With the Author's Compliments.

A CENTURY OF MEDICINE AND CHEMISTRY.

A LECTURE

INTRODUCTORY TO THE

COURSE OF LECTURES

TO THE

MEDICAL CLASS IN YALE COLLEGE.

DELIVERED SEPTEMBER 14, 1871,

BY

PROF. B. SILLIMAN, M.D.

NEW HAVEN, CONN.:
PRINTED BY CHARLES C. CHATFIELD & CO.
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The author has to ask a kind indulgence of his readers for the typographical errors in this Lecture, which was printed during his absence and without adequate supervision.

NEW HAVEN, CONN., January, 1872.

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LECTURE.

A century has now nearly passed since on August 1st, 1774, Dr. Priestley first recognized the distinctive properties of oxygen gas which he called "dephlogisticated air." Lavoisier in the same year and shortly after the discovery of oxygen by Priestley, published a memoir in which he showed that in common combustion and in the calcining of metals it was not the whole of the air but only one part of it which was active in producing these changes. He at first called the active portion of the air "vital air," or "air eminently adapted for supporting combustion and respiration." Up to this time chemists had distinguished what we now call metallic oxides as the "*calx*" of metals. Lavoisier in preparing oxygen from what was then called "mercurial calx" (mercuric oxide, or "red precipitate *per se*",) as Priestley had done before him, took a most important step in advance of his English predecessor, and beyond his time, and proved that the "mercurial calx" was a compound of "vital air," or the new gas, with mercury, and hence he concluded, by analogy, that all metallic calxes must have a like constitution. Starting thus upon the legitimate, but until then untried path of inductive reasoning in chemistry, he advanced from the fact already made known some years before by the researches of Dr. Black of Edinburgh on "fixed air:" namely that metallic calxes when heated with charcoal were converted into the metallic state with escape of "fixed air," or carbonic acid ;—the great French philosopher reached the important deduction that "fixed air" must itself be composed of charcoal (carbon) and "vital air" (oxygen). This latter conclusion he soon after established by a brilliant synthesis, by burning a diamond in "vital air" and proving that the sole product was "fixed air," which from that time was known as carbonic acid. The Florentine academicians in the days of Cosmo de Medici had indeed burned the diamond by means of a powerful burning glass, but these philosophers were so completely occupied by the phenomenon of the burning, physically considered, that they did not see in this remarkable experiment its chemical teachings, nor was the world then sufficiently advanced to comprehend the problem in its chemical relations. Thus, well advanced, in his course of chemical research, Lavoisier continued his investigations upon the constitution of acids by examining in 1777 the acid produced by the combustion of phosphorus. In this research he first demonstrated that the active agent of combustion constituted one fifth part of the air, thus adding the accuracy of quantitative determinations to phenomenal or qualitative observations. And finally in 1778, in a memoir in furtherance of the same line of research, he for the first time, in the literature of chemistry, distinguishes the "air eminently adapted for supporting combustion and respiration" by its present name of OXYGEN.

Prior to the discovery of oxygen, and with it the methods of reasoning and investigation peculiar to chemistry, there was no science of chemistry properly so called. The alchemists and the Iatro Chemists had indeed accumulated a great number of important data and had observed many interesting and valuable facts; but men's minds were then preöccupied by an hypothesis, which to a certain extent methodized facts, but completely misled the judgment and blinded the eyes of observers, when considering those chemical changes which accompany the phenomena of combustion. This was the so called *Phlogistic Theory* of Stahl. George Ernest Stahl was a German physician and chemist, (born in 1660, died 1734) of original power and whose medical theories were quite as prominent as his chemical. His phlogistic theory in chemistry was the first attempt at a systematic and philosophical arrangement of facts in the science, and held its ground for more than fifty years. Like all theoretical systems, which have had more than an ephemeral existence, there was in it a substantial element of truth, obscurely perceived it is true, but firmly held. Stahl's phlogiston was only another name for heat (φλογιστὸς, burnt) and so long as the material nature of heat was an article of scientific faith the phlogistic theory served to classify phenomena into generic groups and to furnish a plausible explanation for chemical changes. The fact that the loss of phlogiston, which by this theory was what happened whenever a body was burned (combustible bodies being such by reason of their holding phlogiston in combination;) that this loss was invariably accompanied by an increase of weight in the *calx* or body burned, appears to have offered no serious difficulties to those who had accepted the phlogistic theory. If pushed for an explanation of this undeniable fact, they found a ready refuge in the absurdity of assigning to this mysterious and unseen principle of phlogiston the quality of *specific levity!* Strange that men of such sagacity as Drs. Black and

Priestley should have been able to content themselves with a resort so completely unphilosophical! It was by the use of this weapon that Lavoisier attacked and destroyed the phlogistic theory, introducing for the first time in chemistry methods of experiment which admitted of rigorous exactness and demonstrating that in every case when, in the act of combustion, there was a gain of weight in the body burned, the increase was exactly equal to the loss sustained in a given volume of air concerned in the reäction. In fact the so called phlogiston was proved to be, not the principle of heat, but an element ever present in the air as one of its component parts and upon the presence of which all cases of common combustion depended. This element was *oxygen*, a name invented by Lavoisier to express what all chemists then believed to be true respecting the acidifying power of this wonderful agent.

It is well nigh impossible for us now from our present advanced position to recall the condition of chemical and medical science as it existed before the discovery of oxygen had rendered it possible to understand the most simple and frequently occurring phenomena of our daily experience, and before the nomenclature of the French Academy, propounded chiefly by Lavoisier, had supplied to us the forms of speech in which to clothe our notions of what takes place in even the simplest chemical changes. But we must not permit ourselves to look with disrespect upon the theoretical views which for nearly half a century held almost universal sway in the minds of chemists. The phlogistic theory of Stahl was the first great generalization of facts in chemistry. Led captive by the splendor of the phenomena which attend combustion, these chemical Fire-Worshipers lost sight of the fact that the change of weight in the body burned was quite as important, and demanded as satisfactory an explanation, as the light and heat sent out in the act of burning. The one set of phenomena are in fact just as important as the other and both must be explained before the philosophical mind can feel satisfied. The swing with which the chemical world moved away from the phlogistic theory to follow the new views set forth in the so called anti-phlogistic theory of Lavoiser was natural enough, but like all extreme movements became in its turn one-sided.

Viewed in the light of modern science the phlogistic theory is seen to involve, as before hinted, an important element of truth. Combustible bodies in burning do lose *something;* not an ideal phlogiston truly, but a *potential energy* which has a definite mechanical value and is capable in each case of an exact numerical statement in terms of work done or to be done. In a unit of carbon we recognize the equivalent of 8080 French units of heat evolved when the carbon burns in air to form carbonic acid; and we know that when the carbon has lost this something in the act of burning, which the older chemists called phlogiston, it can regain it only by the reverse process of *unburning*, which for its perfect accomplishment must borrow the same amount of power from some other source. Every body which is capable of burning may be likened to a force in a condition of unstable equilibrium, like a weight held at a height by a cord against the force of gravity, and which will reproduce by its fall the same amount of power which had been expended in raising it to its present position. What is the source of the power which we find in a mass of anthracite, or of wood when these substances burn? The answer is they exist in their present potential condition only by reason of the exercise at some former time of an amount of force equivalent, necessarily, to that which they in turn can now exercise in the act of burning. The sun has wrought out this problem with his silent power, unburning factors, which have, under his chemical agency, given up their carbon and hydrogen to form vegetable fibre and endow it with these reserves of force, which however great they may seem to us, are all precise equivalents of the energy employed in their production.

I sometimes think with how much satisfaction George Ernest Stahl would contemplate this view of his phlogistic theory, which assigns to it a definite philosophical basis, far more profound indeed than he could ever have dreamed of, and one which would have enabled him to meet his antagonists, had he been permitted to revisit the earth half a century after his death, and to have dealt them blows, which to say the least, would have been as well delivered as those which he had to receive. The triumph of a theory is its power to embrace and co-ordinate the greatest number and variety of facts. Now the theory of phlogiston was equally applicable to two opposite orders of phenomena and united them by a theoretical bond, but it failed while considering the phenomena of combustion and the calcination of metals to regard the part which the air bore in these changes, and precisely here was where it was successfully attacked by Lavosier, and brought to grief.

But let us consider more particularly a few points which are of more specific interest to us in view of what medicine has gained from the introduction of the

Lavoisierian methods in Chemistry. It is too obvious to require comment that until we knew the composition of the atmosphere, the functions of respiration and the aeration of the blood were without a rational explanation. The remarkable researches of Black on fixed air, or carbonic acid, and on the alkalis, preceded, it is true, the discovery of oxygen by several years, and offer a fine example of logical method and analytic power in dealing with facts observed for an end. This was the first research which demonstrated the cardinal importance of quantitative determinations in the interpretation of chemical phenomena. Black in fact led the way in these investigations, as also in those ideas of chemical combination and decomposition as connected with the addition or subtraction of a ponderable substance, which Lavoisier afterwards extended to the whole range of chemical phenomena.

The year 1774 was also made remarkable by Scheele's discovery of chlorine in the course of a research, having for its object the determination of the properties of oxide of manganese. He regarded this wonderful element it is true as muriatic acid deprived of phlogiston. Hence his name for it, *dephlogisticated muriatic acid.* By phlogiston Scheele meant in this case, hydrogen gas. In other words, as we now know his theoretical view of the new substance was correct and precisely what Davy in 1810 proved to be true when he gave the new element the name chlorine. The discovery of iodine by Courtois in 1811 and of bromine by Ballard in 1826 filled out, with the addition of fluorine, the remarkable group of which chlorine is the type, and supplied to the materia medica and the resources of the healing art, agents of wonderful efficacy and varied applications, the powers of which are yet far from being exhausted.

After the discovery of the different gases and the investigation of their properties by Dr. Priestley it occured, seemingly almost at the same time, to several different persons that the use of various gases, or mixtures of them, in the atmospheric air, might offer new and powerful means of curing or of ameliorating disease Dr. Beddoes, at that time Professor of Chemistry at Oxford, was a zealous advocate of these notions, and secured the powerful support of Mr. Wedgwood, the celebrated potter, and of Mr. Watt, of Birmingham, who furnished the chief part of the means needful to put these ideas to the test of practice at Bristol; where about the beginning of this century Beddoes was settled as a physician. But this gentleman did not possess the requisite scientific, and particularly chemical skill, to carry out the objects of the Institution, and in casting about for some competent young man of the requisite zeal and ability, a Mr. Davy was fortunately thought of and secured. This was the ever famous Sir Humphrey Davy, then a comparatively unknown young man who had formerly been apprenticed to an apothecary. He devoted himself for about a year to investigating the effects of various gases when employed in respiration. His characteristic habits of original research would not permit him to confine himself to the mere routine of a perfunctory duty, but with accustomed zeal he undertook, at great personal risk, the inhalation of every sort of gas, nearly paying the foreit of his life for his rashness in attempting to breath gases of known poisonous qualities. It was in this series of experiments that Davy discovered the now familiar properties of nitrous oxide, or laughinggas. His results were published in 1800, in a volume entitled "Researches Chemical and Philosophical; chiefly concerning nitrous oxide, or dephlogisticated nitrous air and its respiration."

