali was rendered mild. I was partly led to these experiments by some observations of Dr. Hales, in which he says that breathing through diaphragms of cloth dipped in alkaline solution made the air last longer for purposes of life.

Little did Hales or Black realize that this principle would be applied to the ventilation of submarines. Incidentally one must pause to reflect upon the fact that the most famous pupil of Black was James Watt, who invented the modern steam engine and professed that his added improvements were due to knowledge which he obtained from Black.

When Cullen was called to the chair of chemistry at Edinburgh, Black succeeded him at Glasgow in 1766. His discoveries were ended. He had discovered carbonic acid gas at the age of twenty-six.

Of Henry Cavendish (1731–1810) it was said that he was the most wealthy of the learned and the most learned of the wealthy. In 1766 he prepared "inflammable air" (hydrogen) as the result of placing zinc, iron or tin in sulphuric or hydrochloric acids. According to prevailing theory he thought that he had captured the phlogiston driven off in the reaction. He therefore identified "inflammable air" as pure phlogiston. Later, in 1783, after Priestley's discovery of oxygen (1774) Cavendish mixed one volume of Priestley's "dephlogistigated air" with two volumes of his pure phlogiston and exploded them with an electric spark with the production of a dew which formed on the glass and which he identified as water. Cavendish mentions that when these experiments were recounted to Lavoisier by a friend, Lavoisier was sceptical as to the possibility of two gases uniting to form water. Cavendish concluded the water was dephlogisticated air united with phlogiston. It remained for Lavoisier to give a satisfactory explanation of this. In 1785 Cavendish showed that, if dephlogisticated air were mixed with the irrespirable portion of the atmosphere and sparks were then repeatedly passed through the mixture when over water, this irrespirable portion was almost completely converted into nitric acid.

This irrespirable portion of the atmosphere was first separated by Daniel Rutherford (1749–1819), one of Black's pupils and the uncle of Sir Walter Scott. In 1772 he burned a candle in an enclosed space and then removed the "fixed air" which had been produced by introducing alkali. The "residual air," which was nitrogen, extinguished the life of a flame or of an animal immediately.

Both Priestley and Scheele independently discovered oxygen at about the same time. There was no pressure for rapid publication of results in those days, and Scheele's work, though performed earlier, was published three years after that of Priestley.

Joseph Priestley (1733–1804) was a Unitarian clergyman who found great interest in laboratory experiments. In 1766 he became a Fellow of the Royal Society and in 1772 was elected foreign associate of the French Academy of Sciences. In the same year he became librarian and companion to Lord Shelburne and traveled with him on the continent. Priestley dined with Lavoisier in Paris in October, 1774, and told him how he had produced "pure dephlogisticated air." However, the story began earlier.

Priestley contemplated the exhaustion of the air by animals and by flames and wondered what mechanism existed for re-vitalizing it. He thought that a sprig of mint put into a glass jar inverted under water might also vitiate the air, but after some months he found that both a flame could burn and a mouse could live in the air within the jar. He then burned a candle in a jar until it went out and introduced a sprig of mint into the jar. Ten days later (in 1771) another candle burned in the enclosed space perfectly well. "This restoration of air depended upon the vegetating state of the plant." In the terms of the phlogiston theory, the burning candle had filled the space with phlogiston, and the growing plant had absorbed the phlogiston, with the production of dephlogisticated air.

Then in 1774 he began treating with the heat of the sun, focused by means of a burning glass, various substances placed in the top of a vessel filled with mercury and inverted in a dish containing mercury. In this way he obtained a copious evolution of gas from *mercurius calcinatus per se* (mercuric oxide). In the gas evolved, a candle burned with an intensely vivid flame, and mice could live in it. He had therefore shown "the superior goodness of pure dephlogisticated air." He gratified his curiosity by breathing it himself and fancied that his "breath felt peculiarly light and easy for some time afterward." He reflected that this pure air might become a fashionable article of luxury. "Hitherto only two mice and myself have had the privilege of breathing it." We shall see how the penetrating mind of Lavoisier transformed Priestley's "pure dephlogisticated air" into the oxygen gas which we know today.

Priestley, at the time of the fall of the Bastille, espoused the cause of the French Revolutionists. His house and church were burned in England by an infuriated mob, and he fled to America in 1794. While he was at sea his great co-laborer Lavoisier was beheaded in Paris. Priestley was an intimate personal friend of Benjamin Franklin, who was his senior by thirty years. Franklin, writing to a friend, said:

> Remember me affectionately to that honest heretic Dr. Priestley. I do not call him honest by way of distinction, for I think all the heretics I have known have been virtuous men. . . . Do not however mistake me. It is not to my good friend's heresy that I impute his honesty. On the contrary 'tis his honesty that has brought upon him the character of heretic.

Priestley died at Northumberland, Pennsylvania, in 1804, still believing in "phlogiston or the principle of inflammability."

Scheele (1742–1786) was a poor Swedish apothecary and a very great chemist. He was the first discoverer of glycerin, uric acid, and lactic acid. In 1771 he heated silver carbonate in a retort. He found that two airs were evolved. For he could remove "fixed air" from the bladder by means of lime water and "fire air" remained in which a candle burned brightly. He wrote to Lavoisier in Paris under the date of September 30, 1774, just before Priestley's visit to Lavoisier, and asked him to use the powerful burning glass of Trudaine upon silver carbonate, then to absorb the "fixed air" with lime water and observe whether a candle or an animal would survive in the remaining air.

Scheele did one remarkable metabolism experiment. In 1777 he placed two large bees and a little honey in a small glass box fitted to the top of a larger cylindrical vessel of glass. The whole space was filled with "fire air" and inverted over lime water. After eight days the bees were both dead, but the lime water, which had absorbed the "fixed air" produced, had risen in the cylinder to replace the "fire air" consumed by the bees. But Scheele had no explanation except along phlogiston doctrines. In 1783, three years before his death, he wrote:

> Is it impossible to convince Lavoisier that his system will not find universal acceptance? The idea of nitric acid from nitrous acid and pure air, of carbonic acid from carbon and pure air, of sulphuric acid from sulphur and pure air, of lactic acid from sugar and pure air!! Can one believe such things? Rather will I support the English.

Priestley, Cavendish and Scheele stood by phlogiston to the end of their lives.

And so also did Adair Crawford (1748–1795), who maintained that the opinion of those who reject the ancient doctrine of phlogiston rested on a very precarious foundation. Crawford was the first man to measure animal heat. He was a native of Glasgow and a pupil of Black. He made experiments on animal heat and combustion in the summer of 1777 and explained them to friends at the time and to students, professors, and to the Royal Medical Society during the following winter. He gave a brief account of his discoveries in his book, "Experiments and Observations on Animal Heat," published in 1779,[36] a second and larger edition of which followed in 1788. In the first edition he writes, in the language of his age:

> The quantity of air phlogisticated by a man in a minute is found by experiment to be equal to that which is phlogisticated by a candle in the same space of time. And hence a man is continually deriving as much heat from the air as is produced by the burning of a candle.

In his second edition he states:

> Though the free communication of discoveries is necessary to the advancement of knowledge, yet it is of much

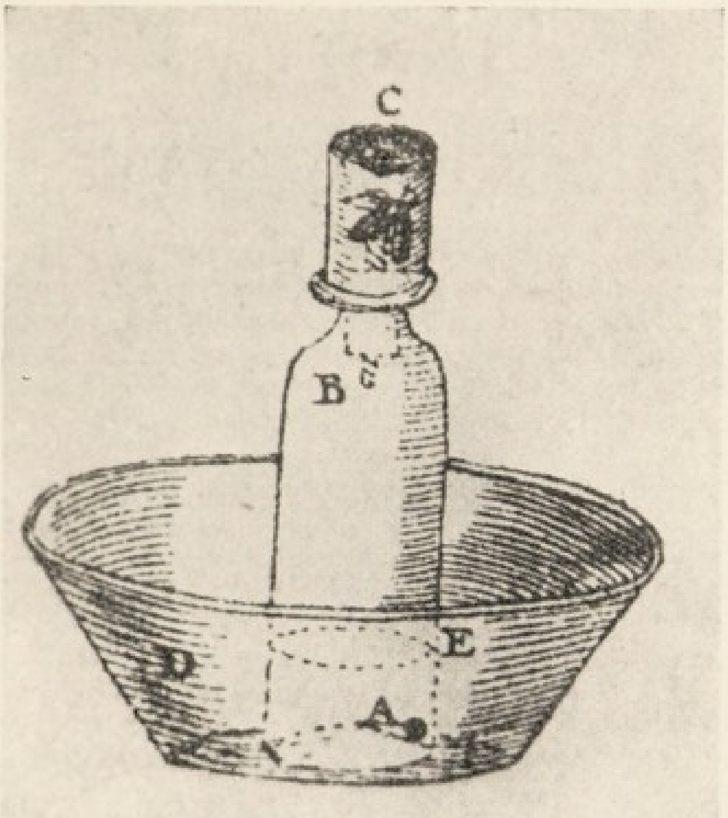

FIG. 4. Scheele's bee in fire air (oxygen); vessel immersed in lime water.

greater importance to the interests of science that facts should be well ascertained than that they should be speedily published.

He burned charcoal in "pure air" (Priestley's dephlogisticated air) by igniting it with a burning glass and found that no water vapor was produced. He burned a candle in pure air and found that water condensed in the interior of the vessel. Therefore the candle contained the "inflammable air" of Cavendish.

He discovered that, when 100 ounce measures of "pure air" were altered by combustion of wax or charcoal or by the respiration of an animal, the quantity of heat communicated to 31 pounds, 7 ounces of water in a calorimeter raised its temperature: by the combustion of wax, 2.1°F.; by the combustion of charcoal, 1.93°; by the respiration of guinea-pig 1.73°. He took care to increase the air temperature surrounding the walls of his calorimeter so that the two remained equal. He concludes that "the quantity of heat produced when a given quantity of pure air is altered by the respiration of an animal is nearly equal to that which is produced when the same quantity of air is altered by the combustion of wax or charcoal." He states that the heat in these processes "arises chiefly if not entirely from the conversion of pure air into fixed air or into water."

The knowledge of what heat really was he left to other philosophers, though he regarded heat as a substance and not a quality. In his opinion "the sensible heat of animals depends upon the separation of absolute heat from the blood by means of its union with the phlogistic principle in the minute vessels."

One experiment, in which he refers to Lavoisier's work, shows how well he knew his art. He describes it as follows:

> If the jar inverted over mercury contain dephlogisticated [oxygen] instead of atmospherical air and if the animal placed in it be removed as soon as it begins to sicken, and the caustic alkali be introduced, a much more considerable diminution will take place, and by the repeated introduction of the animal and of the alkali, almost the whole of the dephlogisticated air may be made to disappear. Hence it follows that it is the dephlogisticated part of the atmosphere which ministers to the support of animal life and which is altered by the action of the lungs. It is extremely probable that this alteration consists in the alteration of pure into fixed air, and of pure with inflammable air.

He also discovers that "when an animal is placed in a cold medium, it phlogisticates a greater quantity of air in a given time than when it is placed in a warm medium."

Crawford moralizes as follows:

> I shall further observe that such speculations have a direct tendency to influence the moral character of man. It is this indeed which stamps them with their principal value; for all the other improvements which may be supposed to arise from the cultivation of Nature if they were unaccompanied with a corresponding advancement in morals, could scarcely be considered as blessings. . . . Could the increase of power be deemed a benefit, if it were used as a scourge; or of wealth if it were made an instrument of corruption; or of knowledge if it were employed to deceive?

The discoveries of carbon dioxide by Black in 1757, of hydrogen by Cavendish in 1766, of nitrogen by Rutherford in 1772, of oxygen by Priestley in 1774, of animal calorimetry by Crawford in 1779, and of the composition of water by Cavendish in 1783, took place within a period of twenty-six years. These notable achievements were all misunderstood, as we have seen.

It required the brilliant mind of Antoine Laurent Lavoisier (1743–1794) to weld these miscellaneous achievements into a harmonious entity.

In the rear of the Madeleine in Paris a monument to Lavoisier bears the inscription:

> Analysis and synthesis of air—Composition of oxides and acids—Composition of water—Theory of combustion—Respiration and animal heat—Permanence of weight of matter and simple substances—Imponderable nature of heat and its rôle in chemistry.

Lavoisier single handed gave interpretations to the knowledge of his time so as to bring from another generation of Frenchmen the justifiable statement, "La chemie est une science française. Elle fût constituée par Lavoisier." Lavoisier was a wealthy state official in receipt of large revenues. These he expended in part upon his laboratory, which was the real home of his mind. His instruments were perfection of their kind. He owned a balance which could weigh 600 grams within 5 milligrams. One may see a collection of his apparatus in the Conservatoire des Arts et Métiers, at Paris. There is a gasometer for the measurement of gases, also the celebrated calorimeter of Lavoisier and Laplace, and a barometer set in polished mahogany, the top of which is crowned with gilded carving, after the fashion of the sumptuous furniture of the period. In the Châteaux de la Carière, near Vichy and the Puy-du-Dom, there is a private collection of apparatus, the property of the descendants of

Lavoisier. Here is a copper face mask which may well have been used by Lavoisier in his first quantitative measurement of the metabolism of man.[46] Here also is a closet filled with metal boxes containing his manuscripts. Only the chemist Dumas has ever read these papers. Perhaps there are unpublished records here which will be given to the world, as were those of Leonardo da Vinci, after several centuries of time. In this home there is a large and magnificent rosewood desk which had been used by Lavoisier.

In 1920 the portrait of Lavoisier and his wife, by David, still hung in the Paris apartment of Monsieur de Chazelles, the grandnephew of Lavoisier, a portrait which now glorifies the library of the Rockefeller Institute. In this same Paris apartment are a portrait of an ancestor of Lavoisier as he appeared at the court of Louis XIV, a portrait of Benjamin Franklin, an intimate friend of Lavoisier, many letters of Franklin, and two sketches by Madame Lavoisier, retouched by David, drawn from memory after Lavoisier's death and showing the first respiration experiments ever performed on man.[47]

Lavoisier was elected to membership in the Académie des Sciences in 1768 at the age of twenty-four. There were men in those days who still believed the old Greek doctrine that water could be converted into earth, and Lavoisier in 1770, in his first paper before the Académie, solved the problem. He boiled rain water 101 days in a hermetically sealed flask. The whole did not change in weight. The loss of weight in the flask itself exactly equalled the quantity of mineral matter gained by the rain water.

Courtesy, Rockefeller Institute

FIG. 5. Lavoisier and his wife.

In 1775 Lavoisier read before the Académie his celebrated memoir "On the nature of the principle which combines with metals during their calcination and which increases their weight." He[40] put an ounce of red mercuric oxide mixed with 48 grains of carbon in a small retort and heated it. He collected 64 cubic inches of gas in a flask under water and found it gave all the reactions of "fixed air," it precipitated lime water, would not support life nor a flame. Metallic mercury was obtained and loss of weight was noted. However, when he heated the red oxide of mercury alone in the same retort, he found that 78 cubic inches of gas were given off, which had none of the properties of fixed air. The gas did not combine with water to acidulate it, it did not precipitate lime water, it did not combine with alkali, it could be used to calcine metals, it maintained the respiration of animals, a candle burned in it with a brilliant flame, carbon burned in it with the luminosity of phosphorus in air, and all combustible bodies burned in it.

Lavoisier concluded that it was proved that the principle which combines with metals in their calcination and augments their weight is the "pure air" which surrounds us and which we respire. Since carbon disappeared completely in the reduction of the mercury calx and nothing but mercury and "fixed air" remained, he concluded that fixed air was a combination of "air eminently respirable" with carbon. The great mind of Lavoisier had penetrated the mystery of Priestley's "dephlogisticated air" and thus sounded the death knell of phlogiston.

Lavoisier confirmed the old observation of Jean Rey that tin increased in weight after calcination and that this increase was due to absorption of "air eminently respirable." A similar absorption took place when phosphorus and sulphur burned, the products of which in the presence of water produced phosphoric[41] and sulphuric acids.

In 1777 Lavoisier[42] found that, if a sparrow were placed in a confined space, the "air eminently respirable" was exhausted by respiration and fixed air replaced it. If this latter were absorbed by alkali, the remaining "foul air" ("spoiled air," Scheele called it) was identical with the air obtained when metals were calcined in a closed space. The lost properties of foul air could be restored by adding "air eminently respirable."

Proceeding farther in collaboration with Laplace, an ice calorimeter was invented. With this apparatus it was possible to measure the quantity of heat produced from combustion of a unit of carbon when it was transformed into "fixed air." Lavoisier and Laplace[44] in 1780 determined the quantity of oxygen and carbonic acid in the respiration of a guinea-pig. The animal produced 226 grains of carbon dioxide in ten hours, and what Pflüger later called the "respiratory quotient" was 0.84. The authors noted that more oxygen was absorbed than was needed to produce the "fixed air" found. They put another guinea-pig into their ice calorimeter and the animal melted 13 ounces of ice in twenty-four hours. They estimated, on the basis of the first experiment, that the oxidation of an amount of carbon necessary to produce 226 grains of "fixed air" would have caused 10.4 ounces of ice to melt in

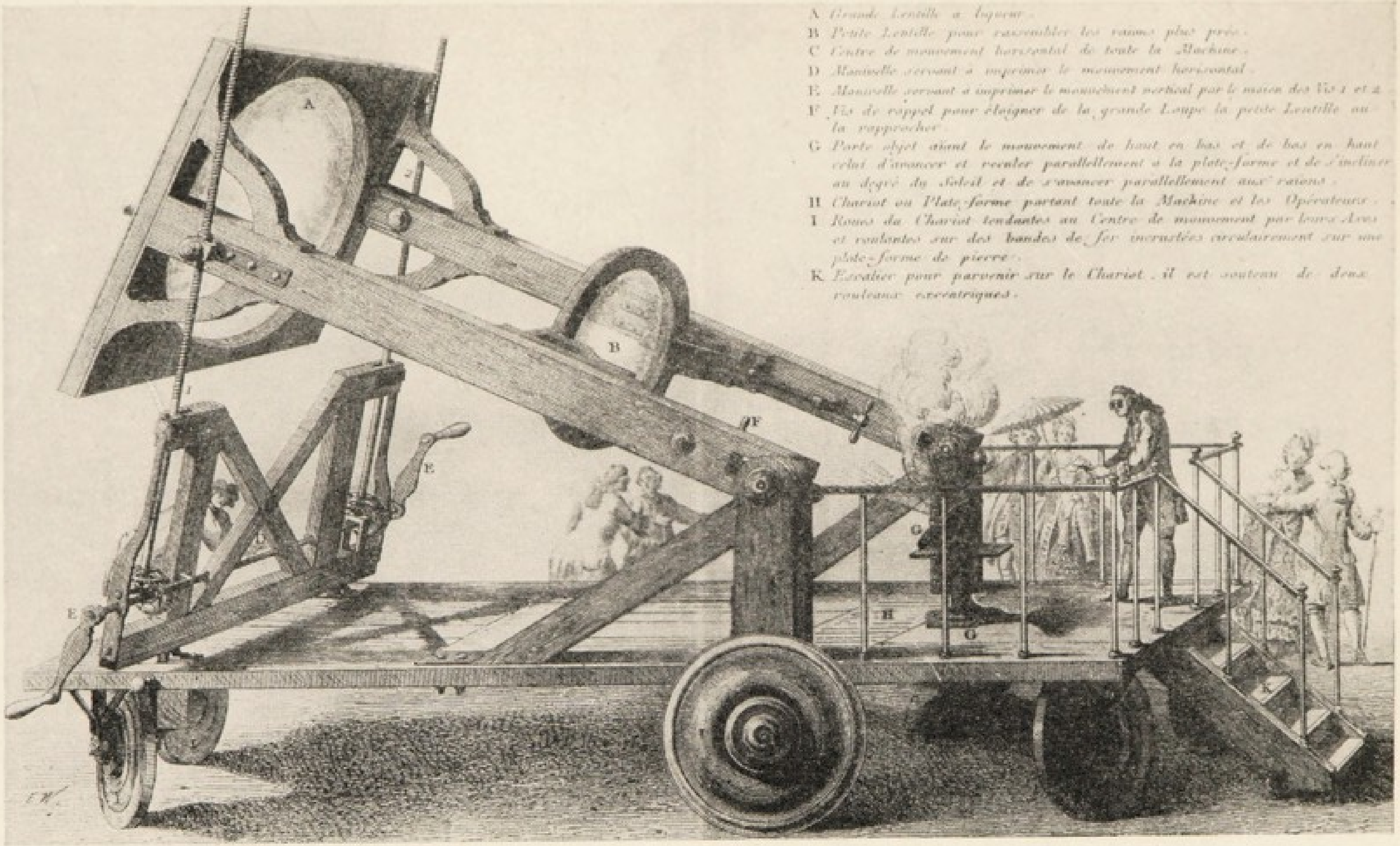

FIG. 6. Burning glass of Trudaine used by Lavoisier.

their calorimeter. They realized that there were errors here. They knew that exposure to cold increased metabolism, also the legs of the animal became chilled and the water of respiration was added to that of the melted ice. But they saw the following vision:

> Since we have found in the preceding experiments that the two quantities of heat obtained are nearly the same, we may conclude directly and without hypothesis that the conservation of animal heat in the body is due, at least in greater part, to the transformation of *air pur* [oxygen] into *air fixe* [carbon dioxide] by the respiration.

A year later Cavendish discovered that hydrogen ("inflammable air" supposed by him to be phlogiston), when mixed with dephlogisticated air and exploded by an electric spark, yielded water. Into the merits of the "water controversy" it is not necessary to enter, but be that as it may, it is certain that Lavoisier[43] was the first to understand the fact that water was formed from the chemical union of the two gases. In 1785 he stated that the discrepancy between his calculation of the heat produced and heat found in his experiments with guinea-pigs was probably due to the fact that the oxygen absorbed, which did not unite with carbon, was used to oxidize hydrogen in the lungs, so that the sum of the heats produced by these two processes should be used in the calculation of the total heat production of an animal. And this method of calculation persisted for three-quarters of a century thereafter. He found also that nitrogen and hydrogen gases mixed with oxygen, and pure oxygen itself had no influence on the respiration, circulation, or intensity of combustion of guinea-pigs.

In 1783 Lavoisier, in a memoir entitled "Reflections upon Phlogiston," dealt with the subject as follows:

> My object in preparing this memoir has been to record the new developments of the theory of combustion which I published in 1777, to show that the phlogiston of Stahl, which he gratuitously supposed existed in metals, sulphur, phosphorus and all combustible substances, is an imaginary creation. All the phenomena of combustion and calcination are much more readily explained without phlogiston than with phlogiston. I understand that my ideas will not be suddenly adopted. The human mind conforms to a certain manner of vision and those who during a portion of their lives comprehend nature from a given point of view have difficulty in acquiring new ideas. In good time the opinions I have set forth will be confirmed or destroyed. In the interim, it is a great satisfaction for me to see that young, unprejudiced minds among those who are commencing to study science, such as mathematicians and physicists who have a new sense of chemical truths, no longer believe in phlogiston as presented by Stahl but regard the whole doctrine as scaffolding which is more embarrassing than it is useful for the continuance of the structure of the science of chemistry.

Finally Lavoisier measured the metabolism of a man. His results may be seen in the table on p. 61.

Lavoisier,[50] the first discoverer of what oxygen really meant, actually found that the intensity of oxidation in a human being was dependent on (1) food, (2) environmental temperature, and (3) mechanical work. We know many more details than Lavoisier knew, but we also know that these three factors are the essential influences governing the oxidative variations which occur within us.

TABLE I
RESULTS OF EXPERIMENTS ON MAN

Condition	*Environmental temperature, degrees*	*Oxygen absorbed per hour*	
		Pouces	*Liters*
1. Without food	26	1210	24
2. Without food	12	1344	27
3. With food	..	1800–1900	38
4. Work (9195 foot pounds) without food	..	3200	65
5. Work (9750 foot pounds) with food	..	4600	91

Lavoisier says the results were due to the exact method of gas analysis used by Seguin, who was the experimental subject during these researches. Seguin in 1791 said the older method of gas analysis of Priestley had twenty sources of error. The new method consisted in collecting the gas to be analyzed in a eudiometer filled with mercury and inverted over mercury. The volume of air caught was measured, phosphorus was introduced, the burning of which completely utilized the oxygen present, and then potash was introduced to remove the carbon dioxide.

The clouds were darkening over Paris at this time. The portents of coming disaster were numerous. The great Frenchman wrote:[45]

This kind of observation suggests a comparison of forces concerning which no other report exists. One can learn, for example, how many pounds of weight lifting correspond to the effort of one who reads aloud or of a musician who plays a musical instrument. One might even value in mechanistic terms the work of a philosopher who thinks, the man of letters who writes, the musician who composes. These factors, which have been considered purely moral, have something of the physical and material which this report allows us to compare with the activities of a man who labors with his hands. It is not without justice that the French language has united under the common expression *work* the effort of the mind with that of the body, the work at the desk with the work at the shop. . . .

Thus far we have considered respiration only as a consumption of air, the same kind for the rich as for the poor, for air belongs equally to all and costs nothing. The laborer who works enjoys indeed in great measure this gift of nature. But now that experiment has taught us that respiration is a true process of combustion which every instant consumes a portion of an individual, that this combustion is greater when the circulation and respiration are accelerated and is augmented in proportion to the activity of the individual life, a host of moral considerations suggest themselves from these determinations of physical science.

What fatality ordains that a poor man, who works with his arms and who is forced to employ for his subsistence all the power given him by nature, consumes more of himself than does an idler, while the latter has less need of repair? Why the shocking contrast of a rich man enjoying in abundance that which is not physically necessary for him and which is apparently destined for the laboring man? Let us take care, however, not to calumniate nature and accuse her of faults undoubtedly a part of our social institutions and perhaps inseparable from them. Let us be content to bless the philosophy and humanity which unite to promote wise institutions which tend to bring about equality of fortune, to increase the price of labor, to assure to it just recompense, to offer to all classes of society and especially to the poor more pleasures and greater happiness. Let us trust, however, that the enthusiasm and exaggeration which so readily seize men united in large assemblies, that the human passions which sway the multitude, often against their own interest, and sweep the sage and the philosopher like other men into their whirlpool, do not reverse an outlook with such beautiful vistas and do not destroy the hope of the country. . . .