His discovery of the peculiar physiological effects of nitrous oxide when inhaled was verified by trial upon a great number of persons contributing, (beyond any real importance it had) more than all his former researches, to his celebrity, and was the starting point of his great subsequent success. Medically considered, the chief interest of this research is the remarkable fact that neither Davey nor any of his medical associates or their successors discovered the anæsthetic power of nitrous oxide. It was exhibited in probably thousands of cases, and among these beyond all reasonable doubt hundreds of patients, Davy among them, must have been brought to a condition of anæsthesia, and the wonder is that no one of them was the accidental subject of a discovery which had yet to wait nearly half a century for a herald. We cannot read the evidence which Davy details of the affects of nitrous oxide gas, not only on himself but upon others, without seeing clearly in the light of our present knowledge that the effects of anæsthesia from this agent were completely produced. Among those whose experience is given in their own language are many of the most distinguished men of the time: Southey and Coleridge the poets, Dr. Kinglake, Dr. Roget, Dr. Blake, Mr. Lovell, Mr. Edgworth, Mr. Wedgewood, and others equally well known. To quote an example, Dr. Kinglake says, speaking of his own case: "The effects produced by a second trial of its powers, were more extensive, and concentrated on the brain. In this instance, nearly six quarts undiluted were inhaled. As on the former occasion it immediately proved agreeably respirable, but before the whole quantity was quite exhausted, its agency was exerted so strongly on the brain, as progressively to suspend the senses of seeing, hearing, feeling and ultimately the power of volition itself. At this period the pulse was much augmented both in force and frequency; slight convulsive twitches of the muscles of the arms were also induced; no painful sensation, nausea, or languor, however, either preceded, accompanied, or followed this state, nor did a moment elapse before the brain rallied, and resumed its wonted faculties, when a sense of glowing warmth extending over the system was speedily succeeded by a re-enstalement of the equilibrium of health." Dr. Roget says, "I felt myself totally incapable of speaking and for some time lost all consciousness of where I was, or who was near me."

Davy's account of his own repeated experience is particularly instructive and full. He noted especially the increase of the animal heat in the early stages of the inhalation; its subsequent fall to a point below the natural average, the increase in the frequency of the pulse, foreshadowing the observations of Dr. Richardson, in his recent researches on the general effects of anæsthetics, as we shall presently see. Davy's account of his sensations when inhaling the pure gas, he thus states: "A thrilling extending from the chest to the extremities was almost immediately produced. I felt a sense of tangible extension highly pleasurable in every limb; my visible impressions were dazzling and apparently magnified. I heard distinctly every sound in the room and was perfectly aware of my situation. By degrees as the pleasurable sensation increased I lost all connection with external things; trains of vivid visible images rapidly passed through my mind, and were connected with words in such a manner as to produce perceptions perfectly novel. I existed in a world of newly connected and newly modified ideas; I theorized; I imagined that I made discoveries. When I was awakened from this semi-delirious trance by Dr. Kinglake, who took the bag from my mouth, indignation and pride were the first feelings produced by the sight of the persons about me. My emotions were enthusiastic and sublime; and for a moment I walked round the room perfectly regardless of what was said to me. As I recovered my former state of mind, I felt an inclination to communicate the discoveries I had made during the experiment. I endeavored to recall the ideas, they were feeble and indistinct; one collection of terms, however, presented itself; and with most intense belief and prophetic manner, I exclaimed to Dr. Kinglake, "*Nothing exists but thoughts!—the universe is composed of impressions, ideas, pleasures and pains.*"

Davy, however, most distinctly recognized the power of nitrous oxide to allay pain, having, as he minutely describes, breathed it specifically to allay great pain from inflammation due to the pushing of a wisdom tooth (p. 465, Researches.) *Lucus a non lucendo*—the wisdom tooth did not impart wisdom enough to invite the forceps of the dentist, or nearly half a century of needless anguish might have been saved to humanity! To show how near the discovery of anæsthesia he was, he adds, in his final summary (p. 556): "As nitrous oxide in its extensive operation appears capable of dislodging physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place." Was it not the fault rather of the surgeons of Davy's time in London (many of whom were entirely familiar with his experiments and results) that *they* did not follow up so distinct a suggestion as that last quoted!

Dr. Christopher Caustick* in a contemporaneous statyrical poem called "The Modern Philosopher; or terrible Tractoration!' in four cantos" makes fun of Dr. Beddoe's and Davy's experiments in rather a feeble imitation of Hudibras. A few verses will serve as a specimen of his wit:—

What then occurs? A lucky hit—
  I've found a substitute for wit;
On Homer's pinions mounted high,
  I'll drink Pierian puddle dry.

Beddoes (bless the good Doctor) has
  Sent me a bag full of his gas,
Which, snuffed the nose up, makes wit brighter,
  And eke a dunce an airy writer.

This precious gas, Sirs, is the pink
  Of pure philosophy,—the link
With which great metaphysicians bind
  To worlds of matter, worlds of mind.

That vital principle, which one
  Promethus plundered from the Sun,
It forms the intellect or *nous*
  Of man, of mammoth, or of mouse.

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* The Dr. Darwin, quoted by Dr. Caustick was Erasmus Darwin, author of the "Botanic Garden," in verse, London 1781, born 1731, and died 1802. He was the grandfather of Charles Darwin, our renowned contemporary and author of the "Origin of Species by Natural Selection, &c," born 1809.

As animals (so Darwin said)
In Nile's *organic mud* were bred,
But rose each generation, one key
To Adam, who was but a monkey;

So Beddoes' gas, Sir, I'm inclined
To think, will burnish into mind,
By dint of chemical gradations,
And Dr. Darwin's fine filtations.

With this a brother bard, inflated,
Was so stupendously elated,
He tower'd like Garnerin's balloon
Nor stopp'd, like half wits, at the moon:

But scarce had breath'd three times before he
Was housed in Heaven's high upper story,
Where mortals none but poets enter,
Above where Mah'mets ass dare venture.

Good Sir, enough! enough already!
No more, for Heaven's sake!—steady!—steady!
Confound your stuff! why have you sweat me!
I'd rather swallow all Mount Etna!

How swiftly turns this giddy world round,
Like tortur'd top, by truant twirl'd round;
While Nature's capers wild amaze me,
The beldam's crack'd or Caustick's crazy.

I'm larger grown from head to tail
Than mammoth, elephant, or whale!—
Now feel a "tangible extension"
Of semi-infinite dimension!

Inflated with supreme intensity,
I fill three quarters of immensity!
Should Phœbus come this way no doubt,
But I could blow his candle out!

This earth's a little dirty planet,
And I'll no longer help to man it,
But off will flutter, in a tangent,
And make a harum-scarum range on't.

Stand ye appall'd! quake! quiver! quail!
For, lo, I stride a comet's tail!
If my deserts you fail t' acknowledge,
I'll drive it plump against your college!!

But if your Esculapian band
Approach my highness cap in hand,
And show vast tokens of humility,
I'll treat your world with due civility.

As Doctor Young foretold, right soon
I'll make your earth another moon,
And Phœbus then, an arrant ass,
May turn his ponies out to grass.

But now alas a wicked wag
Has pulled away the gaseous bag;
From Heaven, where thron'd, like Jove I sat,
I'm fall'n! fall'n! fall'n! down, flat! flat! flat!

Can we have a finer illustration than these researches afford us of the important truth that great discoveries are the legitimate fruit of leading ideas, by which facts are sought out and arranged in order to science. The history of science is replete at every turn with examples of the power of preconceived ideas to shut out from our eyes the most obvious truths. Davy was then preöccupied with the phenomena of respiration of various gases as affecting the general health. If it had occurred to him to test the effect of these powerful agents in producing partial paralysis, suspension of the heart's action, or upon the sensorium generally, he could hardly have failed to have anticipated the observation of Horace Wells, of Hartford, when seeking for an agent to subdue pain, he for the first time recognized the anæsthetic power of this same agent in 1844.

Another illustration of the same principle in matters of observation is within the personal knowledge of the writer, who during the years 1835–40 had frequent occasion to observe the effects of a general and profuse exhibition of ether to hundreds of Academical Students for the purpose of a frolic. This kind of etherial debauch was carried on for some time in the open fields about New Haven, and in the presence of hundreds of spectators — the wildest exhibitions of excitement being often manifested — but in no case was the anæsthesia, as such, observed, although the inhalation was often carried up to the point of insensibility. It is true none but a skilled professional man was prepared to recognize the phenomena of anæsthesia, even when it existed in the most unequivocal condition; and when the existence of this physical state was as yet practically unknown how could it be discerned by a crowd of youthful unprofessional observers? If it is true that what we find is often better than what we seek, it is equally true that it may require more sagacity to see what is found than it does to direct a search for a definite object.

We will not pause here to rehearse the history of facts now familiar to all respecting the actual discovery of anæsthetics, nor attempt to decide what share of merit shall be awarded to the several claimants to this honor.* Suffice it to say, that to chemistry, the honor

* It is well known that a private individual not long since entered a costly memorial monument, in the Boston Public Garden commemorating the discovery of etherization. It is adorned with bass-releivos in illustration of the blessings conferred by the use of anæsthetics, and is surmounted by a symbolic statue; but there is, a studied silence on the personal question of the discoverer. A well known physician of Boston, when showing this monument to a stranger, was asked to whom it was intended to assign the honor of discovery, to Morton or Jackson? The witty reply was, "To Ether" (either).

must belong of rendering it possible that such a discovery could be made. If the discovery was accidental, the researches which have furnished the agents upon which it rests were no accident. And this brings us to consider some points bearing upon this subject which serve to illustrate the fact that researches which may appear of little practical moment, and are seemingly of interest only to the theoretical chemist, may never the less be fruitful, when least expected, of the most precious results for the medical profession.

We have already alluded to the discovery of chlorine in 1774, by Scheele of Sweden. So powerful an agent could not fail to manifest remarkable relations to other substances, and we need not therefore be surprised to find how much the attention of chemists has been occupied in studying these relations, and that these researches have been fruitful of the most important results, both theoretical and practical, in every department of chemical science and therapeutics.