> We end this memoir with a consoling reflection. To merit well of humanity and to pay tribute to one's country it is not necessary to take part in brilliant public functions that have to do with the organization and regeneration of empires. The naturalist may also perform patriotic functions in the silence of his laboratory and at his desk; he can hope through his labors to diminish the mass of ills which afflict the human race or to increase its happiness and pleasure; and should he by some new methods which he has opened up prolong the average life of men by years or even by days he can also aspire to the glorious title of benefactor of humanity.

In August, 1793, the Communists closed the Académie des Sciences as being dangerous to the welfare of the state. In November, 1793, Lavoisier was arrested in his laboratory. In May, 1794, he was executed by his enemies, chief of whom was Marat who had borne him a grudge since 1780 when Lavoisier had attacked Marat's statement: "A candle in a confined space is extinguished because the violent expansion of the air caused by the flame compresses it and puts it out." He was condemned to death for permitting the sale of tobacco containing water, for the disturbance of the peace and the disorganization of the national defense. Charles Richet[51] characterizes the execution of Lavoisier at the age of fifty-one as the most criminal act of the Revolution. Lavoisier's friend Lagrange whispered to another friend, "It took but a second to cut off his head; a hundred years will not suffice to produce one like it." And perhaps that was a true statement.

Lazzaro Spallanzani[35,37] (1729–1799) was a contemporary of Lavoisier and watched his work carefully. He took holy orders when he was twenty-six years old, but most of his work was scientific. He was professor at Pavia for many years at the same time that Volta was studying electricity there. He found that fluids boiled in sealed vessels remained sterile, thereby destroying the idea of spontaneous generation. He introduced a sponge tied to a string into the stomach of a hawk and on its removal obtained gastric juice for the first time, and it was clear to him that putrefaction did not occur in the stomach, for the juice thus obtained dissolved flesh, bones, and bread without putrefaction when these materials were put into vials and were warmed by the heat of his arm pits.

He was the first to fertilize the ova of frogs in the laboratory with sperm obtained from the male and, in like manner, he artificially fertilized a bitch. He showed that respiratory exchanges and oxidation belonged to all tissues and to animals without lungs. The stomach, liver, and ovaries of fishes all absorbed oxygen and gave off carbonic acid. He thus discovered the internal respiration. Magendie in 1822 still taught the doctrine of Lavoisier that carbon and hydrogen were oxidized in the lungs, though Lagrange in 1791 had placed the seat of oxidation in the blood on the ground that otherwise the lungs would be overheated.

The manifold researches into gases during the last quarter of the eighteenth century led to the founding of the Pneumatic Institute by Thomas Beddoes[49] (b. 1760), a lecturer on chemistry at Oxford, an institute for the medical application of manufactured gases. He and Humphrey Davy manufactured nitrous oxide which, administered to the latter in 1800, made him unconscious. They stated that it destroyed physical pain and might be used in surgical operations.

CHAPTER V

DIETETICS

It may be well to pause at this point and consider the question of dietetics.

Tiedemann[58] states that the early Romans partook of a light luncheon of bread and fruit, then before dinner indulged in exercise and baths. When the luxury period set in five meals daily were taken.

Coffee was introduced into Europe at the end of the sixteenth century from Constantinople. In 1652 the first coffee house appeared in London, and there were many of them in the reign of Charles II. When newspapers began to be printed during this reign the coffee houses were frequented by the politically disaffected and had to be closed for a time.

An Arabian poet sang "Coffee is the drink of the children of God. Drink thereof confidently, and listen not to the talk of fools who groundlessly seek to condemn it."

When long voyages began to be taken it was noted that scurvy set in among the crews of the vessels. It is stated by Garrison that lemon juice was used as a curative by the Dutch as early as 1564. In 1747 John Huxham, a pupil of Boerhaave, recommended a vegetable diet for 1200 sailors who had scurvy. In 1779 the Channel Fleet had 2400 cases after a ten weeks' cruise, and it was not until 1795 that the introduction of lemon juice into the British navy led to the disappearance of the disease among the sailors.

A case of scurvy experimentally produced occurred in one William Stark[57] (1740–1770), who, having been told by Benjamin Franklin that the latter had lived in health and strength on a diet of bread and water for a period of two weeks when he was a journeyman printer, was inspired to undertake a similar diet. Stark took between 20 and 30 ounces of bread and 2 to 4 ounces of water daily and lost 17 pounds in weight in forty days. He then took between 26 and 34 ounces of bread, 4 to 8 ounces of sugar, and 2 to 3 pounds of water daily for a further period of twenty-eight days. After sixteen days of this diet the gums began to bleed and abscesses appeared in the gums. Two days thereafter, having been very ill, he took a few ounces of meat and drank some wine and felt much better. Nine days later he dined heartily on meat and fruit and drank some wine.

Then for twenty days he lived on a diet of bread, water, and olive oil. After fifteen days he was so weak he could hardly walk across the floor. The gums were swollen. A diet of meat, bread, water, milk, and wine effected a recovery in five days. Bread, water, and roast goose made him "hearty and vigorous, both in mind and body."

A second series of experiments, carried on with a diet of bread, flour, and honey, were his undoing, and he died.

Stark reached the following conclusion:

> A very spare and simple diet has commonly been recommended as most conducive to health, but it would be more beneficial to mankind if we could shew them that a pleasant and varied diet was equally consistent with health as the very strict regimen of Cornaro or the Miller of Essex.

These and other abstemious people, who having experienced the great extremities of bad health, were driven to temperance as their last resource, may run out in praises of a simple diet, but the probability is that nothing but the dread of former sufferings could have given them resolution to persevere in so strict a course of abstinence.

Friedrich Tiedemann, in his "Human Physiology" of 1836,[58] in commenting on this, states that the diets in question are evidently unable to furnish all the complex materials necessary for the nutrition of the organism.

About the time of Stark's death William Cadogan[55] published in 1771 "A Dissertation on the Gout and All Chronic Diseases." He recommends for patients:

. . . new-laid eggs boiled so as not to harden the white creamy part of them, tripe, calves' feet, chicken, partridge, rabbits, ... skate, cod, turbot, etc. and all sorts of shell-fish, particularly oysters raw. Very soon he [the patient] will be strong enough to eat beef, veal, mutton, lamb, pork, venison, ... eaten with their own gravies without any compounded sauces or pickles whatever: instead of which, boiled or stewed vegetables, and sallads of lettuce . . . light puddings, custards, creams, blanc-manges, etc. and ripe fruits of all kinds. . . . But because wine undoubtedly produces nine in ten of all the gouts in the world, wine must be avoided, or taken very sparingly, and but seldom. How is this to be done? Can a man used to it every day, who thinks he cannot live without it, and that his existence depends upon it, leave it off safely? If he thinks he must die of the experiment, doing it all at once, he may do it by degrees, and drink but half the quantity of yesterday till he has brought it to nothing. But the danger of attempting it in this manner is, that it will never be done; and, like a procrastinating sinner, he will for ever put off his penitential resolution till to-morrow. If he did it all at once, I would be hanged if he died of the attempt; he would be uneasy for three or four days, that's all. He may change his liquor, and drink a little good porter, or soft ale, and by degrees come to small beer, the wholsomest and best of all liquors except good soft water. I do not mean that this rigorous abstinence from wine is to last for life, but only during the conflict with the disease. As soon as he has recovered health and strength to use exercise enough to subdue it, he may safely indulge once a week, or perhaps twice, with a pint of wine for the sake of good humor and good company, if they cannot be enjoyed without it; for I would not be such a churl as to forbid, or even damp, one of the greatest joys of human life.

Is it not better to have a little gout than go to all this trouble, he asks. No, because it becomes worse, cripples a man, shortens his life by twenty years, and embitters it. Better therefore self-denial for a year or two. Activity, temperance, peace of mind, are the three great principles of health and long life.

One is struck with the good judgment with which the German physiologist Tiedemann in 1836 writes on the subject of diet, which may here be quoted.

Moderation in the enjoyment of food and drink is undeniably the most important consideration for the preservation of health and the attainment of a happy and efficient old age. People with weak and delicate constitutions find that moderation in diet makes life tolerable. As Hippocrates has pointed out, moderation never leads to illness but makes illness less likely, and when it occurs less virulent and more even in its course. A regulated regimen in the use of foods is favorable under all conditions and preserves the energy of both body and mind. Both Aristotle and Cicero recognized and described its influence upon temperament and genius. It tempers excessive sensory excitement and prevents the awakening of violent desires. It preserves intellectual activity, productive imagery, reflective power, free-will, and self control. Finally moderation causes mildness and strength of character and preserves a joyous spirit and the acquirement of true wisdom.

On the other hand, Tiedemann points out that excessive eating and drinking lead to a weakness in imagination, memory, and judgment, as Cicero and Galen both realized. The old Greek physicians, Hippocrates, Celsus, and Galen, in their medical treatment carefully controlled the diet of their patients and prescribed only few and simple drugs. Sydenham and Boerhaave trod in their footsteps.

The students of Boerhaave sang,

> Hermann Boerhaave schreibet ja
> Acqua paullo frigida
> Potio est optima.

To deal with the subject of dietetics in general or of the story of the vitamins in particular would lead one too far for the restricted limits of this volume. The works of McCollum,[53] of Mendel,[54] and of Sherman [56] are available.

CHAPTER VI

THE NINETEENTH CENTURY

French Era

The intellectual conquests of Lavoisier, the turmoil first of revolution and then of the Napoleonic wars, were followed by a period of splendid scientific achievement in France. In 1823 Laplace and Berthollet, both of whom had been associates of Lavoisier, were living in Paris. Gay-Lussac, a pupil of Berthollet, was there, and in this year Gay-Lussac, the greatest chemist of his day, received young Liebig, aged twenty, into his laboratory, a youth who in his turn became the greatest living chemist. Thénard, Cuvier, Ampère, Laennec, and Magendie lived there also, as did the great German traveler-scientist Alexander von Humboldt. The interesting point is the directly transmitted intellectual inheritance from Lavoisier through Berthollet and Gay-Lussac to Liebig, through Liebig to Carl Voit, and through Voit to many who are still alive and are still busied with the problems originated by their distinguished predecessors.

Whether conditions now exist for intellectual cultivation similar to those which occurred a hundred years ago, is not determinable. It is certain, however, that the present arrangement of well-meaning patrons, by which a series of representatives, boards, and agents appointed by boards to carry out certain educational formulae, does actually constitute a series of successive

FIG. 7. Lavoisier and Berthollet.

FIG. 8. Louis-Joseph Gay-Lussac (1778–1850).

shock absorbers, by which any turmoil induced by the action of the patron at one end of the line returns to him only in the form of subminimal stimuli which cannot be felt. This mechanistic method is entirely different from the personal touch of Lorenzo di Medici, or of Napoleon who took a hundred scientists with him to Egypt. The modern method is much to be regretted in that it induces a sense of intellectual subservience of superior minds to men who are often of an inferior or non-creative type.

Liebig tells us how, after Gay-Lussac and he had made a new discovery, they danced around a table together, the lad of twenty and the old boy of forty-five. When the spiritual will of such people dominates the American university, as it has in Germany and in England in the recent past, then and then only will our rightful Anglo-Saxon inheritance of freedom from wrongfully imposed control be assured. This has to do with the formulation of conditions for the development of great men. Charles Richet[51] has written: "I do not consider that beautiful laboratories, splendid show cases, and complicated apparatus are impracticable, but I prefer a physiologist of genius in a miserable laboratory to a magnificent laboratory with a mediocre experimentalist."

The Germans have the *Sprichwort:*

"Es kommt nicht auf den Käfig an
Wenn nur der Vogel singen kann."

The dying Marcus Aurelius exclaimed "Laboremus." Let us work—in laboratories.

It may be of interest to continue here the story of the blood gases. Humphrey Davy (1778–1829) was the first to obtain oxygen from arterial blood by warming it to 93°C. He stated in 1799 that he had obtained "phosoxygen," which was a combination of heat and light. He showed that this gas could be absorbed by venous blood in the dark without any liberation of light, and he noted the color change in the blood. Carbonic acid was also obtained. "Respiration then is a chemical process, the combination of phosoxygen with the blood, and the elimination of carbonic acid and aqueous gas from it." The rest of his explanation was crude, unenlightened by the results of Lavoisier.

Robert Magnus in 1837 shook blood in a hydrogen atmosphere and also placed it in a complete vacuum and obtained a large volume of the gases, oxygen and carbon dioxide, much more than the blood could have held in solution. There was more oxygen and less carbon dioxide in arterial than in venous blood. From that time on it was generally believed that oxidation took place in the blood, with the production of carbon dioxide.

Carl Ludwig (1816–1895) failed to pass his examination in physiology. This stimulated his interest. He had but one master, Bunsen, in whose laboratory he worked a year. "His papers are epoch making, and he founded the largest school of physiologists of modern times" (William Stirling[52]). Ludwig had over 200 pupils. Bunsen had perfected gas analysis, and in 1859 Ludwig and Setschenow published a description of an apparatus which allowed the boiling of blood at body temperature *in vacuo* and which resulted in the complete expulsion of all the gas contained in arterial blood. The gases thereby evolved could be collected in a eudiometer and exactly analyzed after the method of Bunsen. Sixty volumes per cent of gas were found in arterial blood, of which 20 per cent was oxygen, 40 per cent carbon dioxide, and a small remainder nitrogen. The paper appeared under the name of Setschenow. Although Ludwig personally wrote nearly every paper and designed every bit of new apparatus, his pupils' names appeared in connection with the published announcements. Bowditch's clock, and the *Stromuhr* described by Dogiel were already invented before either had entered the laboratory (personal information from Leon Asher, one of Ludwig's youngest pupils). Ludwig once said, "What is fame, who is famous? Helmholtz is famous. I know of no one else," and to his students he exclaimed, "It is sad, meine Herren, to think how many times I have lied in my lectures in the course of my life time." A quiet, noble, distinguished man, well dressed, but always oldfashioned, with a stock around his neck such as Goethe would have worn, he ranked as one of the finest types produced by our civilization.

The question of animal heat agitated the scientific world of Paris from the time of Lavoisier and led the Académie des Sciences to offer a prize for the best thesis on this subject. The prize was competed for by Despretz[61] (1792–1863) and by Dulong[62] (1785–1838) and was awarded to Despretz, although a modern jury might have awarded it to Dulong.

Despretz determined the heat production of three guinea-pigs which were placed in a water calorimeter. The atmosphere within the calorimeter was saturated with water. The animals raised

23.31 liters of water 0.63°c. in two hours. The production of carbon dioxide was 2.59 liters. The volume of oxygen taken in, which was not united with carbon in the expired carbon dioxide, amounted to 0.71 liters, which was adjudged to have been combined with hydrogen to form water. Despretz then struck the following balance:

Heat from three guinea-pigs as measured..........		100
Heat from formula C + O..................	69.9	
Heat from formula H + O..................	19.4	
Total heat calculated..........................		89.3

This deficit between the heat as calculated (indirect calorimetry) and the heat actually found (direct calorimetry) was noted by both Despretz and by Dulong. Both authorities state that nitrogen gas is exhaled by an animal, a mistake due to imperfect gas analysis. Liebig later pointed out that, if a dog had expired as much nitrogen gas as Dulong found, the animal would have been converted into a mass of mineral ash in seven days.

The heat value of carbon oxidized employed by Despretz was quite accurate, but that of one gram of hydrogen oxidized was taken at 23.64 calories instead of 34.46 calories, the more nearly modern figure found by Favre and Silbermann in 1852. Using these values, Gavarret[64] in 1855 found that the calculated calories in all the experiments of Despretz would have averaged 90.2 per cent of the heat found. Moreover, in seven out of sixteen experiments reported, these calculated heat values were 101.8, 96.8, 94.1, 96.5, 99.2, 99.2, and 93.8 per cent of the values directly found. The corrected values of Dulong's work showed that an average of 90.6 per cent of the heat directly determined could have been calculated from the heat of the oxidation of carbon and hydrogen.

If modern methods had been employed in Despretz's experiment with the three guinea-pigs, the consumption of oxygen would have been 3.30 liters, the respiratory quotient 0.78, the calculated heat 15.86 calories, that directly measured 14.68 calories, or 8 per cent more calculated heat than was directly measured, instead of 11 per cent too little as estimated by Despretz. The computation does not include the heat absorbed by the vaporization of water in the lungs, which must have been small in amount on account of the humidity of the inspired air.

Despretz concluded that, although oxidation is the main source of animal heat, assimilation of food, movement of the blood, and friction in different parts can easily account for the remainder. In his "Elements of Physiology" in 1836, Magendie accounted for the discrepancy by these same factors and included the heat produced by the friction of the blood corpuscles upon one another. This was before the day of the enunciation of the law of the conservation of energy.

The great French physiologist François Magendie (1783–1855) reported in 1816[65] that, when he gave dogs sugar alone, or butter, or olive oil, or gum arabic, together with distilled water, the animals died within thirty to thirty-six days. Evidently the protein element was necessary. Magendie also found that a supplementary ration of gelatin would not take the place of meat protein in the diet. These were animal experiments akin to those of Stark upon himself fifty years before and showed that no one could live on simple organic compounds as a steady diet.

The chemists of the day were busy isolating organic compounds, so called because it was believed that they were derived only through the activity of living things. Thus Michel Eugène Chevreul (1787–1889), who lived to the great age of one hundred and two years, longer than any other scientist in the record, and lectured regularly at Paris when over one hundred, discovered in 1814 that fats were made up of fatty acid and glycerine. In 1832 he isolated creatine. Urea had been found in the urine in 1773 by Ruelle, and in 1823 Prévost and Jean Baptiste André Dumas (1800–1884) extirpated the kidneys of dogs and cats and witnessed a great accumulation of urea in the blood, which showed that urea was not produced in the kidney. In 1828, two hundred years after Harvey's announcement of the circulation of the blood, Wöhler produced urea synthetically from ammonium cyanate. Wöhler wrote to his close friend Liebig; "I must tell you that I can make urea without the aid of the kidneys or indeed of an animal." With that sentence the term "organic" chemistry became mistaken usage, although it persists to this day as descriptive of the chemistry of the carbon compounds.

In Gmelin's "Human Physiology" (1836, vol. 3) the word "*Stoffwechsel*" appears, as indicating the changes which take place when foodstuffs undergo destruction in the body. This word was not used by Liebig in his "Thierchemie"[72] in 1842, although it begins to appear frequently in Johannes Müller's *Archiv für Physiologie* in 1843. It is the German equivalent of the word "metabolism."

The first balance of the intake and outgo of the elements in food and excreta was made by Boussingault, a Frenchman who employed the methods used in organic chemical analysis which had been developed by Lavoisier, Gay-Lussac, and Thénard, an art finally perfected by Liebig in 1830. Boussingault in 1839[60a] determined the elements contained in the fodder given to a cow and the quantity of the same elements eliminated in the urine, feces, and milk, and obtained the following results:

	C	*H*	*O*	*N*	*Salts*
In the fodder..........	4813	595	4035	201.5	889
In the urine, feces, and milk................	2602	332	2083	174.5	921
	−2211	−263	−1952	−27.0	+32

Boussingault united the 1952 gm. of oxygen with all the hydrogen available to form water, and a balance of 19 gm. of hydrogen was left which required inspired oxygen to convert it into water. He estimated that the 2211 gm. of carbon available for oxidation would require 4052 liters of oxygen to convert it into 7999 gm. of carbonic acid gas. This cow received a maintenance ration, that is, one which maintained her weight under the conditions outlined. As far as the factor of nitrogen was concerned, Boussingault said that from one analysis it was impossible to state whether atmospheric nitrogen entered as a factor or not.

He repeated this experiment with a horse and found some of the nitrogen of the food was retained in the body.

In 1843 he used a turtle dove[60b] and found, by his indirect method of calculation, that 0.211 gm. of carbon should have been expired whereas 0.209 gm. actually had been expired in the form of carbon. These were the beginnings of the determination of respiratory metabolism.

Liebig applied the same principles to the determination of the metabolism of a company of the grand ducal guard of Hesse-Darmstadt, to prisoners at Giessen and at Marienbad.

Barral[59] (1819–1884) used the same method in 1849 for determining his own metabolism and that of his family. He likewise calculated the heat production from the union of oxygen with carbon and hydrogen. His values are not abnormal.

Subject	*Calories 24 hrs.*	*Calories per kg.*
Barral (29 yrs.)	2312	49
His son (6 yrs.)	1224	82
A servant (59 yrs.)	2559	44
A woman (32 yrs.)	2541	42

The most notable respiration experiments of their day were those of Regnault and Reiset.[66] "The closed circuit system of Regnault and Reiset" is today the common term for the method used in conjunction with modern respiration apparatus.

Henri Victor Regnault (1810–1878) was professor of physics and chemistry in Paris. He also became chief engineer of mines and director of the Sèvres porcelain manufactory. He held the students so strictly to their tasks that, following his examinations, they organized an annual street procession of protest, a custom which outlived him and which is said to persist today.

Regnault and Reiset in 1849 introduced animals into a bell jar of 45 liters capacity, in which they were sealed. Carbonic acid, as produced, was removed by a pumping apparatus which brought alternate portions of the air in contact with potash solutions and then returned this air into the bell jar again. As the animal used the oxygen in the air a new supply of oxygen was admitted to replenish that consumed. They were able to determine what Pflüger later called the "respiratory quotient," that is to say, the volume of carbon dioxide expired divided by the volume of oxygen inspired. They obtained the following values:

	R. Q.
Rabbit	
After carrots and fresh plants	0.919
After bread and oats	0.997
Dog	
After bread	0.928
After raw meat	0.745
After mutton fat	0.694
Fowl	
After bread	0.976
After meat	0.677

Gavarret[64] in 1855 remarks concerning these results that the relative volume of carbonic acid to oxygen diminishes when the food becomes entirely vegetable and increases when animal food is given, which is in complete accord with elementary composition of the materials ingested and oxidized under these variations of nutritive conditions.

Regnault and Reiset found that the respiratory quotient in fasting animals is a little less than when they are fed with meat, and noted that the similarity is due to the fact that in starvation they live off their own flesh. All fasting animals are similar to carnivora. They were convinced of the fact that heat was entirely derived from chemical reactions. They said that the substances oxidized in the body are composed of carbon, nitrogen, and hydrogen, and often contain a large amount of oxygen. Hence their own content of oxygen is employed in part in the oxidation which yields carbonic acid and water as end products. Therefore the heat liberated must be different from that calculated on the assumption of Lavoisier that carbon and hydrogen are oxidized as such. Moreover, the foodstuffs are not completely destroyed, for urea and uric acid are found as waste in the urine. All the processes involved in metabolism were accompanied either by the liberation or absorption of heat, but they were evidently so complex that it was very unlikely that anyone would ever be able to evaluate them.

This was not true prophecy, for probably even at that time, and certainly three years later, Bidder and Schmidt had grasped the secret of the interpretation. In the same way, in 1840 the great physiologist Johannes Müller stated that the velocity of the nerve impulse would never be measured, and ten years later his pupil Helmholtz measured it.

Some of Regnault and Reiset's animals expired nitrogen, others absorbed it, and what happened

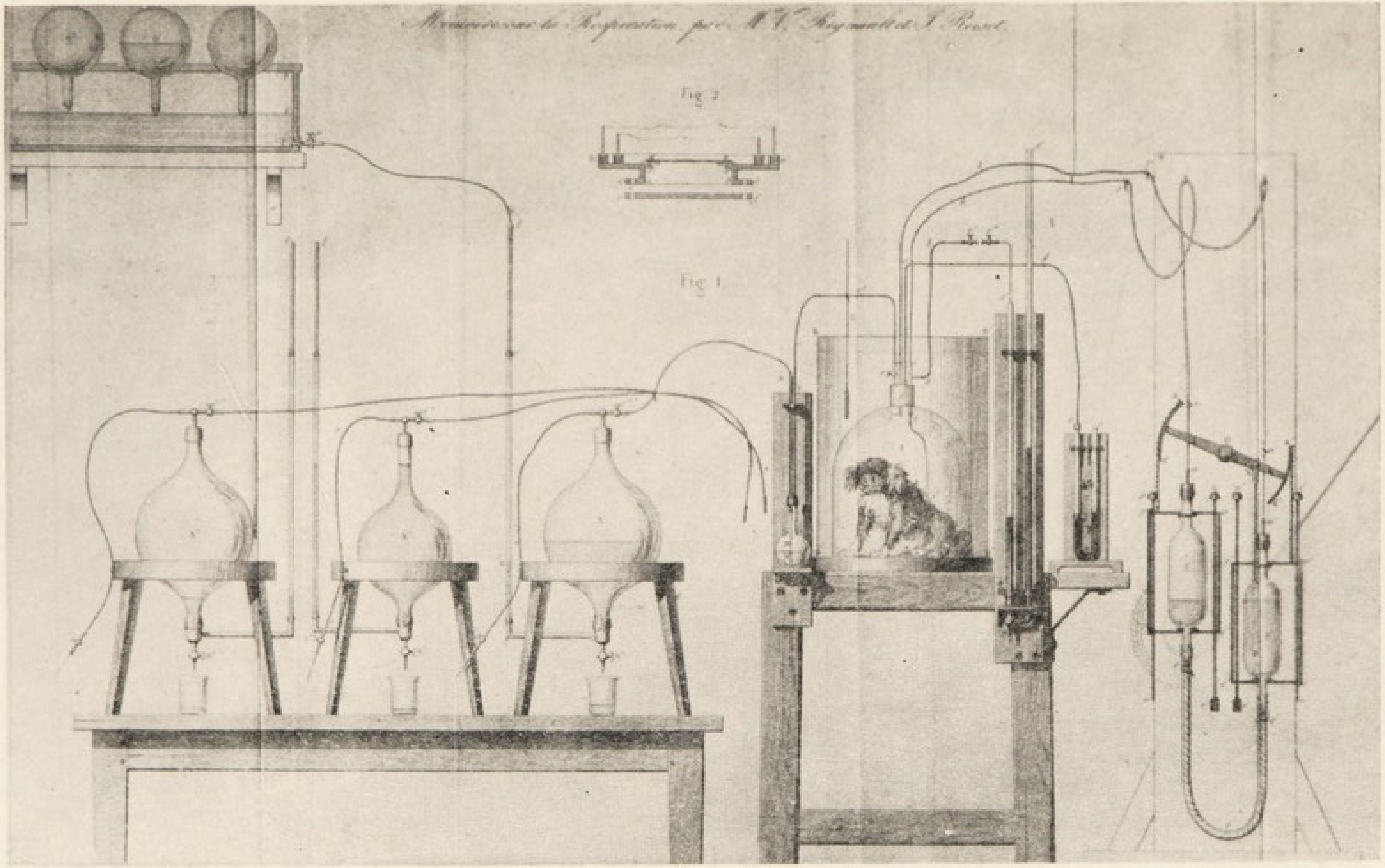

Fig. 9. Closed circuit apparatus of Regnault and Reiset.

was the resultant action of the two processes, they said. The respiratory processes were carried on perfectly in an atmosphere made up of hydrogen and oxygen.