So early as 1796, an association of four Dutch chemists, who had already discovered the rich hydrocarbon gas, long known as heavy carburetted hydrogen gas, or olefiant gas, and now called ethylene or hydrogen-di-carbide (C_2 H_4); studied the effects produced from mingling this hydro carbon with an equal volume of chlorine gas over water. They saw that the volume of the mixed gases rapidly diminished, with a notable elevation of temperature and the appearance of a dense oily looking liquid, collecting on the sides of the bell jar and the surface of the water, and quickly sinking to the bottom. Collecting this oily liquid and washing it clean of adhering chlorine, in alkaline water, and in pure water, it was found to be a new substance of a highly agreeable etherial odor, and distinctly sweetish aromatic taste, neutral to tests, and nearly insoluble in water, to which however it imparts its taste and odor, but quite soluble in ether and alcohol. It was wholly unaffected by concentrated sulphuric acid even with the aid of heat. For many years its real constitution remained unknown, and it was shown only as one of the curiosities of the chemist's laboratory, under the name of "Oil of the Dutch Chemists;" the name olefiant gas, having had its origin from the oil-producing property, which this gas developed in its action with chlorine. Analysis has long since shown that this chlorine compound of the Dutch chemists, is a simple union of one molecule of ethyline with two of chlorine, and that it may properly be called the chloride of olefiant gas. I have been the more particular in noticing the discovery of this remarkable substance because it has acquired considerable notoriety from the fact that it was early and most naturally counfounded with chloroform, to which, in sensible and physiological properties, it bears a remarkable resemblance. It was long known as "Chloric Ether," a name which conveys a false impression, since there is nothing in the constitution of the body, which in the least resembles the ethers.

In 1831 appeared the 2d volume of "Silliman's Elements of Chemistry," in the order of the lectures then given in Yale College, in which the Dutch liquid was spoken of in its physiological relations, with the remark that, "Its medical powers have not been ascertained, but from its constitution and properties it is highly probable it would be an active diffusive stimulant."

This remark immediately attracted the attention of

Mr. Samuel Gutherie, of Sackett's Harbor, New York; a man of an active and original mind, much devoted to practical chemistry, who at once conceived that he might obtain the so-called "chloric ether" in greater abundance and at a cheaper cost by distilling together alcohol and chloride of lime (bleaching powders.) His success was remarkable, and he obtained the alcoholic solution in great abundance, describing his process in a short article in Silliman's Journal of Science, for January 1832; and subsequently, in July of the same year, he states with more detail the precautions he adopted to obtain the product pure, and especially, free from alcohol. It is remarkable that in his second paper he describes in full the method of testing the purity of the substance by agitation with concentrated sulphuric acid. There is no question that Mr. Gutherie was entirely original in his method of producing "chloric ether," as it was then called, and it is no abatement of his sagacity that he was not aware that, earlier in the same year, in which he described his process, a French Chemist, Mr. Souberaine, had devised and described the same method in a memoir entitled, "*Researches on some combinations of Chlorine*," which appeared in the *Ann.-de Chimie et de Phys:* for Feb. 1831." Souberaine calls the product "a new etherial liquid of a constitution unlike any before known to chemists," and also gives us the name chloric ether (*ether chlorique.*) Dr. Thos. Thomson also applied the term chloric ether to the oil of the Dutch chemists in his System of Chemistry for 1820. Souberaine gave two analyses of this product which while they prove that the body is not the "Dutch liquid," failed to reveal its true constitution, which was first given by Dumas in 1834, in a memoir published by him in the same journal, and in this paper he then gave to the new body the name by which it has ever after been known, *chloroform*.

Such, in brief, is the history of one of the most remarkable bodies ever discovered. You will understand that while the "chloric ether" of Gutherie was a misnomer, the substance which he produced was *chloroform*, and that the first use made of this agent in medical practice was at the suggestion of Prof. Silliman, to Dr. Eli Ives, formerly Professor of Theory and Practice in this college in 1832. Dr. Ives's note on his experience will be found in Silliman's Journal, vol. 21, for July 1832, and the first case in which he employed it was one of asthma in an aged person, who was relieved of a severe paroxysm by its use, "more suddenly than she had been in any previous illness of the kind." Thus the therapeutic history of chloroform had its commencement from the teachings and practice of the Yale Medical School.

But the great discovery of its anæsthetic power yet remained undeveloped. The article was here in all its purity and strength in 1832, and in no stinted quantities. Mr. Gutherie, in an interesting letter published in the *New York Commercial Advertiser*, eighteen years after his discovery, and when the world rang with the excitement consequent upon Professor Simpson's use of chloroform as an anæsthetic says, "To give an idea of how easily and rapidly chloroform may be made, and of great purity and strength, I will detail one operation made in 1832, from which course I have never since had occasion to deviate:—Into a 500 gallon copper-still I poured 100 gallons of common whisky, and then plunged in 240 lbs. of chloride of lime. The still became instantly hot ; and before I had luted on the head, I had a full stream of chloroform flowing from the still-worm. It continued to run freely for some time without fuel. When the product ceased to come over sweet, I removed the receiver, and run off the remainder of the spirit for further use. The product was re-distilled from a profusion of water, or was well washed in some five or six waters, when it had reached a specific gravity of 1,437. From 2000 lbs. of ordinary chloride of lime I obtained nearly 100 lbs. of chloroform," (quoted by Channing: Etherization in Childbirth, 1849, p.p. 29.)

Thus many years before the discovery of its anesthetic powers had chemistry supplied to the materia medica a full knowledge of chloroform, while ether had been in familiar use for centuries, having been known, it is believed, to Raymond Lully in the 13th century. Valerius Cordus certainly described the method of making it in 1540, and called it *Oleum vitreoli dulce;* and yet it was left for the Dentist Morton, who was neither chemist nor physician, to be the first to administer ether in 1846, by inhalation up to the point of insensibility to pain, acting as is believed, at the suggestion of Dr. C. T. Jackson, and certainly with almost criminal boldness ; a thing which no prudent physician would have dared attempt until he had first tested its power on the lower animals.

The materia medica was thus enriched with two anæsthetic agents of very unlike chemical origin and constitution, one being a salt of an alcohol radical, oxide of ethyl or common ether, the other a substitution product, by the action of chlorine in replacing three atoms of hydrogen in the constitution of methylic, ethylic, or amylic alcohol. It was obvious to chemists as soon as these remarkable physiological results from the inhalation of the vapors of these agents was known, that a wide field was opened for the study of the powers of a large class of analogous compounds, among which might be discovered some of equal or greater value to medical use, embracing many other effects as important as anæsthesia. But the union of chemical knowledge with medical skill, physiological or biological power, and with accurate habits of observation and research in these difficult and critical experiments, is a rare conbination, and consequently for many years after the discovery of the anæsthetic powers of ether and chloroform, very little was done in this field of research of any practical or scientific value. Surgeons and practitioners seemed content to "use the gifts the Gods allow," without venturing upon the limits of the unknown. Consequently it is only within the last few years that Medical Science has been enriched by the results of systematic research in this department. In Germany Leibreich, of Berlin, has labored assiduously, and with eminent success in this field, his crowning discovery in 1869 being of the narcotic power of chloral hydrate, of which more anon.

In Great Britain we are largely indebted to the sagacity and industry of Doctor Benj. W. Richardson, of London, for most systematic researches upon the anæsthetic and other physiological powers of a great number of substances whose effects he has studied with care. As his results are but little known in this country it it seems appropriate to devote to them here more than a passing allusion. Dr. Richardson's results have been communicated in the form of Annual Reports to the British Association for the Advancement of Science, year by year, since 1864. Commencing with the nitrite of amyl, the study of which has occupied several years, he has gradually extended his researches over a wide field upon a systematic plan, embracing not only anæsthesia, but the study of all the physiological effects of these reagents with a precision not before known. Much of his work is purely physiological, and the details are therefore more appropriately discussed elsewhere than here. But the basis of all his researches has been an intelligent comprehension of the chemistry of the problem with which he is dealing, and his example in this regard is invaluable as pointing out how it is possible to substitute the accuracy of systematic investigation for the blind gropings of empyricism in therapeutics.

The substances studied are grouped in a tabular form under the five divisions of hydrides, nitrites, alcohols, chlorides, and iodides respectively, of the methyl, ethyl, butyl and amyl series of alcohol radicals ; the propylic compounds being purposely omitted, owing to the difficulty of obtaining pure specimens.

Dr. Richardson's table is exhibited on the following page :

We will pass briefly in review some of the more important results of Dr. Richardson's researches following the order of the table.

Hydrides. This term is applied in modern chemistry to the compounds of hydrogen with metals, alcohol radicals, and organic acid radicals, of which the second only has any present interest for us. Their composition is shown in the fourth column of the table.

The Hydride of Methyl or Protylen, familiarly called *Marsh gas* is a natural product, being the "fire damp" of coal mines and is given off also abundantly from the oil wells of Pennsylvania. Being a gas it can be administered for physiological purposes by inhalation only. It is a pleasant gas to inhale, producing no irritation,

	Name.		Chemical Composition.	Vapor Density. $H_2 = 1$.	Specific Gravity Water=1000.	Boiling-point.		Percentage of Iodine in Iodides.
	Old.	New.				C.	F.	
Hydrides.	Methyl . .	Protylen .	$C\ H_3\ H$	8	Gas.	. . .	. . .	
	Ethyl . . .	Deutylen.	$C_2\ H_5\ H$	15	Gas.	. . .	. . .	
	Butyl . . .	Tetrylen .	$C_4\ H_9\ H$	29	Gas.	. . .	. . .	
	Amyl . . .	Pentylen.	$C_5\ H_{11}H$	36	.625	30°	86°	
Nitrites.	Methyl . .	Protyl. . .	$C\ H_3\ NO_2$	30.5	Gas.	. . .	. . .	
	Ethyl . . .	Deutyl . .	$C_2\ H_5\ NO_2$	37.5	.917	18°	64°	
	Butyl . . .	Tetryl. . .	$C_4\ H_9\ NO_2$	51.5	. . .	64°	147°	
	Amyl . . .	Pentyl. . .	$C_5\ H_{11}NO_2$	58.5	.877	96°	205°	
Alcohols.	Methylic.	Protylic. .	$C\ H_4\ O$	16	.814 at 0° C	60°	140°	
	Ethylic . .	Deutylic .	$C_2\ H_6\ O$	23	.792 " 16° C	78°	172°	
	Butylic . .	Tetrylic .	$C_4\ H_{10}O$	37	.803 " "	110°	230°	
	Amylic . .	Pentylic .	$C_5\ H_{12}O$	44	.811 " "	132°	270°	
Chlorides.	Methyl . .	Protyl. . .	$C\ H_3\ Cl$	25.25	Gas.			
	Ethyl . . .	Deutyl . .	$C_2\ H_5\ Cl$	32.25	.921 at 0° C	11°	52°	
	Butyl . . .	Tetryl. . .	$C_4\ H_9\ Cl$	46.25	.810 " 16° C	70°	158°	
	Amyl . . .	Pentyl. . .	$C_5\ H_{11}Cl$	53.25	. . .	102°	216°	
Iodides.	Methyl . .	Protyl. . .	$C\ H_3\ I$	71	2.240 at 16 C	42°	108°	89.4
	Ethyl . . .	Deutyl . .	$C_2\ H_5\ I$	78	1.946 " "	72°	162°	81.4
	Butyl . . .	Tetryl. . .	$C_4\ H_9\ I$	92	1.604 " "	120°	248°	69.4
	Amyl . . .	Pentyl. . .	$C_5\ H_{11}I$	99	1.511 " "	146°	295°	64.1

nor yet giving rise to any of those feelings of excitement which are induced by nitrous oxide gas, or vapor of chloroform. It produces anæsthesia and for this purpose it must be inhaled nearly pure. Recovery from it, if stopped in time, is rapid and complete, a few seconds being sufficient to restore consciousness and muscular power. It can kill only by negation and by replacing air requisite for oxidation of the blood. No spasms accompany its inhalation. As it is often the cause of most melancholy disasters in coal mines, it became a curious question how much of it could be breathed with impunity, and this point Dr. Richardson tested experimentally by use of a glass chamber through which an atmosphere charged with known quantities of the gas could be passed. To his surprise he found that even pigeons, animals peculiarly susceptible to the influences of narcotic gases, could live in an air charged with not less than 35 per cent of the gas for the space of half an hour. When by pushing the inhalation further death is induced, it is a very gentle sleep, so gentle indeed that it is difficult to say when the action either of the respiration or of the circulation is over. The lungs are left with blood in them, the heart has blood on both sides, and the blood itself retains its normal character. Death from fire damp must be of the easiest kind, must be in fact as easy as going to sleep, which accounts probably for the sleep-like placidity and posture in which the dead have been found after fatal accidents from inhaling this gas. It is not so easy to account for the placidity of countenance observed in those who have perished from explosions of fire damp when mingled with common air. In this case it is true the bodies are often blackened from the burning flames, but if they escape disfigurement from this cause the carbonic acid resulting from the explosion, and which miners know as "choke-damp," is also a narcotic, and those who perish by inhaling it may die as quietly as by the marsh gas alone.

From the circumstance that the hydride of methyl is found in the air of marshes it has been taxed as the cause of malarial fevers. There is no evidence whatever to support this view; none that the gas is anything more than an immediate and simply negative poison, the effects of which cease as soon as the body is removed from its influence. We must therefore seek for some other cause to account for the true origin of malarial fevers—probably some organic poison containing nitrogen, derived from decomposition, to which the hydride is a harmless concomitant. The best means of recovery of those under the influence of fire damp is exposure to heated air and the use of warm, nourishing drinks like milk. Alcoholics do decided harm.

Hydride of Amyl or *Pentylen*, exists nearly pure as one of the lighter products of Pennsylvania petroleum. It is a light fragrant fluid, boils at 86° F., and has a density of 0.625— is in fact what has been called rigoline. It is very agreeable to breathe and creates no irritation. This hydride was first used in this country about four years ago as a general anæsthetic and was reported on favorably. Dr. Richardson confirms this report in general terms and adds a number of interesting particulars. It is particularly useful for producing local anæsthesia, especially when mingled with absolute ether, to reduce somewhat its extreme volatility. In this form it is the best agent which can be employed for producing rapid local insensibility. When inhaled it produces in the human subject rapid insensibility, from which the recovery is also rapid and complete, no nausea, headache or chilliness ensuing. As a vehicle for solution of iodine it is the best known, whether for topical application, deodorizing, or inhalation. Its solution in ammonia is an excellent antiseptic for the preservation of animal substances in a fresh state in a closed jar, and the solution can be used medicinally by inhalation in cases where the physician wishes to administer ammonia rapidly, as in scarlet fever, and in states of great prostration. The ammonia can be so diluted in this manner as to render it agreeable for inhalation. Many other uses of the hydride of amyl might be named, but suffice it to say, so soon as its value is known and appreciated it must become as common an agent in medicine as ammonia, ether or alcohol.

Two other hydrides of the petroleum series have been studied by Dr. Richardson lately; they are hexyl and heptyl, caproylic and ænanthylic hydrides, whose formula are respectively $C^6 H^{13}$, H, and $C^7 H^{15}$, H; boiling points respectively 154° F. and 201° F; vapor density 43 and 50 hydrogen, being unity.

Dr. Richardson, says "I should consider the hydride of caproyl in the light of a narcotic which acts by reducing the respiratory process of change of blood rather than by any direct influence of its own on the nervous centres. In the absence of chloroform it might be used as a substitute for it; and had it been tried pure in the early days of anæsthetic research it would possibly have obtained position over ether." This is assigning it a pretty high anæsthetic value, and considering their great abundance and cheapness in the United States it may well be asked if it is not worth while for American practitioners to pay more attention to these very light petroleum spirits below the density of 0.700?

If there was a demand for these products for medical use they could readily be furnished, quite free of all disagreeable odor, at a price not exceeding, probably, one dollar per gallon, crude light naphtha being worth about ten cents.

It may be interesting here to record our American commercial classification of the light petroleum products.

The prime crude petroleum of 45° B. yields of:—

"Rigoline"	boiling at	65° F.	about	½	per cent.	
"Gasoline"	"	" 120° "	"	1½	" "	by volume
"C Naphtha"	"	" 180° "	"	10	" "	

On a daily average crude product of 15,000 barrels it is easy from these data to calculate the abundant supply of these anæsthetics.

Neither the Nitrite nor the Nitrate of Methyl produce true anæsthesia. Both are derivatives of methylic alcohol or wood spirit. They both produce intense excitement and rapid action of the heart and arteries. In the human subject the face becomes red, the vessels of the head seem full and distended and the pulse is readily brought up to 120 and even 130. On the inferior animals the same excitement is manifested, and death is preceded by convulsive jerks. After death the lungs are found collapsed and white, and the heart flaccid and full of blood on both sides. On exposure to the air the heart recommences to contract, and continues its contractions for long periods, in one case (a rabbit) for 40 minutes. The blood in the vessels remains fluid for an hour or more, but coägulates readily on exposure to warm air. The muscles are flaccid but will contract for an hour or two under the excitement of voltaic electricity. The power of nitrite of methyl is so marked and general in producing muscular relaxation that Dr. Richardson suggests that its use in cases of a desperate spasmodic character, as in tetanus, would be a rational scientific procedure. Passing the nitrites of ethyl and butyl we will next consider briefly the more remarkable:

Nitrite of Amyl. This is an amber colored fluid with an odor and taste of over ripe pears, resembling, in this respect, the acetate of amylic oxide a body sold commonly under the name of "essence of pears." It is the product of the action of nitrous acid gas upon amylic alcohol (fusel oil). When pure its density is .913 and it boils at 182° F. Its vapor extinguishes flame and acts as an antiseptic. When inhaled it acts in a wonderful manner to excite the circulation—the action of the heart in man, and in warm blooded animals, being doubled in rapidity in thirty seconds. This intense action is followed by great suffusion of the skin, by breathlessness like that produced by violent running, by a peculiar sensation and fullness of the head with throbbing , and ultimately by failure of muscular power of the extremest kind. It produces no destruction of the nervous sensibility, and in animals no increase of sensibility up to the moment of death. It is not an anæsthetic. In cold blooded animals this remarkable agent suspends animation for many hours and even for days; and in young warm blooded animals after exposure to the nitrite of amyl until they seemed to be dead, the action of the heart continued for so long a period as eighteen hours. This agent administered by inhalation acts with great promptness and precision and the phenomena are among the most striking in the whole range of physiological experience. It appears to act by arresting the progress of oxydation in the tissues.

As a remedy for disease the great virtue of nitrite of amyl is its specific power of removing muscular spasm. Beneath its first and most conspicuous power of producing excessive action of the heart and apparent excitement there is another and more permanent condition produced, namely a temporary paralysis of muscle and a suspension of all outward manifestations of life which in the lower animals (frogs) can be sustained without actually destroying life. This observation of Dr. Richardson led him to point out the importance of this nitrite to control spasms, and especially to meet the spasmodic disease tetanus (or locked jaw) over which he inferred it would have a direct controlling power. This sagacious suggestion, the fruit of pure scientific reasoning, and as far removed from empyricism as light from darkness, has since been completely verified, first by Dr. Brunton, of Edinburgh, in *angina pectoris*, and subsequently by others in the same disease, as also in terrible pain from spasm of the bowels, where, when the nitrite was administered, the patient exclaimed that he "was transformed from agony to heaven in a moment." Mr. Foster, an eminent practitioner of England, administered it to a man suffering from tetanus where the spasms were so severe that the patient is described as "having been rolled up like a rigid ball." Five drops of the nitrite inhaled from a handkerchief induced immediate lessening of the spasms. This treatment was assiduously renewed on each return of the spasms for *nine days*, when he had inhaled an ounce of the fluid, and the case was a complete recovery. Mr. Foster states that of seven like cases of tetanus in his 31 years practice, all had died; he had met with no success until he had recourse to the nitrite of amyl. This is a splendid triumph of science! Nitrite of amyl was not introduced into use as a remedy, against spasmodic diseases, including tetanus, by any mere accident, nor by a lucky guess. It was introduced on method of pure scientific investigation; its powers as a remedy were discerned and estimated, stated before it was applied for the cure of disease, and the results obtained were the simple expositions of the predictions made concerning its value. Dr. Richardson has no occasion to apologize for an expression of a just pride of feeling at these wonderful results which so well indicate the worth of scientific experimental inquiry, as preliminary to practical application, for certain and systematic relief and cure of human suffering.

The form preferred by Dr. Richardson for exhibition of nitrite of amyl by inhalation, is an etherial solution, or tincture, in which five grains of the nitrite are contained in one drachm of absolute ether.

The nitrite of amyl is believed to produce its effect by its paralyzing action upon the nerves which govern the contraction of the blood vessels; and this view of its action explains, by the reverse, the mode of action of those agents which it neutralizes, such as strychnia, and the influence which excites the disease known as tetanus. These agencies either excite extreme action of the nerves which keep up the contraction, or paralyze the counter nervous supply which causes ditalation of vessels; and the convulsive movements induced by such agents as strychnine are due to the removal of blood by contraction of vessels in a manner analogous to the convulsion which follows free abstraction of blood.