The beginnings of the Law of Surface Area appear in the following statement by Regnault and Reiset:

> The consumption of oxygen absorbed varies greatly in different animals per unit of body weight. It is ten times greater in sparrows than in chickens. Since the different species have the same body temperature, and the smaller animals present a relatively larger area to the environmental air, they experience a substantial cooling effect, and it becomes necessary that the sources of heat production operate more energetically and that respiration increase.

Bergmann,[68] in Müller's *Archiv für Physiologie* (1845, p. 300), presented an article entitled "Non-chemical note of criticism concerning *calor animalis*." In this he remarks, "The preservation of a constant temperature in a given volume of substance with a constant surface area but under conditions involving heat loss such as low environmental temperature, requires a measured amount of heat to be added to such a body or to be produced within it." In later papers about this time Bergmann developed a theory that the heat production was proportional to the surface area, and Rubner thinks that Regnault may have heard of the idea. Regnault had worked with Liebig at Giessen.

Be that as it may, a clearer statement of the case occurs in Bidder and Schmidt's great book, "Die Verdauungssäfte und der Stoffwechsel,"[69] published in 1852, which reads as follows:

The extent of the respiration, like every other component of the metabolism process, is to be regarded as a function of one variable, the food taken, and one constant, a distinctly typical metabolism (*Respirationsgrösse*) which varies with the age and sex of the individual. This factor characterizes every animal of a given race, size, age and sex. It is just as constant and characteristic as the anatomic structure and the corresponding mechanical arrangements of the body. It is in the main determined by the heat consumption in the organism; that is to say, the replacement quota for heat lost to the body through radiation and conduction to the environment in a given unit of time. It may therefore be used to determine this, or in case the factor of heat loss is known, one can deduce the extent of the metabolism.

This typical metabolism . . . is that of the fasting animal. It must be nearly the same in animals having the same body volume, surface and temperature; the larger the body surface, the body volume and temperature remaining constant, or the higher the body temperature with surface and volume constant, the higher will be the metabolism as determined by the laws of static heat.

Of course a sharp mathematical treatment of this phenomenon can be thought of only after very numerous and exact experimental determinations on animals of most varied form, size and temperature.

Magendie's most distinguished pupil was Claude Bernard (1813–1878), the discoverer of glycogen. Bernard was both philosopher and physiologist. Richet[67] declares that from 1850 to 1870 it appeared as though Claude Bernard were preaching in a desert, but that his ideas made their way in the world and medicine now perfectly well understands that physiological experimentation is the master-key which reveals the science of medicine. For Bernard himself declared "Do not think that there are two physiologies nor two chemistries, one for the normal, the other for the abnormal; the laws are the same in both cases."

Richet[67] tells us that Magendie tried to discover whether the lymphatics of the intestines played as large a part in the absorption of foods as did the veins. This problem aroused the interest of Bernard, and it was incidental to this investigation that he discovered that an extirpated liver forms sugar whether food had been given or not before its extirpation. It also formed sugar if meat had been administered before extirpation. He noted that the blood of the hepatic vein might contain more sugar than that of the portal vein and concluded that the liver formed sugar in the living animal. He perfused the liver with saline until it no longer showed a sugar reaction and then, after waiting three hours, found that further washing removed sugar once more. He sought for the mother substance, found it, and named it "glycogen," the producer of glucose. He coined the term "internal secretion" and said that the liver could secrete glucose into the blood.

And in recent years the study of glycogen, both in health and in disease, would have fortified Claude Bernard in his conviction that there was but one chemistry for health and for disease.

Claude Bernard did most of his finest work in a cellar under the street. And Sir Michael Foster[63] relates that Claude Bernard's wife left him because he, though one of the greatest men in France and an associate of the Emperor, could not provide her with a horse and carriage.

CHAPTER VII

THE NINETEENTH CENTURY

GERMAN ERA

We have witnessed two eras of English discovery in the seventeenth and eighteenth centuries; we have seen the glittering rise of French science during the era from Lavoisier to Gay-Lussac; and now Liebig transfers from Paris to the small town of Giessen power which was innately his own but which was developed within him by Gay-Lussac, Thénard and Dulong, an obligation which he acknowledged all his life. The time was propitious in Germany. The universal genius of Goethe and of Beethoven had touched the spirit of the whole land, and these two men were still alive when Liebig, Wöhler, and Johannes Müller were young professors. Goethe's patron, Grand Duke Karl August, had said in 1819, "Freedom of opinion and freedom in teaching must be retained in all the universities, for truth is discovered by open conflict of opinions, and a scholar must be protected from reliance on authority and must be given independence." Goethe further interprets this statement by saying that conflict of opinion does not determine truth but states the problem to be solved.

The first meeting of the Deutsche Naturforscher, which was attended by Purkinje, was held in Leipzig in 1822, the year Liebig went to Paris.

Justus von Liebig[74] (1803–1873) was made professor of chemistry at the University of Giessen

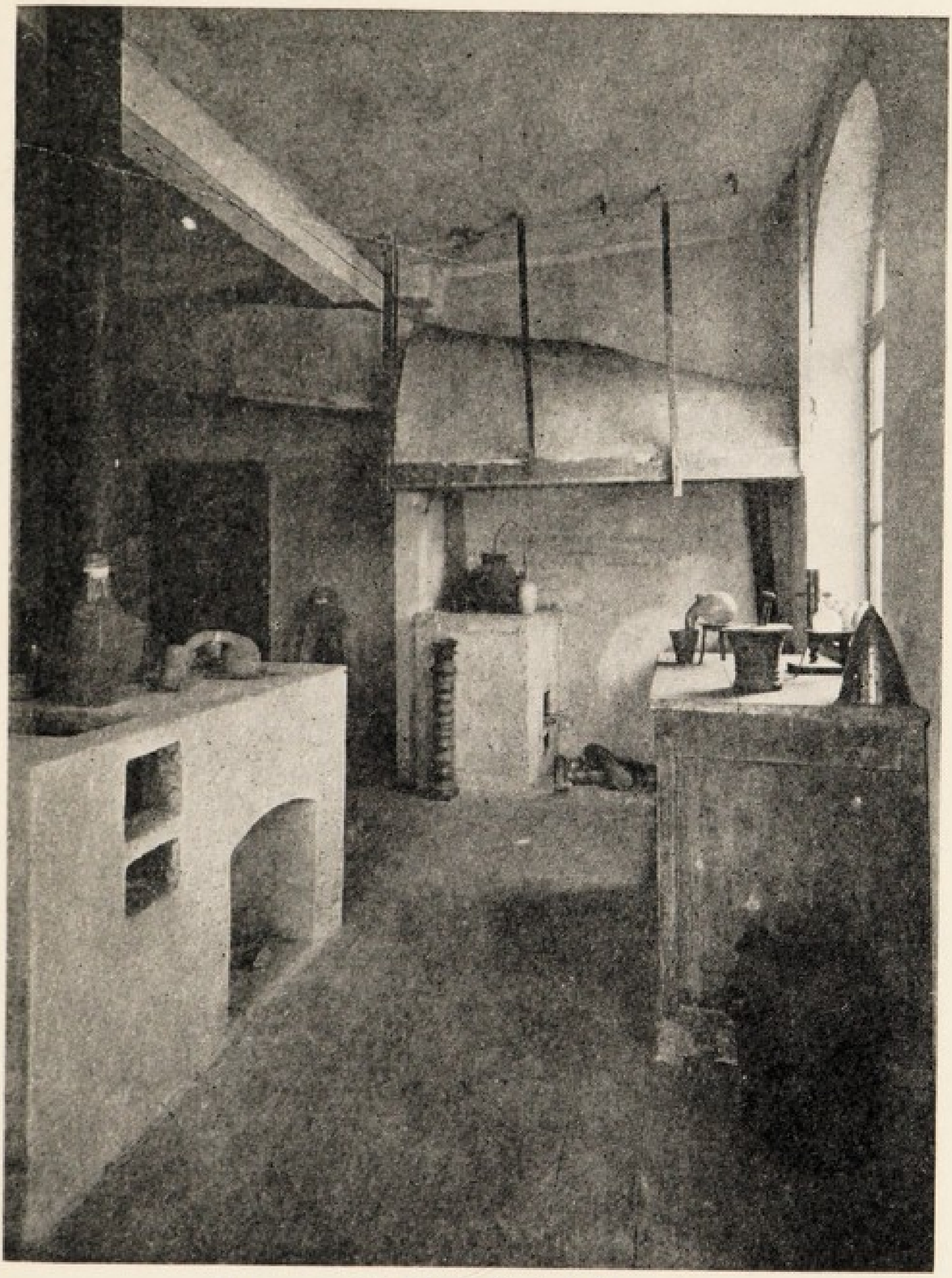

FIG. 10. Liebig's first laboratory.

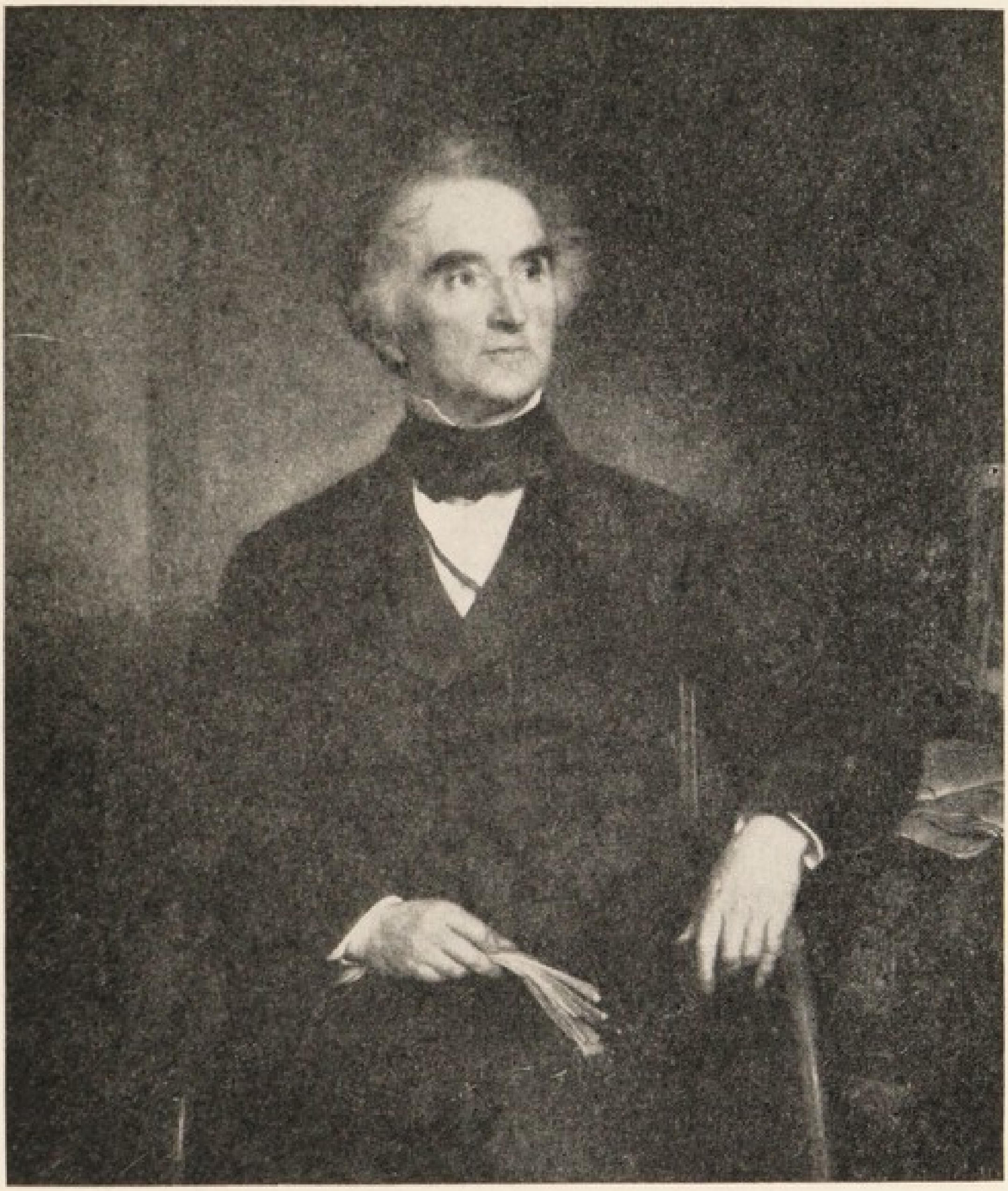

FIG. 11. Justus Liebig (1803–1873).

in 1824 when he was twenty-one years old. His original laboratory, now a museum, was improvised in a military horse barracks. Here the Liebig method of the analysis of organic substances was perfected. In it organic chemistry was being created by Liebig. Pupils from all over the world came to him, for his name filled the earth. Agricultural chemistry and physiology also felt the magic of his touch.