THE ALCOHOLS. *Methylic alcohol.* Several of the derivatives of methyl are already familiarly known in their physiological relations. Marsh gas has already been considered, while chloroform, the terchloride of methyl, is historic, and the tetra-chloride of carbon has also of late attained some notice as an anæsthetic. The methylic alcohol or wood-spirit has been long known both to chemists and to the materia medica. It is obtained from the dry distillation of wood; and when pure, is a colorless spirit boiling at 140° F. and having a densitity of 0.810, nearly the same as wine alcohol. Its physiological effects may be obtained either by direct administration with water or by inhalation of the vapor. The first symptoms from administration of methylic alcohol are those of excitement followed by languor. These symptoms are succeeded by labored breathing, and soon by gaspings and by deep sighs, which occur at intervals of about four seconds; followed by want of power in the limbs, with rolling movements on the side and complete intoxication. If the dosing is pushed beyond this, the animal relapses into utter prostration, and the breathing becomes blowing, with the bronchial râle, due to the passage of air through fluid in the finer bronchial passages. Throughout all these stages of intoxication there is imperfect anæsthesia and, up to what would seem the extremity of living action, some evidence of reflex sensibility is seen when irritation is applied. Brought to the lowest stage of prostration by methylic alcohol, an animal will always recover, slowly, in a warm atmosphere, the period for recovering being from four to six hours at a temperature of 65°. During recovery there are no active convulsive movements and tremors are not marked symptoms. When methylic intoxication is pushed to death, the respiration and circulation cease almost instantaneously. The lungs are left with a fair amount of blood and both sides of the heart contain blood. The brain is much engorged with blood and all the vascular organs are in the same state. The blood is not objectively changed in character, its coägulation is somewhat prolonged, but is not prevented. The evidence is, on the whole, to the effect that methylic alcohol influences principally the motor centres of the nervous system. At all events, these centres are prominently influenced, and it is probably only when they begin to fail that the centres of conciousness and sensation succumb. In this respect the methylic, the ethylic and the amylic alcohols have a common action. But on comparing the effects generally of methylic alcohol with those of amylic and of ethylic, or common alcohol, Dr. Richardson finds the methylic spirit much less potent. It produces prostration and muscular paralysis more quickly, but from the prostration, recovery is far more rapid.

Amylic Alcohol. When the loss of animal power from amylic alcohol is complete, a peculiar sympton is developed, namely ; universal tremor accompanied with a very deep inspiration. There is no spasm, no rigidity, but rigors of an intense kind. These rigors are soon established in regular rhythm, and by maintaining the experiment cautiously, may be kept up for several hours. Dr. Richardson has observed them for one hour at the rate of 16 in a minute as regular as possible, and by the reduction of the agent has lowered them to twelve, eight, and four per minute. The breathing is tranquil and the action of the heart good throughout. The rigor occurs as described, spontaneously, but it can be excited at any moment by touching the animal, or blowing upon it, or even by a sharp noise as the snap of the finger. When the animal is reduced to entire insensibility, if it be laid in the open air, it begins to recover its sensibility at once, but the power to move is suspended for two or three hours, and the rigors also continue, but with decreasing force and frequency. Ultimately the animal recovers and is always eager for food. When these urgent, and, as they would seem, extreme symptoms are carried to their full extent, even an experienced observer would think recovery impossible; but in truth the animal cannot be killed by any fair play with amylic alcohol. In order actually to kill, it is necessary to complicate the experiment by reduction of air, or by closing the chamber and retaining the carbonic acid of the breath. By ethylic alcohol (*common alcohol*) the same symptoms are developed but in a minor degree in Dr. Richardson's experiments.

In poisoning by *Methylic* alcohol these symptoms of amylic alcohol are nearly altogether absent. The recovery is not only rapid, but easy; approaching in fact, recovery from inhalation of ether.

Butylic alcohol manifests physiological actions like those of common alcohol, but exerted in a slower and more marked degree, and with some symptoms added. The time required for producing intoxication is full double that required by ordinary spirit, and the time for recovery is proportionally still longer. The same depression of animal heat is observed as in ethylic alcohol, but in the third stage of intoxication after the temperature is depressed to a minimum, distinct tremors of the muscles appear, which continue for ten or twelve hours without further administration of this alcohol, and so slowly do they subside that Dr. Richardson has observed them in the pigeon thirty-six hours after the intoxication. "There cannot, I think," he adds, "be a doubt that these tremors, produced in animals by the heavier alcohol, are identical with the tremors observed in the human subject during the disease known as *delirium tremens.*"

The reduction of temperature observed by Dr. Richardson, in exhibiting methylic alcohol to pigeons was, when the third degree of intoxication was produced, that in so short a period as ten minutes the temperature was lowered four degrees F., and that the decline of temperature continued during the whole period of recovery, reaching at the lowest a decline of eight degrees on Fahrenheit's scale. The temperature begins to rise about two hours after the first indications of recovery; but a period of seven to eight hours is required to restore the body, even under favorable conditions, to the natural temperature.

He has demonstrated, also, the tendency to decrease of animal heat in all stages, after the first stage, of intoxication by common alcohol. In the progress toward complete intoxication under alcohol, however administered, there are as under chloroform, four degrees or stages. The first is a stage of simple exhilaration, the second, of excitement, the third, of rambling insensibility, and the fourth of entire unconsciousness, with muscular prostration.

The following paragraphs from Dr. Richardson's Reports on the alcohols are quoted in full as offering a beautiful example of the fruits of scientific research drawn from a careful study of chemical, physical, and physiological phenomena, as applied to medical investigations; while at the same time they clearly indicate the possibility of dethroning king alcohol completely in medical practice, by the use of an alcohol possessing a far higher medical value than common acohol, and from the exhibition of which, it is to be hoped, no evil habits can be entailed as a sequel to the use of these stimulants when called for in practice. It will also not escape the notice of the profession, that Dr. Richardson distinctly confirms the doctrine formerly held, but unfortunately, of late, discountenanced by many, that alcohol, in the human system, acts only at the cost of the vital power, adding nothing to this force as an aliment, and ultimately lowers the animal heat, passing out of the body as it entered it, chemically unchanged.

"I notice especially this difference of action of the three analogous alcohols for two reasons; first—because the fact is an exposition of a general physiological law in relation to bodies of the same series: and secondly, because there is a practical fact behind bearing upon the employment of these substances. The physiological law is this; that the period of time required by these bodies to produce their effects and the period of time required for recovery, turns altogether on the evaporating point of the fluid used. This is so certain, that, when in an analogous series of fluids, the action of one of the series is well learned, the action of the others may be safely predicted from the boiling point. In illustration, here are these four alcohols, amylic alcohol, butylic alcohol, ethylic alcohol, and methylic alcohol; the first boils at 270° F., the 2d at 230°, the 3d at 172°, and the 4th at 140°. If we intoxicate four animals of the same kind with these alcohols, carrying the symptoms in each case to the same degree, and then leave the animals to recover in the same temperature, say 60°, then if the animal in the methylic alcohol be four hours recovering, the one in ethylic alcohol will be seven hours, the one in butylic alcohol will be fourteen hours, and the one in amylic will be sixteen hours.

"The explanation of this fact is very simple, and reduces the phenomenon to a question, I had almost said, of mechanical force. The alcohols taken into the body enter into no combination which changes their composition. They pass out of the body chemically as they entered it, and their evolution and the time of their evolution is a mere matter of so much expenditure of force (caloric) to raise them and carry them off. To test this more directly, intoxicated animals were placed in different degrees of temperature with the unerring result of a quickened recovery in the higher degrees.

"The practical lessons I would refer to are two in number. I would suggest that in all cases of alcoholic poison in the human subject, the most important condition for recovery is a high temperature. The use of the hot air bath raised to 150° or even 180° F. would be the most perfect means of recovery. Next I would point out that as methylic alcohol is much more rapid in its action, and much less prolonged in its effects than is common alcohol, it would be used with great advantage by the physiological physician in all cases where he feels a demand for an alcoholic that shall act instantly and with the least possible ultimate expenditure of animal force for its elimination. It must be observed that in the end all these alcoholic bodies are depressants, and although at first, by their calling vigorously into play the natural forces they seem to excite, and are therefore called stimulants; they themselves supply no force at any time, but take up force, by which means they get away and therewith lead to exhaustion and paralysis of power. In other words the calorific force which should be expended on the nutrition and sensation of the body is expended on the alcohol.

"Reviewing the alcohols as a class we find their physiological action, less extended in regard to particular organs than the nitrites, and more extended than the insoluble hydrides, as expressed both on the organic and cerebro spinal centers, reducing the active functions of both systems and at last so reducing the functions of the cerebral hemispheres as to remove consciousness altogether. The leading peculiarity of the action is the slowness with which those centers, which supply the heart and diaphragm with power, are affected. In this lies the comparative safety of alcohol; acting evenly and slowly, the different systems of organs fall together, with the exception of the two on which the continuance of mere animal life depends. But for this, every deeply intoxicated man would die. The alcohols are strictly anæsthetics; and indeed the first published case of surgical operation under anæsthetic sleep was performed in 1839 by Dr. Collins on a person who was rendered insensible by breathing the fumes of alcohol. But the anæsthesia is not commendable; it is too slow and too prolonged. Methylic alcohol, if it could be entirely purified and made inodorous, might be used and with methylic ether it would be one of the safest of agents; but as yet its inhalation is disagreeable.

"The difference of action of the alcohols, as they ascend in the series and as the carbon increases, is most striking. The slowness of action, as the prolongation of action step by step, from the lighter to the heavier compounds, is a fact as definite as any in physiology. Curious it is also that neither the methylic nor the ethylic alcohols produce those tremors in the inferior animals which we recognize in and especially name from their occurrence in man; while the butylic and the amylic most effectively call them forth. Considering how much of the heavier alcohols is distributed for consumption, especially among the lower orders, I think it is possible that the heavier fluids may also be the cause of delirium tremens in the human subjects, as they are frequently the cause of that continued coldness, lassitude and depression which follow the well known dinner with bad wine.

"Speaking honestly, I cannot by any argument yet presented to me, admit the alcohols through any gate that might distinguish them as separate from other chemical bodies. I can no more accept them as foods than I can chloroform, or ether, or methylal. That they produce a temporary excitement is true, but as their general action is quickly to reduce animal heat, I cannot see how they can supply animal force. I see clearly how they reduce animal power, and can show a reason for using them in order to stop physical or to stupify mental pain, but that they give strength, *i. e.*, that they supply material, for the construction of fine tissue, or throw force into tissues supplied by other material, must be an error as solemn as it is wide spread.

"The true place of the alcohols is clear; they are agreeable temporary shrouds. The savage, with the mansions of his soul unfurnished buries his restless energy under their shadow. The civilized man, overburdened with mental labor, or with engrossing care, seeks the same shade, but it is shade, after all, which in exact proportion as he seeks it, the seeker retires from perfect natural life. To search for force in alcohol is to my mind equivalent to the act of searching for the sun in subterranean gloom until all is night.

"As yet alcohol, the most commonly summoned of accredited remedies, has never been properly tested to meet human diseases. I mean by this, that it has never been tested as alcohol of a given chemical composition, of a given purity, and in given measures. Wines, beers, spirits, are mixtures—compounds of alcohols, and compounds of alcohols with ethers and other organic substances. It is time, therefore, now for the learned to be precise respecting alcohol, and for the learned to learn the positive meaning of one of their most potent instruments for good or for evil; whereupon I think they will place the alcohol series in the position I have placed it."

The Sodium and Potassium alcohols (ethylates of sodium and potassium) formed by the direct action of metallic sodium and potassium, respectively, with absolute alcohol, and in which the alkali metal replaces one atom of hydrogen in the alcohol $\left[\begin{matrix} C_2H_5 \\ M \end{matrix}\right\} (O)$, appear to offer the way to obtaining one of the greatest needs of medicine, a sure, rapid, and painless caustic, applicable in local anæsthesia, for subcutaneous injections, to destroy the virus of poisoned wounds as of snakes or rabid dogs. The action of these salts is also remarkable in producing almost instant crystallization of the crystalloidal matter of blood cells, in acicular and arborescent forms. They are also remarkable antiseptics especially adapted to the preservation of nervous matter, as brain and other soft animal pastes.

Sulphur Alcohol or *Mercaptan.* The study of the physiological relations of this body, long since made known to chemists by Zeise, has revealed among other curious and suggestive facts, one which Dr. Richardson considers entirely new. While all other narcotic and paralyzing agents which have been studied, produce paralysis of the voluntary muscles before they cause paralysis of the muscles of respiration and of the heart, and in recovery the heart first lights up, then the respiration, and finally the muscles of voluntary power — it proves that under mercaptan the reverse obtains, the voluntary muscles lose their irritability last and regain it first during the recovery. It produces in the lower animals a perfect simulation of death which may be prolonged in the frog, after half an hour's immersion in its vapor, and subsequent washing in water, and exposure to fresh air ; for an hour and a half to two hours, when they begin to breathe, next the heart begins to beat, and in a short time they recover perfectly, precisely as if awakening from the torpor of cold.

The Chlorides of the Alcohol Radicals. —The whole of the bodies in the chloride series are simple and pure anæsthetics, and the power of their action increases with the number of atoms of carbon in the radicals. They act most readily and determinately on the cerebrum, and on the centers of volition and common sensibility. They have little action on the organic nervous system, and they interfere, even in full doses, but very gradually with the movements of the heart and respiration.

The Chloride of Methyl being a gas, made by the direct action of chlorohydric acid upon methylic alcohol, can only be used properly by inhalation. With atmospheric air 15 per cent. of methylic chloride produces good anæsthesia without excitement and with excellent recovery. Carried to the extent of causing death, the action of the heart outlives the respiration ; the lungs are left with blood in the pulmonic circuit, and both sides of the heart are filled with blood which is little changed in color. The muscles retain irritability after death, and respond to the voltaic current two or three hours after death, and the heart continues to pulsate spontaneously for half an hour or even forty minutes.

The Chloride of Ethyl acts much as does the methylic chloride, but its action is much more prolonged and is longer in coming on. With absolute ether it forms an excellent compound, objectionable only by reason of its instability.

The Chlorides of Butyl and Amyl have yet, in Dr. Richardson's opinion, to take a very important part in medicine. Their action is very similar. Both are simple and efficient anæsthetics and both are pleasant to inhale, the butylic chloride being most agreeable. They admit of being applied in many cases where a prolonged sleep is required; for this purpose they may, to a considerable extent, replace opium. The deep sleep they induce is especially characteristic of the amylic chloride in accordance with the well established law that these agents have effects prolonged in proportion as they contain mere atoms of carbon and as their boiling points are higher.

Pigeons put to sleep by breathing an air containing ten per cent. of chloride of amyl require from ten to twelve minutes to produce perfect sleep, passing the three stages of anæsthesia easily and without convulsion, but invariably with slight vomiting. The temperature of the body falls fully four degrees F. This sleep continues in common air at 90° F. for fifteen minutes profoundly; the awakening is quick and the recovery perfect.

In rabbits, seven minutes are required to produce safe narcotism, and the sleep produced is very profound.

The breathing is tranquil, and the eyes usually remain open. Thus narcotized, a rabbit will lie five and thirty or even forty minutes in this state before showing signs of recovery, and the temperature of the body falls 3° to 4° F. If the inhalation is pushed too far this profound sleep passes into death, the sleeping prolonged in common air at 90° F., a full hour and a half prior to death. During this time the respiration remains for the most part natural, with occasional double breathing ; but the temperature of the body is all the time falling, and is reduced even while the animal is yet alive 21° F. below its natural standard. Thus in one case the rabbit fell from 103° to 82° F. This is the lowest reduction of temperature I have seen, says Dr. Richardson, in connection with symptoms of living action ; but from this extreme condition recovery is yet possible if the respiration be sustained in a warm air. After death from amylic chloride both sides of the heart are charged with blood, and the action of the auricles and ventricles is long persistent. The blood is very slow to coägulate ; but the venous and arterial bloods retain their color. The lungs are natural. The blood corpuscles are much changed ; they are shrunken, stellate, and elongated with truncated ends. The brain is bloodless and of the purest white, which seems characteristic of the effects of all the chlorides of the alcohol radicals.

It is obvious from these statements that there is a most important unexplored field of physiological research in this direction, especially in the study of the effects of these higher chlorides of the alcohol series upon the human subject to which the researches of Dr. Richardson have opened the way.

Bichloride of Methylene ($C\ H_2\ Cl_2$). This new anæsthetic has come into very general notice since 1867, both in this country and Europe, and is considered safe to the extent of one fatal case in ten thousand according to Dr. Richardson's report of 1870, and probably to one in 20,000, the two fatal cases noted in that report being of doubtful relation to the anæsthesia. Its boiling point is 104° Fh. and it differs from chloroform, from which it is derived, by the substitution of one atom of hydrogen for one of chlorine in the tri-methylic chloride, giving us di-methylic chloride. It is best administered by a peculiar form of inhaler adapted for all fluids which boil at a low temperature. This instrument is so constructed that the fluid can be admitted grain by grain, and distributed in the form of spray on a surface of thin flannel spread over a mouth piece of vulcanite. Compared with chloroform its anæsthesia is more quickly produced, and when produced is more prolonged, while recovery, when it commences, is far more rapid, never exceeding in Dr. Richardson's experience four minutes, and there are no prolonged or painful after effects. When animals are allowed to sleep to death in vapor of bichloride of methylene, the lungs are found containing blood but not congested, while the heart contains blood on both sides. In this respect the vapor acts differently from both chloroform and ether. After death in chloroform vapor the lungs are left bloodless, and the right side of the heart is gorged with blood. After death from ether vapor, the lungs are found intensely congested, and the heart containing blood on both sides. Dr. Junker who has used the bichloride of methylene safely in 200 cases of ovariotomy expresses the opinion that it is practically free from danger when pure, and used with ordinary care. Dr. Richardson's opinion is that it is safer than chloroform, but not actually safe, belonging like chloroform to a dangerous family of chemical bodies. The difficulty of obtaining a supply of this anæsthetic, and at a reasonable price, seems to be an important bar to its more general introduction at present.

Chloroform. It is in order here to add a few words respecting this historic member of the series of chlorine derivatives of the alcohol :— thanks to the late Sir James Y. Simpson, of Edinburgh,—now that a quarter of a century has recorded its abundant testimony for and against what in every judgment must be regarded as one of the most wonderful agents added to the materia medica by chemical research. The cautious teachings of experience, and in Dr. Richardson's case of 87 experiments, conducted specifically to determine the direct influence of chloroform on the heart ; the result has been the conviction that the cause of death from chloroform is in every case due to arrest of the nervous function, and that the idea of any direct action of the agent on the muscular structure of the heart is without foundation. This opinion is in direct contradiction to the weight of professional opinion entertained prior to Dr. Richardson's researches and to his own as expressed in his report in 1866, page 178, in which he says "chloroform kills by its paralyzing influence on the heart." But the more mature judgment now quoted being sustained by numerous physiological experiments is entitled to the greatest consideration. The main disadvantage of chloroform is its high boiling point, requiring a great amount of vital force to eliminate it from the body, so that it is probably never eliminated entirely by the lungs, but only with the aid of all the excreting organs, any deficiency or derangement in which may consequently lead to such suppression of elimination that the nervous systems may be overwhelmed, with consequent arrest of their activity. Nevertheless, many surgeons greatly prefer chloroform to ether or any other anæsthetic, and I am permitted to cite the experience of my distinguished friend Dr. Samuel D. Gross of Philadelphia, who assures me that in an experience of over twenty-five years, in which he has administered it almost daily in his extensive surgical practice, he has had no fatal result. Still we must remember that chloroform belongs to a family of unenviable reputation. The best means of restoration in impending death from chloroform is the introduction into the lungs by artificial respiration of air heated to 130 F., by means of a bellows and coil of metal tube heated by a spirit lamp, injecting through one nostril.

The Tetrachloride of Carbon ($C\ Cl_4$). This body is the final result of the action of chlorine upon marsh gas, all the atoms of hydrogen in methyl being replaced by chlorine. It is a fluid of high density (1.6) not very pleasant odor, and boils at 172° Fh. In its physiological action it resembles chloroform, but is slower in inducing anæsthesia and much slower in passing off, a result fully in accordance with its high boiling point, (chloroform boiling at 142° Fh.) It is Dr. Richardson's distinct enunciation, as the result of experiments, that it is more dangerous than chloroform, and if it were generally used it would act fatally in a much larger number of cases. The last chlorodized member of this important family is also the last in point of introduction to medical use and one of the most interesting, viz:—

Chloral Hydrate, ($C_2\ H\ Cl_3O$.) This powerful narcotic was first brought to the notice of the profession by Liebreich of Berlin, in 1869, and has since obtained a world wide reputation. This agent affords another illustration of the comparative slowness with which the discoveries of chemistry make their way into medical usage. Liebig discovered chloral and its hydrate in 1832, the same year in which Gutherie discovered chloroform in this country. Chloral is the final product of the action of chlorine gas upon absolute alcohol, and also, more cheaply, by the action of chlorine upon starch or sugar. The first exact knowledge the readers of English had of its physiological relations was communicated to the British Assocation at Exeter in August, 1869, by Dr. Richardson, who has since continued his researches upon it in the report of 1870. The calm result of opinion based on a great number of observations is that it holds its place only as the rival of the old and time-honored organic compound opium: that its results in some respects are subordinate to this drug and its derivatives; and that it is less potent in relieving acute physical pain than in calming the senses and producing deep, but not insensible sleep, is also probable. But whatever modification of opinion may arise concerning it, "it is an established messenger between science and disease, and must henceforth find its place in the pharmacopœia of all civilized peoples. "If I were to say," writes Dr. Richardson in 1869, "that a million of persons in sleepless pain had been made to rest quietly and painlessly under its benign influence, I should certainly not overate the extent of its usefulness." That its incautious use should have produced some disastrous results cannot be wondered at, especially when we remember how often it is used without medical advice, by patients who are completely ignorant of the potency of the agent they so rashly tamper with.