Sir William Ramsey, writing in 1910, tells us that in the days of Liebig and Wöhler there were no overgrown universities. Life in their laboratories was like that in a family. The teacher was a true father caring for his children. All worked together. The great size of universities has now made this life impossible. When the students exceed fifty in number it is impossible to know them all personally, and a department becomes a machine shop. One can make screws by the million in a factory, but men cannot be created like screws. And the owner of the factory, that is the professor, may have to take care of the machinery instead of coming into intimate personal contact with the young people.

In 1840 Liebig delivered a course of lectures in England when he was but thirty-seven years old. In these lectures on "Organic Chemistry,"[71] he declared:

> All discoveries in physics and chemistry, all explanations of chemists must remain without fruit and useless because, even to the great leaders in physiology, carbonic acid, ammonia, acids and bases, are sounds without meaning, words without sense, terms of an unknown language which awaken no thoughts and no sensations. They treat these sciences like the vulgar, who despise a foreign literature in exact proportion to their ignorance of it; since even

when they have had some acquaintance with it, they have not understood its spirit and application. . . . It is too often forgotten by physiologists that their duty really is not to refute the experiments of others, . . . but to discover the truth and that alone. It is startling when we reflect that all the time and energy of a multitude of persons of genius, talent and knowledge is expended in endeavors to demonstrate each other's errors.

In this volume we read that "all superabundant nitrogen is eliminated from the body as a liquid excrement, through the urinary passages; all solid substances incapable of further transformation pass out by the intestinal canal, and all gaseous matters by the lungs." If we substitute for the first sentence "all soluble substances are eliminated in the urine," this paragraph, written nearly a century ago, becomes one transmitted to me by Voit and by me to students for forty-one years.

In 1842 Liebig published his famous "Thierchemie."[72] In this he clearly states that the nitrogen of flesh and blood which has been involved in metabolism is found in the urine as urea and uric acid, and that the quantity of nitrogen in the urine is directly proportional to the mass of the destroyed organ tissue. He finds the relation of N:C in the urine to be 1:1. All that part of carbon and hydrogen in protein which is not needed to form urea and uric acid is eliminated as carbon dioxide and water. Inspired oxygen is the direct cause of the oxidation of fat and carbohydrate in the body, whereas muscle work is the cause of protein metabolism.

He states, "The heat generated by oxidation is entirely sufficient to explain the constant temperature of the body and its loss of heat," and

Liebig estimates relative caloric values of different foodstuffs which, as far as carbohydrate and fat are concerned, are not far different from those of Rubner, though Rubner had a more accurate biological basis for his knowledge. One may read a crude forecast of the isodynamic law of Rubner in the following statement:

> In England servants receive daily a certain amount of beer, or in consequence of temperance societies, the equivalent of beer in cash. One of my friends tells me that when the supply of beer is stopped, the household increases its consumption of bread, so that the beer is paid for twice, once in cash and again in bread containing the same equivalent of carbon and hydrogen.

It is seen from this example that Liebig's hypotheses, though based on no experimental evidence, were the brilliant ideas of a poet who was a prophet, and they therefore had a remarkably stimulating effect upon his time.

Liebig dedicated his book ("Thierchemie") to Berzelius, who was then over sixty. Berzelius wrote Liebig that British adulation had turned his head, had caused him to make a purely literary effort in which the poetical tendencies of his mind, combined with a readiness of literary expression, had led him into the limitless realm of theory in which the temper of a poet was a most dangerous companion. Liebig replied that Berzelius, when a young man, had changed the opinions of others through his own experimental evidence and should not now criticise others. He acknowledged the high and enduring esteem in which Berzelius was held by all who knew of his immensely valuable work.

A generation later, in 1870, Liebig at the age of sixty-seven, wrote an article critical of Voit's conceptions. As a turning-point in physiology, Voit[76] replied, only the immortally memorable work of Lavoisier, which a hundred years previously had elucidated the process of oxidation, was in any way comparable with that of Liebig. Also that the ideas of Liebig had always been his guiding star. But Voit said his own work had been based, not on pure chemistry or on theoretical reasoning, but rather on asking the living animal itself to reveal the real truth about the processes of cell life. The attack of the younger man of thirty-nine upon the older Liebig was so sharp that I have been told that Liebig, who all his life had most vigorously assailed all opponents, broke down and cried.

Theories are often held tenaciously and are often overvalued by their proponents. Willstätter defines their true importance: "A hypothesis may vary in value according to the mentality and temperament of the investigator and according to its utility in suggesting and co-ordinating new observations. A hypothetical explanation of incompletely understood phenomena is often a necessary condition of scientific progress." Measured in these terms, the thoughts of Liebig had the profoundest influence upon his day and generation.

Of great significance in the history of nutrition is the work of Friedrich Bidder (1810–1894) and Carl Schmidt[69] (1822–1894). Bidder, a farmer's son, was born in Livonia, Russia, and graduated in medicine in 1834 at Dorpat. He traveled for a year, hearing the lectures of Johannes Müller and of Henle in Berlin. In 1835 he returned to Dorpat where he taught for thirty-four years. His pupils produced seventy-seven doctors' dissertations. Carl Schmidt was born in Mitau, Courland, Russia. He took his PH.D. degree under Liebig at Giessen in 1844 and also worked with Wöhler. He went to Dorpat in 1846 where he taught for forty-five years. These two young men came together there, one a pupil of Liebig, the other a worker under Johannes Müller. The harmony was so complete that they wrote, "As the result of mutual exchange of ideas and intellectual metabolism, we are in entire agreement." In 1852 they published their celebrated "Die Verdauungssäfte und der Stoffwechsel." This volume was issued only three years after the work of Regnault and Reiset was published. Regnault and Reiset had a better respiration apparatus than Bidder and Schmidt, but the latter had a keener insight into the problems of metabolism, undoubtedly derived from Liebig.

They report the following balance sheet regarding the fate in the body of 100 gm. of dry muscle protein, free from ash, beef and cat muscle being almost identical in composition.

	C	*H*	*N*	*O*	*S*
100 gm. meat protein......	53.01	7.02	16.11	22.86	1.00
Less 34.52 gm. urea........	6.91	2.30	16.11	9.20	
Rest of 65.48 gm..........	46.10	4.72	0	13.66	1.00

They let a cat fast for eighteen days and made the following computation from the analysis of the excreta and of carbon dioxide expired. As

Liebig had taught them, the nitrogen in the urine was made the measure of protein metabolized. The carbon expired, less that attributable to the oxidation of protein, must have arisen from fat.

From the metabolism of	*C*	*H*	*N*	*O*	*S*	P_2O_5
Body protein, 204.43 gm.	102.24	13.43	30.81	43.81		
Body fat, 132.75 gm.	103.72	15.59	.....	13.45		
	205.96	29.02	30.81	57.26	2.17	3.76
Excreted by lungs, urine and feces	205.96	4.67	30.81	18.42	1.13	3.57
Rest for respiration	......	24.35	.....	38.84		

	O_2, *gm.*
190.78 gm. expired C required to produce CO_2	508.74
24.35 gm. expired H required to produce H_2O	194.78
	703.52
Less O_2 contained in the other products of metabolism	38.84
O_2 which must have been used	664.68

One may see here the pattern of organic chemistry, as expounded by Liebig, applied to the elucidation of the problems of life.

The respiratory quotient by this calculation was 0.765 for the fasting cat. Regnault and Reiset had found 0.744. Pettenkofer and Voit later found 0.69 in a fasting man, using a procedure

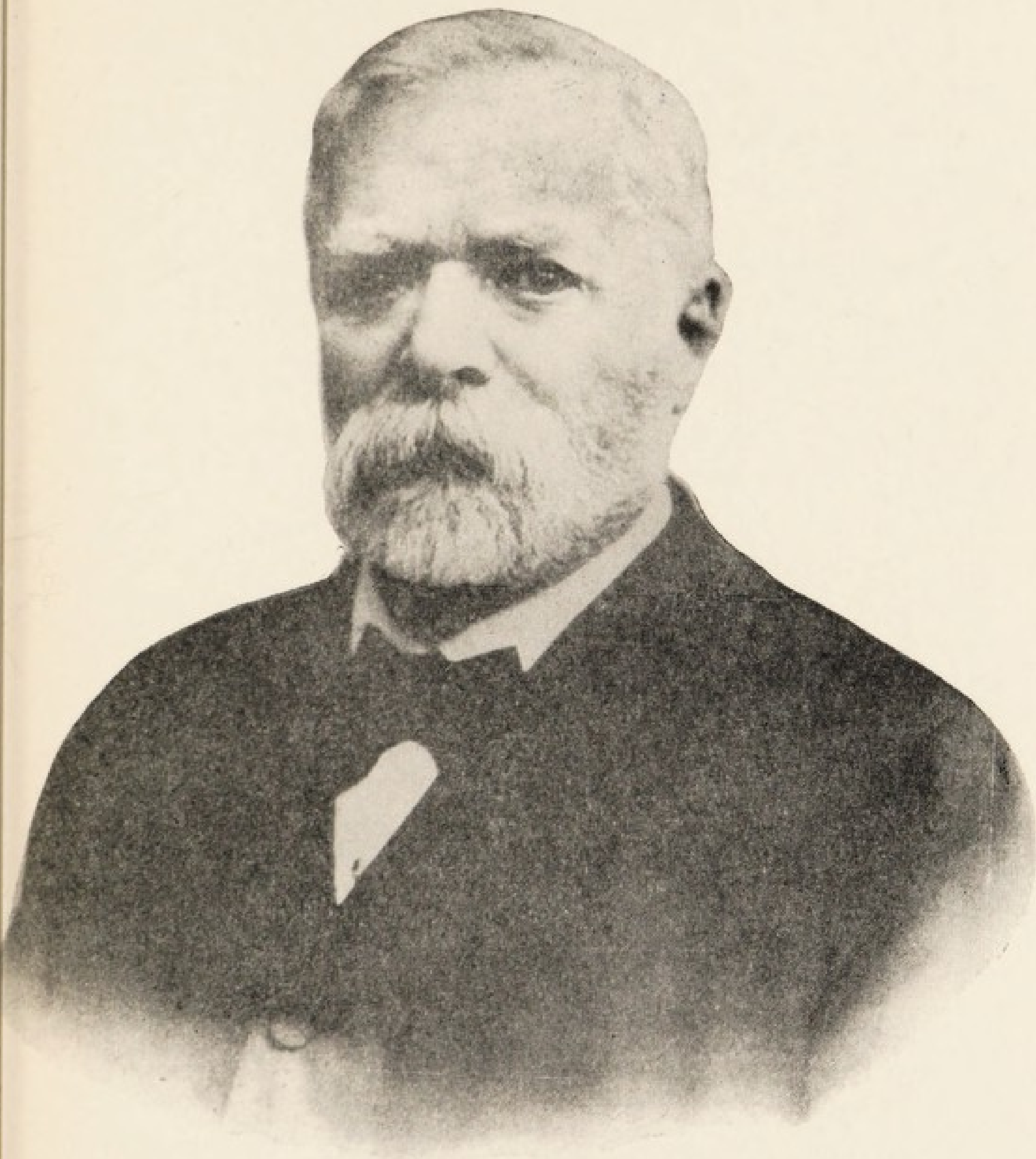

Fig. 12. Carl von Voit (1831–1908).

similar to that of Bidder and Schmidt. The true value is about 0.72 to 0.73.

We have more refined data, but the fundamental ideas were present in this work of Bidder and Schmidt, the physician and the chemist working hand in hand.

They gave to another cat all the meat it would eat and calculated that its "typical" metabolism doubled. Their views upon this typical metabolism have already been set forth.

Responding to Liebig's suggestion that bile was reabsorbed and was for the most part a "respiratory stuff," that is to say, could be oxidized to carbon dioxide and water, they made many experiments upon this subject and concluded that Liebig was right. They furthermore discovered that, when bile was removed from the body by a fistula, bread or meat could be perfectly digested and absorbed by a dog. But when 113.6 gm. of fat were given, 72.2 gm. of fatty substances were recovered in the feces, which smelled foul on account of the putrefaction of unabsorbed fat. Modern textbooks do not refer to these notable observations.