The Iodides and Bromides of this series are anæsthetics comparable with the corresponding chlorides for activity, but objectionable on account of the irritating qualities which accompany them. But the *Iodide of Methyl* has been found to possess remarkable powers as a sedative when administered in solution, and has proved serviceable in treatment of cancerous ulcers and in allaying pain, especially in case of extreme sensitiveness of the skin, as in hyperæsthesia. Mr. Nunn, of Middlesex hospital, states that it can be safely administered for long periods for the removal of pain, and that cancerous ulceration may heal under its use, but he is not prepared to say that it will prevent the deposit of cancer. As the iodides of this series exert an eliminating as well as an anodyne power on glandular structure, they promise to be of great service in medicine. *Iodide of Butyl* will probably be found the best of the series. They are best exhibited in the form of syrup, but may be also used by sub-cutaneous injection. *The Bromide of Ethyl* has also developed remarkable narcotic powers, there being almost no nervous or muscular irritation preceding the narcotism, but an almost immediate transition from the first to the third degree of anæsthesia. It is however an unstable compound and produces a certain degree of local irritation and dryness of the throat.

Ether. In the present state of knowledge there are few who will feel disposed to controvert the opinion that the oxyd of ethyl or pure rectified ether is the best of all known agents for the production of general anæsthesia by inhalation. Almost the only objections to its use are those which have arisen from impurities which the official article is permitted by the absurd rule of the pharmacopœias to contain. The subject is too familiar to require further comment here.

The Nitrite of Ethyl or Nitrous Ether was not spoken of in connection with its congeners. Its action is perfectly analogous to that of the nitrite of amyl. The introduction of nitrogen into these ethers seems to give to them properties like those found in certain alkaloids, as strychnia. The same power to produce suspended animation which was described in the amylic nitrite, is found in the ethylic salt with another yet more remarkable which Dr. Richardson thus describes: "If a young animal, say a kitten, is subjected so suddenly to the ethylic nitrite as to fall sensless and to appearance dead in or within a minute, it will remain in the same state for six or even ten minutes yielding no evidence of life; it will not breathe and the most delicate oscultation will fail to detect motion of the heart. But after a period varying from six to ten minutes it will spontaneously recommence to breathe, and with every movement of expiration a breath sufficient to dull a mirror will pass from the rabbit. As the breathing recommences, the heart also begins its work, making a series of distinct intermittent strokes. This condition, looking like an actual return of life, will last so long as half an hour, and will then cease gradually, the animal lapsing again into a state of actual inertia, or death.

In the Acetate of Ethyl and *Hydrofluoric Ether* we have two most remarkable bodies, unsuited to inhalation, but capable of being largely and usefully employed for the destruction and removal of morbid growths. Directed upon the blood they break it up absolutely, destroying alike the corpuscles, the fibrine and the albumen. Hydrofluoric Ether may be looked upon as a universal solvent of the animal tissues, nothing escapes its action except the gelatinous structures, and those not altogether.

Two other ethers demand a passing word, they are *Triethylic and Trimethylic Ether* formed when chloroform is made to act on sodium or potassium ethylate or on sodium or potassium methylate. A chloride of the metals is formed and an ether is liberated either Ethylic or Methylic according to which salt was the one employed. Triethylic ether is supposed to be homologous with an ether of a triatomic alcohol, triethylic $C_7 H_{16} O_3$, so called by Dr. Richardson. The second is homologous with trimethylic ether.

"Triethylic ether is a heavy aromatic fluid boiling at 174 F., and having a vapor-density of 71. It passes into vapor very slowly, unless the temperature of the air be considerably raised, and hence at ordinary temperatures the action of the ether is very faint when it is administered by inhalation. But in making the ether I observed that the first distillation yielded as a product a volatile chloride, of very delicate aromatic odor and without exception the most perfect general anæsthetic I have ever employed or seen. This compound is so quick in action that it may be diluted with half its volume of absolute ether, and still yield a vapor of a sufficient narcotic power to be available for long or short operations. Exposed to the vapor, pigeons and rabbits glide into the deepest sleep and unconsciousness without a movement and in a state more strikingly resembling natural sleep than any other condition. Administered in a case of strabismus the action was simply perfect. After inhaling the vapor, the patient subsided into what seemed a natural sleep, without a convulsive or disturbed movement; the operation was performed without the faintest manifestation of sensation, and recovery was perfect in one minute after the vapor was withdrawn. The experience of the action of the narcotic I have here described is so good that I could not let it pass silently; but I am not yet sure whether the application can be brought into general use. The production of the fluid is troublesome and costly, and after a time, if exposed to the air, it loses its efficacy. In brief it is not a homogeneous substance, and is therefore open to the objections urged against other compound fluids.

"The part played by the heavy ether is excellent, in that it equalizes diffusion and prevents pungency of vapor. Further research may improve it.

"*The trimethylic ether* of which I have spoken is a much lighter fluid than the triethylic, boils at 140° F., and has a vapor-density of 53; but the odor of its vapor is not agreeable, and although it produces safe anæsthesia, it is not perfect in its action."

We will close our notice of these most interesting researches by citing, from Dr. Richardson's Report for 1870, a remarkable passage upon the relation of consciousness to sensibility, equally instructive to the psychologist as to the physiologist.

"The metaphysicians, in treating of conscious and unconscious states of mind, have long taught that there may be periods of consciousness with an absence of common sensibility. The truth of this inference is sustained by physical inquiries. In a previous report on amylene I pointed out that the vapor of amylene while it destroys sensation, does not destroy all conscious acts; and in my later observations on the action of methylic ether the same fact has been more perfectly elicited. In several cases where I administered this ether for removing pain in surgical operations, the patients, when quite insensible to pain, were so conscious that they were able to obey every request asked of them, and in some instances were even anxious to reason, stating that they knew what was going on, and arguing that they were not ready for the operation because they were sure they should feel pain. Nevertheless in this state of mental activity they were operated on, and afterwards, while remembering every incident, were firm in their assertion that they felt no pain whatever during the operation. One patient, who sat for the extraction of two teeth, selected the tooth to be first extracted, putting her finger on it, and afterwards reärranging her position for the second removal. To the looker-on it seemed in fact as though no change in her life had occurred, yet she affirmed that she was sensible of no pain whatever; and several other less striking but hardly less singular examples came before me. We may then, I think, fairly assume that in course of time we shall discover manageable and certain anæsthetic substances which will paralyze sensation only, leaving the muscular power unaltered and the mental little disturbed; and we gather from this either that in the cerebral hemisphere there is some distinct and simple center of common sensation, which may be acted upon by certain agents, without involving all the cerebral mass, or that the peripheral nervous matter may be influenced without involving these portions of the nervous system. On the whole I incline to the view that the action of those agents which destroy pain before they remove consciousness is primarily in the peripheral system;

for we know, from the process of local anæsthesia, that it is easy to destroy sensation at the extremities, without destroying, or even interfering with consciousness, while those who have inhaled the vapors which destroy common sensation before interfering with the mental condition invariably describe the experience of a numbness and insensibility in the extreme parts of the body. That which we medical men most require is an agent that shall be easily applied and shall admit of being so applied generally as to induce insensibility to pain with or without destruction of consciousness, as the case before us may demand.

"There are many minor surgical operations for which consciousness need not be destroyed, although pain ought to be; there are other operations in which the consciousness of the person operated upon is of great service to the operator: and there is a third class of cases in which it is essential to suspend both sensation and consciousness.

"Now those agents which first destroy common sensation can always be pushed to the extent of destroying consciousness, so that if we could get a perfect agent of this kind we should have the full requirements in our hand. Up to the present moment we have been content with two classes of agents, one which destroys consciousness and sensation at the same time, the other which locally destroys sensation, and has no influence on the consciousness. I look hopefully for a method in which, by means of a single agent, we shall be able, at will, to suspend common sensation alone, or to exalt the process into suspension of consciousness. When this object is attained, with safety and facility, the science of anæsthesia may be considered as perfected."

You cannot fail to see that with the close of this century of chemistry and medicine a new era has opened upon medical science, in which the resources of chemistry are being made available through the researches of the physiologist with a degree of certainty in their medical results hitherto unknown. By the more thoughtful of the profession it has long been felt that the use of drugs and other articles of uncertain value, applied in an expectant manner without a definite knowledge of the disease or its remedy was equally irrational and unscientific. I have cited largely the labors of Dr. Richardson, because he is one of the few physicians who adds to the skill of an expert chemist, an accurate knowledge of physiology and abundant medical experience, the fruit of a varied practice, combining all these qualities with the rarer gift of an original investigator. To such a man, all things are possible which it is in the power of the human mind to grasp. From the contemplation of such examples we learn the important lesson that *truth* yields her secrets only to labor,—that she is (as Lord Bacon long since declared) the daughter of time and not of authority.

As students of medicine you will also learn, by the study of such results as we have been considering, that truth is one, however varied the factors which enter into the grand total, and that it is never safe to disregard even the least of her teachings. Thus guided, gradually but surely the curer of disease will learn from the chemist and physiologist, that remedies rapid in action, easy in administration, positive in result, must all come from organic nature.

Thus learned the physician exchanges dogmatism for wisdom, faith for knowledge, doubt for certainty. He will compete with his fellows by the pure struggle of intellect, he will be responsible for results without evasion, and his duties will be more solemnly his own. Standing where he never stood before, a conscious master of his art, he will know in what he doth believe, and the world assured by his exactitude will learn to know none but him in his vocation. Coming from an investigator who has himself done so much to give them value, these words of Dr. Richardson have great force in concluding his report of 1869. "The leading idea of the report is that of studying the action of substances which are to become remedies, not by the old and faulty method of so-called experience, but by proving physiological action. I am certain the time must soon come when the books we call Pharmacopœias will be everywhere reconstructed on this basis of thought, and when the chemist and physician will become one."

Life and Death.—In the use of many of the remarkable agents we have been considering it is obvious we are treading very close upon the shadowy border which separates life from death. The simulation of death in some of them is so perfect as to lead us to ask whether the marvelous stories told of the Fakirs of India, may not have a foundation in substantial truth. Dr. Richardson conceives it quite reasonable to presume that the Fakir holds in his hand some substance derived from the vegetable world which even more than the amylic nitrite possesses the power when introduced into the human body of suspending the common signs of animation for a certain number of hours, and that in this borrowed likeness of shrunk death the facts of the phenomenon are presented and explained. The result of experiments like those of Pasteur, Wyman and others, on the limits of life and its possible development and maintainance under conditions once believed to be wholly inconsistent with vitality, teach us that there is yet much to learn which will probably greatly enlarge our knowledge of those mysterious conditions, partly physical, partly spiritual, which we include in the comprehensive words, life and death. It may not please Him with whom are the issues of life to delegate to us, His creatures, powers which are divine, but is it presumptuous in us who are made in His likeness to believe that by taking hold of the ways of life in the humble spirit of devout searchers it may be granted to us to enter far more closely within the veil which yet shrouds the connection between matter and spirit?