We have now reached the day of Carl Voit (1831–1908). He passed his *physicum* examination in medicine in 1851 and went to Würzburg, in those days far more celebrated as a medical center than Munich. A year later he returned to Munich, the same year in which Liebig, at the urgent solicitation of Pettenkofer, left Giessen for Munich. Liebig shared with Wagner the idolatry of the town. Voit graduated in medicine in 1854 after the usual requirement of six years of study. He then attended lectures in physics, zoölogy, anatomy, and chemistry, a reversal of modern educational methods. Chemistry was taught him by Liebig and the practical course was given by Pettenkofer, who was then Liebig's assistant. Voit's laboratory desk was next to that of Brush, who subsequently became celebrated as director of the Sheffield Scientific School. Voit worked with Pettenkofer on the quantity of urea in muscle tissue in cholera during an epidemic in 1854. He spent a year with Wöhler, on Liebig's advice, and he planned to go to Bidder and Schmidt, whose work fascinated him, but this plan was abandoned when in 1856 Bischoff offered him a position as assistant and *Privatdozent* in the new laboratory building in Munich, which had been finished in 1855. This remained Voit's scientific home until his death in 1908, an occupancy of fifty-three years. He became full professor of physiology and director of the institute in 1863 when he was thirty-two years old.[73]

Voit's first important piece of work was published in 1857 and dealt with the demonstration of what is known as "nitrogen equilibrium."[78] Barral had made experiments on himself which indicated that half of the nitrogen content of ingested protein was eliminated as nitrogen gas in the lungs. The experiments of Regnault and Reiset showed that between 0.5 and 2 per cent of the ingested protein nitrogen could have been thus eliminated. Bidder and Schmidt had nourished a cat with meat alone and had found 99.1 per cent of the ingested nitrogen in the urine, 0.2 per cent in the feces, which left a residuum of only 0.7 per cent for the respiratory process. The feces contained no undigested meat fibers.

Voit administered to a large dog 29 kg. of meat for fifty-eight days. The nitrogen content of the meat was 986 gm.; in the urine were 943.7 gm.; in the feces 39.1., a total elimination of 982.8 gm. The difference between the nitrogen of the ingesta and of the egesta was 3.2 gm., or 0.3 per cent. This and similar experiments established the doctrine of nitrogen equilibrium on a strong basis of fact. He used the method for the titration of urine for nitrogen which Liebig had taught him, he tested the reliability of the method, and Liebig himself verified his findings.

Three years later Bischoff and Voit published their "Laws of Nutrition in Carnivora,"[70] which was largely based upon the previous work. When a large dog was given 250, 500, 800, and 1000 gm. of meat, more nitrogen was eliminated from the body than was ingested. Only when 1800 gm. of meat were administered could nitrogen equilibrium be established. When 2000 and 2500 gm. were given the animal retained nitrogen, thereby adding flesh to his body.

Gelatin spared body protein but did not prevent its loss. Sugar reduced the quantity of protein metabolism in the body, reduced the quantity of protein necessary to maintain nitrogen equilibrium, and possessed this power to a greater degree than fat. The authors were in complete agreement with Liebig that oxygen caused the combustion of fat and carbohydrate and that muscle work accounted for the destruction of protein.

But in the same year that this was published Voit found, to his utter astonishment, that muscular work did not increase the protein metabolism in the fasting dog nor in one which had received meat. He wrote "It is of itself so important that I question whether it is desirable to add a word of explanation." And Liebig in 1870 generously wrote:

> The question regarding the source of muscular power has been confused through a conclusion which has been shown to be false and for which I am to blame. . . . When one thinks about the matter it is apparent that the facts could not be otherwise. For if the metabolism of the muscle increased with mechanical work, a man could exhaust his entire supply of muscle tissue, because work is directed by the will.

The other conception of Liebig that oxygen was the cause of the destruction of carbohydrate was also upset by Voit, although credit for this discovery is usually attributed to Pflüger. In 1865 Voit wrote that the life of the body was the sum of the activity of all the thousands of minute workshops of which it was composed; that a combination of oxygen was not the first step, but that there was a preliminary cleavage of materials into simpler materials, which under certain circumstances might remain unoxidized. He pointed out that hydrogen, the most inflammable of all gases, was not oxidized by the body, hence the conditions of cellular oxidation were entirely characteristic of the cells themselves.

Voit discovered that the slow deep breathing which followed section of the vagi had no influence upon the quantity of carbon dioxide expired and therefore concluded that the metabolism was independent of the oxygen supply. In 1870 he thus expressed his ideas:[76]

The oxygen used in the tissues is renewed from oxygen carried by the hemoglobin of the blood, and this is ultimately restored to the hemoglobin in the lungs. This latter renewal is therefore determined by the quantity of oxygen used by the tissues; the rate of respiration is the result of oxidation but not its cause. If more is metabolized in the tissues and more oxygen is used, then more oxygen is taken from the blood, more carbon dioxide is given to it, and these factors stimulate the respiratory center in the medulla to deeper and more rapid respiration in order that the oxygen in the blood may be restored and the excess of carbon dioxide removed.

Pflüger later in 1877 showed that a rabbit, breathing quietly or during apnea induced by vigorous artificial respiration, absorbed the same quantity of oxygen in both cases. It became evident that oxygen did not cause metabolism. The cause of metabolism lay in the secret recesses of the individual cells. The cleavage products of fat, carbohydrate, and protein, formed as the result of the activities of living cells, united with oxygen in direct proportion to the quantity of such cleavage products formed.

The earlier work of Voit and a study of that of his predecessors, which he knew thoroughly, especially the work of Bidder and Schmidt, inspired him with the desire to devise an apparatus for the investigation of the metabolism of man, a wish which Regnault and Reiset had expressed but could not effect for lack of funds. In Voit's case, 8000 guilders ($3400.00) were obtained from the private purse of the reigning King Maximillian II. And the successful construction of the apparatus itself was accomplished by his friend Pettenkofer.[75] Between 1866 and 1873 seven long papers were published under the names of Pettenkofer and Voit upon the subject of the metabolism of men and of dogs under various dietary conditions. These papers are classical, are constantly referred to, and represent the beginnings of the modern science of nutrition. The apparatus consisted of a small room, large enough to hold a bed or a bicycle ergometer. The room was well ventilated with a known volume of outside air. Samples of the air entering the room were continually analyzed for carbonic acid and water, and samples of the air leaving it were analyzed in like manner. The gain in carbonic acid and water by the whole volume of outgoing air gave the amount of these materials eliminated by a man. The accuracy of these measurements was validated by burning candles of known composition within the chamber and by evaporating a known weight of water. For the first time a respiration apparatus had been made in which a subject could live in pure fresh air and whose accuracy could be tested. The quantity of oxygen absorbed was determined by difference, as in the Liebig method of the analysis of an organic compound. A fasting man was thus analyzed:

	Kg.		*Kg.*
Weight at start.......	71.09	Weight at end......	70.16
Water drunk..........	1.06	Carbon dioxide......	0.74
		Water in respiration.	0.83
	72.15	Urine eliminated....	1.20
Oxygen by difference..	0.78		
	72.93		72.93

A total weight of 72.15 kg. was converted in twenty-four hours into a weight 72.93 kg. through the absorption of 0.78 kg. of oxygen. This method was widely used in all experiments of the period and was not completely superseded until Atwater, who had received funds from the Carnegie Institution for the purpose, with the cooperation of F. G. Benedict, designed an accurate method for the determination of the oxygen absorption by a man placed in an apparatus of the chamber type.

Voit has described the delight with which he and Pettenkofer saw the secrets of metabolism unrolled before their eyes. He writes in his famous book on "Stoffwechsel und Ernährung,"[77] published in 1881, as follows:

> The mass and capacity of the cells of the body determine the height of the total metabolism. Protein metabolism dictates the direction which is taken. Protein is the substance which is most readily metabolized, breaking down into materials, one of which is probably fat. If, through protein ingestion alone, the metabolic activity of the cells is exhausted, then this fat is deposited in the body. If, as is usually the case, the capacity for metabolism has not been reached, then sugar is oxidized as the next most readily destroyed material. If no sugar is present, then fat is attacked until the cells are no longer able to metabolize more material. . . . Muscle work raises the power of the organism to oxidize more material, and this is done at the expense of the destruction of more fat or carbohydrate. The requirement of protein is dependent on the organized mass of the tissues; the requirement for fat and carbohydrate is dependent on the amount of mechanical work accomplished.

This outline represented the essence of his opinion at the time of his death. I[73] have elsewhere set forth the conscientious fidelity to truth and duty which operated in the life of this truly great man, to which I as his pupil have the privilege of bearing witness.

One may hear the voice of the influence of the old Voit laboratory in the words written to me in 1923 by Friedrich von Müller, the distinguished professor of medicine at Munich:

> It does not appear to me to be important to start from *theories* or to invent *dogmas*, but to seek facts and true observations according to the fundamental basis of our own honored teacher, Carl Voit, who always said to his students early in his lecture course, "You need not believe anything of what I relate to you in my lectures, you need only believe what I can demonstrate and prove to you." It is astonishing how simple modern theories become when one puts aside everything that is hypothetical and allows only the experimental facts and discoveries to speak for themselves.

CHAPTER VIII

THE MODERN PHASE

The most eminent of Voit's pupils was Max Rubner (1854–1932), for many years professor of physiology at Berlin. When Voit was a young man he spent six months in England and brought home to Munich a Frankland calorimeter for determining the caloric value of food materials. In 1866 he prepared a lecture chart indicating that the fasting man whom he had investigated produced 2250 calories in twenty-four hours, whereas when the man received food 2400 calories were evolved. During the years 1869, 1870, 1871, 1874, and 1884 Voit and his associates endeavored to construct a calorimeter for the measurement of the heat given off by a man but were unable to solve the problem. It was into this atmosphere that Rubner came.

In 1878[79] Rubner determined the daily metabolism of a rabbit which fasted until it died. He then analyzed the whole animal and, with the data available, was able to calculate how much protein and how much fat were present in the animal on each day from the beginning to the end of the fasting period. At the end the animal was almost free from fat and the whole of the life process was carried on at the expense of a greatly increased protein metabolism. Rubner has recently written that at that time he believed that, when the supply of fat failed, the equivalent of its energy was derived from the metabolism of protein for the maintenance of the life process.

In 1883–84 Rubner found that carbohydrate and fat were interchangeable in nutrition on the basis of their energy equivalents. One hundred calories in fat were the nutritive equivalent of the same number in carbohydrate. This is the isodynamic law of Rubner and is valid except when food is given in large quantity and the specific dynamic action appears. His investigations showed:

100 gm. fat =	211 gm. protein
	232 gm. starch
	234 gm. cane sugar
	256 gm. glucose

Rubner turned his attention to the caloric value of the constituents of urine and of feces, so as to obtain values which could be deducted from the heat value of protein when it was oxidized to carbonic acid, water, and nitric acid in the calorimeter. Urine which contained creatinine and uric acid had a higher caloric value than it would have had if its nitrogen content had all been in the form of urea. After this fashion he obtained a biological value of 4.000 calories for the heat of 1 gm. of meat protein when it was oxidized in the body, in contrast with 5.345 calories when burned in the bomb of a calorimeter. He also determined with great accuracy the heat values of various carbohydrates and of fat. In the respiration experiments on Voit's fasting man it had been calculated that 70.8 gm. of protein and 222.1 gm. of fat had been oxidized. The heat production involved could be calculated as follows:

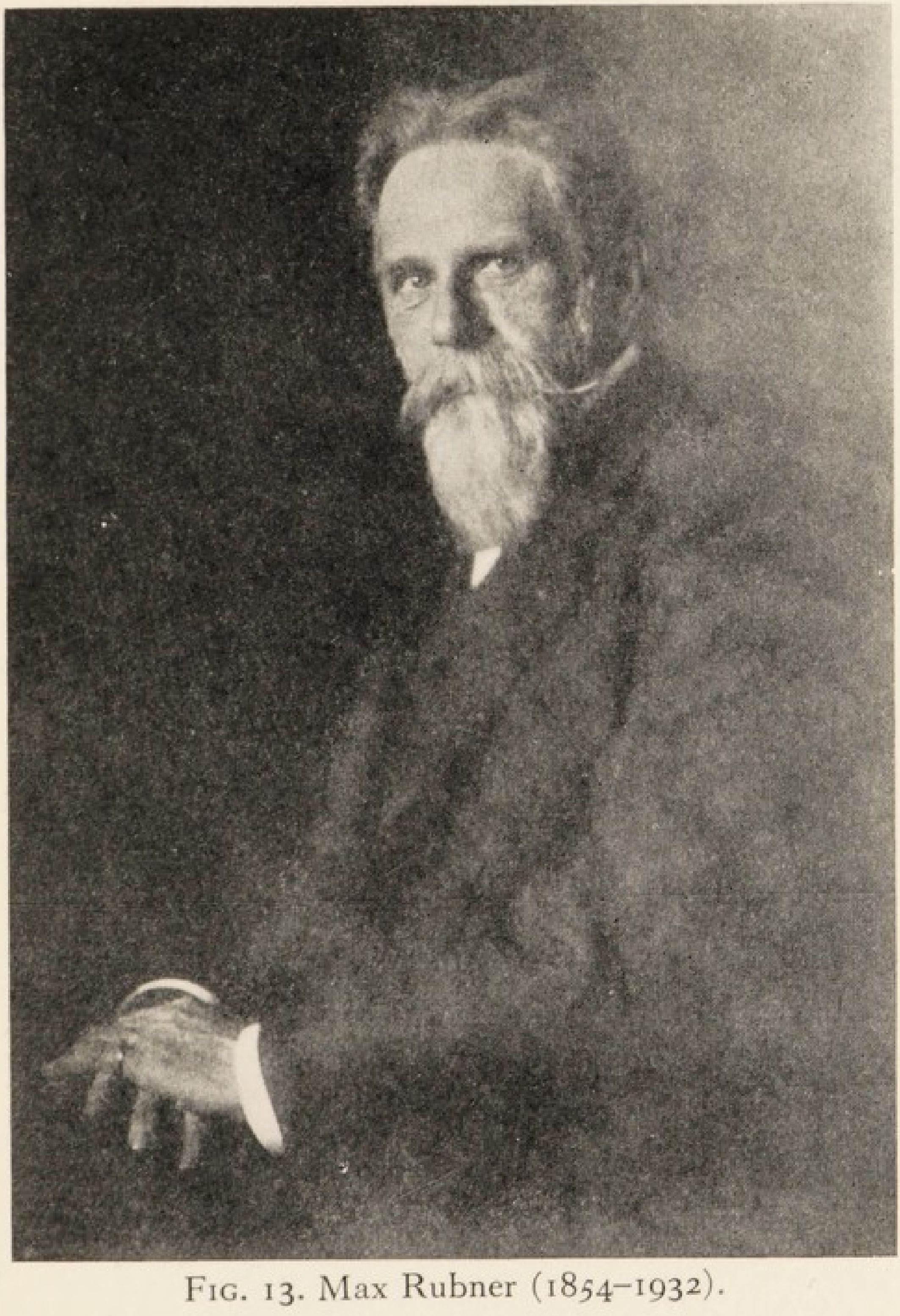

FIG. 13. Max Rubner (1854–1932).

	Calories
Heat from protein (70.8 gm. × 4.0)...	283
Heat from fat (222.1 gm. × 9.423)...	2093
	2376

The value of 9.423 calories was available as representing the heat of combustion of a gram of hog fat.

Rubner applied such methods to the calculation of the heat production of various animals, the

TABLE II

BASIS OF RUBNER'S LAW OF SURFACE AREA

Dogs		*Mammals*		
Weight, kg.	*Calories per square meter*		*Weight, kg.*	*Calories per square meter*
31.2	1036	Hog...........	128	1074
24.0	1112	Man...........	64	1042
19.8	1207	Dog...........	15	1039
18.2	1097	Guinea-pig.....	0.5	1246
9.6	1183	Mouse.........	0.018	1185
6.5	1153			
3.2	1212			
1:10 Variation	1142 Average		1:7111 Variation	1145 Average

respiratory data concerning which were at that time available. He used the small respiration apparatus of Voit, designed on the principle of Pettenkofer's larger machine. He also had the newly discovered helpful formula of Meeh for determining the surface area, and he announced that the heat production of mammals was proportional to their surface areas. The experiments covered periods of twenty-four hours, were not absolute rest experiments, and they were made in cool rooms at about 15°C. No food was given. For comparative values they suffice to tell the tale.

These experiments emphasized the importance of considering metabolism from the standpoint of energy, and this point of view became fixed in Rubner's mind. The energy doctrine, he states, depends upon the fact that loss of energy is unpreventable during active life throughout the entire animal kingdom and even in yeast and bacteria; this energy loss is compensated for by the utilization of disintegrating molecules, the oxidative cleavage of which liberates energy. This doctrine permitted the introduction of the study of comparative nutrition as already outlined. His work on this subject establishes his undying fame.

One may here relate the part of the story developed by some of Rubner's contemporaries. Nathan Zuntz (1847–1920) was the first to introduce a portable apparatus which could determine the respiratory exchange in men under a great variety of circumstances. The determinations were made in short periods and were generally regarded with disfavor by Voit and his school. Notable contributions, however, were made by a pupil of Zuntz, Magnus-Levy, who carried the apparatus to the hospital bedside in 1893 and made the pioneer investigations upon metabolism in a great number of diseases. For example, he made 150 respiration experiments on one myxedematous patient in three years. He also made observations upon hyperthyroidism, obesity, acromegaly, carcinoma, diabetes, gout, pernicious anemia, and, in normal persons, upon the influence of thyroid extracts and in pregnancy. His methods were accurate and his conclusions were usually correct. He began his work with Zuntz in 1892. In 1906 he gave the following definition, "The *Grundumsatz* [basal metabolism] is the *Kraftwechsel* [energy exchange] by which the normal functions of the organs may be maintained when under conditions of greatest possible relaxation." The *Grundumsatz* could be obtained by measuring the respiratory gas exchange twelve hours after the last meal when the subject was in a comfortable resting position, in complete muscular relaxation and avoiding all muscular movement. To this should be added a warm environment. So determined, the maximal variations in the *Grundumsatz* of one individual amounted to between +11 and −8 per cent from the average of many observations. One finds few erratic respiratory quotients in this early work of Magnus-Levy, such as have since tended to becloud the significance of so much which has been published.

When the Russell Sage Institute of Pathology began its activities in 1912 Du Bois and I, after long consideration, decided to translate the German word *Grundumsatz* as "basal metabolism." F. G. Benedict's term, "post absorptive metabolism," is also accurately descriptive. The early work of Du Bois centered around the establishment of a standard of metabolism. He, like Rubner, found that the basal metabolism in normal human beings was proportional to the surface area as measured by Meeh's formula. He and his cousin D. Du Bois discovered a better formula for the measurement of the surface area in man, and this method has been applied by Cowgill and Drabkin to dogs.

Rubner has recently published the following analysis of material taken from Benedict's determinations of the basal metabolism of men.

TABLE III
BASAL METABOLISM OF MEN

No. of individuals	*Class in weights, kg.*	*Average weights, kg.*	*Calories per sq. m. surface in 24 hrs. (Du Bois)*
6	40–50	48.7	922
41	50–60	53.4	914
164	60–70	64.5	927
24	70–80	74.7	924
8	80–90	83.7	924
	Variation....... 1:1.7		Aver. 922

Rubner found it difficult to understand how Benedict, on the basis of such results, could have reached a negation of the law of surface area.

Benedict's work shows an average of 850 calories per square meter of surface in the case of 103 women, or 8 per cent less than the average for men. Du Bois had noted a fall of 7 per cent in women. Cowgill and Drabkin have observed that the heat production of female dogs is 836 calories per square meter of surface (average variation ±5 per cent), which is only 1.6 per cent less than that found in women.

With advancing age there is a tendency of the basal metabolism to fall. Thus F. G. Benedict, at the age of fifty-seven, had a basal metabolism of 772, and Graham Lusk, at the age of fifty-eight, one of 775 calories per square meter of body surface.

It would seem that the law of surface area as a standard of measurement had been placed in an unassailable position. As a biological principle it is of high importance, for by its use Du Bois was able to establish certain normal constants for persons with due regard to their size, sex, and age, drastic variations from which betokened disease.

Rubner analyzed the regulative control which produces the constancy of body temperature. Two factors are active, the physical and the chemical. The physical regulation is accomplished by changes in the distribution of blood to the skin or by the evaporation of water from the skin. The chemical regulation of body temperature is effected by an increased metabolism in the presence of cold. Cannon differentiates this latter mechanism into two factors, the fine adjustment caused by the discharge of epinephrine from the adrenals, and the coarse adjustment produced by shivering.

It was in 1842 that James P. Joule laid the foundations which established the mechanical equivalent of heat. In 1845 J. R. Meyer announced the law of the conservation of energy, and in

1847 Helmholtz independently discovered the same principle and proclaimed its widespread biological significance. This principle was experimentally proved for the mammal by Rubner in 1891. With very little money, in a small laboratory, in the University of Marburg, working with his own hands, Rubner made the first calorimeter which accurately measured the heat production of a dog. Attached to this was a Voit respiration apparatus which could determine the gaseous metabolism. He calculated the heat which should have been produced from the metabolism of the dog (indirect calorimetry) and determined the heat actually given off by the animal (direct calorimetry). The experiment lasted forty-five days and the two methods gave the following results:

Calculated from the materials oxidized in the body	17,406
Actually measured by the animal calorimeter	17,349
Difference	0.2 per cent

An age-long problem was solved.

The delicate hands of an artist were manifest in the production of this machine, for Rubner, to his delight, could paint a picture and seek relaxation and happiness in the company of artists.

Atwater, who had been a pupil of Voit, Rubner and Zuntz, began work in 1892 upon a calorimeter for the measurement of the heat production of man. He had access to large United States Government appropriations and the assistance of an eminent physicist, E. B. Rosa. After years of labor a splendid apparatus was evolved which was technically perfect. The average results of experiments on three individuals during forty days were as follows:

	Calories in 24 hrs.
Indirect calorimetry..........	2717
Direct calorimetry...........	2723
Difference.................	0.2 per cent

The apparatus for the measurement of the gaseous metabolism in this calorimeter was of the Pettenkofer-Voit type. Soon, however, Atwater and Benedict, as before mentioned, applied the Regnault and Reiset closed circuit system to this apparatus and were able to determine the respiratory quotients of a man within it. This respiration calorimeter was copied by H. B. Williams, who added improvements for the physiological laboratory of the Cornell University Medical College in New York City. With this apparatus the metabolism could be determined for the first time in dogs and in babies during hourly periods. Murlin and Lusk, in twenty-two different experiments with dogs, obtained the following results:

	Calories in 24 hrs.
Indirect calorimetry..........	2244
Direct calorimetry...........	2230
Difference.................	0.6 per cent

Then followed the construction of the Sage calorimeter at Bellevue Hospital in New York City, and with this metabolism in disease could be studied. A human subject lay quietly resting on a bed for a period of four hours, quite as comfortably as though he were in a sleeping car.

In one series of investigations by Du Bois and Coleman, in which ten patients with typhoid fever were under investigation, metabolism records during several successive hourly periods were obtained on sixty-five days, some during high fever. The results were as follows:

	Total Calories Measured in Experiments
Indirect calorimetry	12,822
Direct calorimetry	12,540
Difference	2.4 per cent

Even under these difficult conditions direct and indirect calorimetry agreed. If the first hour is excluded from all the determinations involving fever, the agreement is within 0.2 per cent.

It is therefore proved that the heat production in health and in disease is a measure of the total energy derived from the oxidation of chemical fragments of certain substances which are called foods. Behind every physical phenomenon there are causes. It is for the scientist to uncover these relations. The quantitative accuracy of these determinations is notable.

The constancy of the basal metabolism is a feature of the background. Lusk has reported fourteen determinations during a period of fifteen months of the basal metabolism of a well-trained quiet dog, nourished with the same maintenance diet, and found that the maximum variation in the basal metabolism did not exceed ± 2.9 per cent. Since an alcohol flame burning in the calorimeter in frequent tests of its accuracy showed maximum variations of ± 1.9 per cent, it is evident that the flame of fire burning within the dog had nearly the same constancy as it was within the limits of the apparatus to measure. The average percentage variation of the basal metabolism of Du Bois was ± 2.8 per cent during fourteen years. Here also the flame of life pursued its constant course.

Richardson and Mason calculated how much protein, fat, and carbohydrate were being oxidized to furnish the fuel for this flame of life, and then administered to the same subject every two hours just enough to support life during that period. This "replacement diet" was simply oxidized instead of the materials present in the body and there was little or no change in the metabolism of the time.

In 1902 Rubner published his celebrated work on the influence of foodstuffs on metabolism. He found that when 100 calories in meat were ingested by a dog the metabolism increased by 30 calories, and 100 calories in cane sugar raised metabolism 5.8 calories. (His value of 12.7 for the increase after administering 100 calories in fat was too high and should have been about 4 calories.) These values are obtained after administration of fat and carbohydrate in excess, but any increase in protein metabolism leads to a proportionate increase in the heat production. Rubner defined this action as the "specific dynamic action" of the various foodstuffs. These values can be determined only if all the experiments are made when the body is free from the stimulating effect of cold, which itself induces an increase in the heat production. If one enters a restaurant on a cold winter day with a keen sense of chill and one there partakes of a meal of meat, bread, butter, and potatoes, the fires in the body are increased and, on returning to the biting cold of the outside air, one feels it no longer. The heat of the specific dynamic action of the foodstuffs replaces the disagreeable subjective sensation of exposing the mechanism of chemical regulation to cold. This relation was also discovered by Rubner. Among the poor the suffering from cold is intensified by suffering from lack of food. Indeed, of the two, cold may be the more potent cause of distress.

It is quite impossible to follow the history of nutrition in all its myriad by-paths. Only the fundamental background has been presented here. We have the fascinating study of the intermediary metabolism, the influence of the endocrine glands, the influence of vitamins, and a long line of pathological disturbances. All these factors react upon the fundamental background. The nutrition of the family is likewise of supreme importance. During the Great War the nutrition of the army, and finally the nutrition of the nations as entities received attention and was subject to precise scientific calculation based upon energy requirements. In the civilian population of England, France, Italy, and the United States it was calculated that an average man doing an average day's work required 3000 calories daily, which is the old Voit standard for a laborer.

The aggregate money cost of this food reaches colossal proportions. In the United States it must be $15,000,000,000 per annum, and this food is usually taken in sublime ignorance of what it all means. Even in medical schools little thought is given to the subject. The schools of home economics, however, form a group of people who really understand the subject.

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