We have occupied so much time in the review of the labors of Dr. Richardson that we can only allude briefly to some other researches of a like nature. Prominent among these are the researches of Dr. Crum Brown and Dr. Thomas B. Fraser, on the connection between chemical constitution and physiological action.* The pioneer in this line of research was Dr. James Blake (now of San Francisco). His important memoir † "on the effects of various saline substances injected into the circulatory system" proves that there exists a close relation between the chemical properties of the substances experimented upon and their physiological effects: his experiments, going to prove that when introduced into the blood substances

* The results of which are given at length in the Trans. of the Royal Society of Edinburgh for 1868–69.

† Published in the French Archives Génerales de Medicine for Nov. 1839.

which are isomorphous exert similar actions on the living tissues; and that salts with the same base have analogous actions.

He tested the action of salts of magnesia, which were found, when introduced in any quantity into the blood, to arrest the action of the heart, with complete prostration of muscular power. The salts of zinc, isomorphous with those of magnesia, have a similar action, but produce the same effects in smaller quantities. The salts of copper, of lime, of strontia, of baryta, and of lead are considered in the order in which they are more closely related by their physiological actions. The peculiar action which the salts of the three last named substances exercise upon the muscular tissues, occasioning contractions in them during many minutes after death produced by their introduction into the blood. These muscular movements were in some cases observed 45 minutes after the cessation of the heart's action. His experiments on the salts of silver and soda reveal a remarkable similarity in action upon the pulmonary tissue, on the heart, and on the systemic capillaries; for while in the case of all the other salts already mentioned, death seems to be produced by the destruction of the irritability of the heart, the fatal result with the salts of silver and soda is the consequence of their action on the tissues of the lungs. The physiological action of the salts of ammonia and of potassa were found by Dr. Blake not to correspond with any of the preceding. Although agreeing perfectly with one another in their action upon the heart and the systemic capillaries, they differ extremely in their effects on the nervous tissues. Ammonia being particularly distinguished from all inorganic compounds in this respect, and being very analogous to poisons derived from organic products which it also resembles in its chemical properties. This last observation respecting ammonia, a nitrogenous compound, has received ample confirmation in the researches of later chemical physiologists, and especially in those of Dr. Richardson on the nitrites of the alcohol radicals and of Drs. Crum Brown and Fraser on the salts of the ammonium bases, derived from strychnia, brucia, and other alkaloids. In the first part of this memoir Drs. Crum Brown and Fraser detail the results of 134 distinct experiments on dogs, rabbits and frogs, with subcutaneous and stomach exhibition of the iodide of methyl-strychnium, the sulphate, nitrate, and hydrochlorate of the same base and of the corresponding salts of morphium, narcotium, codium, thebaium, brucium, in contrast with strychnia, brucia, thebaia, codeia, morphia, and nicotia, either alone or as the hydrochlorates of those alkaloids, giving the doses used, how administered, the effects produced, the interval between the administration and commencement of symptoms, and their duration.

The second part of the paper is devoted to the action of the ammonium bases derived from atropia and conium. The tabulated results of this research embrace 110 separate experiments upon the same animals. The agents used were iodide of methyl ammonium, iodide of ethyl-atropium, iodide of dimethyl-conium, hydrochlorate of methyl-conia, hydrochlorate of conia, sulphate of methyl-atropium, and sulphate of atropia; the same conditions and results being recorded as in the first part of the memoir. It is well known that doses of strychnia, varying from $\frac{1}{20}$ to $\frac{1}{30}$ of a grain, rapidly produce in rabbits most violent tetanic convulsions and in a few minutes death. But these physicians found that a dose of 12 grains of iodide of methyl-strychnium when administered (by subcutaneous injection) to rabbits weighing 3 pounds produced no effect whatever. Fifteen grains produced symptoms altogether different from those produced by strychnia. In place of violent and tetanic convulsions and muscular rigidity the appearances were those of paralysis with complete general flaccidity. The spinal motor nerves were then paralyzed or speedily became so, and instead of the rapid occurrence of muscular rigidity, the muscles remained flaccid, contractile and alkaline for hours. In short by the addition of iodide of methyl as a chemical factor in the constitution of strychnia the poisonous power of the latter is diminished about 140 times; and the new body formed has the properties of South American arrow poison, known as curare, namely paralysis of the outer ends of the motor nerves.

Our authors have also discovered that the poisonous powers of brucia, codia, and thebia, are proportionately diminished in their corresponding methyl ammonium salts, likewise simulating the action of curare. The convulsive powers of morphia when similarly combined with methyl are destroyed, while the soporific or hypnotic power remains.

Time fails us to follow this interesting research throughout, as it would be most instructive to do. Sufficient has been said to show its general scope, and to establish the broad proposition which is now proved by so many examples that the physiological, and doubtless also the therapeutical power of agents is essentially modified, if not entirely depending on, chemical constitution, using that word in the sense attaching to it in our modern chemical ideas.

If any one yet desires to ask what the century of chemistry now closing has done for therapeutic medicine let him take up any formulary of a century old and look for almost any of the more familiar articles which form the staple of medical practice to-day. He will find set forth in the pharmacopœias of a century agone, with the greatest prominence, such simples and carminatives as balsam of tolu, syrup of marsh mallow, camphor, red coral, castile soap, ginger, worm wood, James' powder, musk, mace, mummy, album græcum, powdered spiders, viper, millipedes, stomachic tincture, and aqua pura. Of the more potent medicines then known but little use seems to have been made. Iron and its salts, opium, mercury, jalap and rhubarb were comparatively rare medicines. Peruvian bark finds its place among astringents, in which category fall also calomel and rhubarb. Burnt sponge is used as an alterative, in all innocence of iodine, which was as yet unknown for more than a generation. Alcohol seems to have been used chiefly for tinctures, and there is no class known as tonics. If we examine the prescriptions it is difficult to say whether a feeling of amusement or disgust at the utter empyricism evinced, is uppermost. Viper broth, and spermaciti for consumption; oak bark and gall nuts for diabetes; musk, decoction of intestines of fowl, red coral, burnt rhubarb, chalk, &c., for diarrhœa; tartar emetic for whooping cough; calomel and sulphur ointment for itch, are a few examples of the therapeutics of the leading physicians of London a century since. Not to do these worthy men the injustice to suppose that they dealt only in such extreme simples it must be remembered that there was one form of iron which was an unfailing *vade mecum* and cure-all with them, and that was the *lancet*, with which they made their practice truly heroic.

It has been well said "that the period of one hundred years ago was the weakest of all eras in medicine. The world then was certainly not killed by its doctors, but assuredly it was not cured by them! And yet, paradoxical as it may seem, the time at once negative and critical was a great period in the history of practical physic."

Groping in the dark for want of guides, blundering over the simplest facts of chemistry and physics, because as yet these knowledges were not developed as sciences — dreaming over the rudiments of physiology, because as yet, physiology as a science was an impossibility;— the art of medicine a hundred years ago was resting on its oars, drifting upon the chartless ocean of its own empyricism, its art, as art, exhausted, and comparatively fruitless, it was waiting as if in obedience to the teachings of the great master Albertus, whose principle of cure *per expectationem* it had adopted, for something new to turn up;—when suddenly the light of Priestley's "dephlogisticated air" broke out on the darkness, and Lavoisier's "oxygen" sharpened the dim eyes of Chemist, Physiologist and Medical man to discern the paths of progress toward the truths of real science, to which thenceforth all art became subordinate. Then for the first time also in the world's history did physics lend its efficient aid to medicine. Galvani proclaims the existence and nature of animal electricity. Volta discovers the pile which bears his name and with which Davy presently resolves the earths and alkalis into their metallic radicals; and the impress of whose electrical nomenclature still stamps the language of chemistry. Cavallo also in his electricity, as early as 1777, had boldly proclaimed the curative powers of electricity.

Then was struck out the new nomenclature of chemistry, the value of which in defining power and in imparting definite ideas, in place of vague and inexact or senseless terms, cannot be too highly estimated. Before the close of the last century, Berzelius of Sweden commenced his immortal labors in chemistry, which closed only with his life in 1848, at the age of 70 years. Reviewing his labors is in fact writing a history of our science for the 50 years of his active career. He gave us the definite data on which the atomic theory of Dalton was established and has supplied the symbolic notation of chemistry substantially as we use it to-day. More than any one else he may be called the Father of modern chemistry.

Prior to 1817 the only alkalis known were those of the group of inorganic bodies of which potassium is the type. In that year Sertürner drew attention to the existence in opium of a substance whose alcoholic solution acted upon vegetal colors like solutions of the alkalis, combining directly with acids to form neutral salts which were soluble in water and reäcted for acids like the salts of the inorganic alkalis. This new substance, Sertürner called *morphine*, and in consequence of its possessing the properties just mentioned, he regards it as a sort of alkali. Immediately following this important discovery it was found that many vegetable products which had long been known for their powerful physiological and therapeutic effects, such as Peruvian bark, tobacco, deadly nightshade, nux vomica, etc., contained similar alkaline principles. Since 1848 a great number of organic alkaloids have been obtained artificially, in addition to the very considerable number which have been drawn from the vegetable kingdom. The total number of bodies referred to this class, now known to chemists, and formulated, considerably exceeds two hundred. Without exception they are compounds containing nitrogen in union with carbon and hydrogen, while a considerable number contain in addition to these elements oxygen also, and all are believed to be derivatives of ammonia, and most of them are formed on the model of ammonia; that is they unite directly with acids to form salts without eliminating water or any other substance.

In 1819 Oersted discovered the fundamental facts of electro-magnetism, and in 1830–31 Henry and Faraday developed the laws of induced currents, reproducing from the pile the intense phenomena of static electricity, and enriching the medical art with a multitude of physical facts and instruments for the early establishment of a new department of therapeutics.

In reviewing the field of modern chemistry, organic and inorganic, in view of its physiological and therapeutic relations, it is simply impossible to form the slightest rational conjecture of the probabilities which are in store for the healing art in the near future. The ground gone over in this lecture may appear extensive, but it is only a corner of the vast domain, in every part of which mines of rich ore are waiting only the exploratory work of the physiological chemist to reward humanity with new blessings even more fruitful of good, perhaps, than those the history of which we have so rapidly sketched.

The time was when chemistry existed only in the hands of the so called *Iatro Chemists*, or Doctor Chemists. This name has often been used as a term of reproach, but the labors of such doctor-chemists as those whose researches we have been considering, are fast teaching us that great discoveries in therapeutics and physiology are to be made only by renewing the bond which make the Physician and Chemist one; and may we not truly say that if every chemist is not a doctor, every doctor must be a chemist, if he would march in the van of the great army of those who by searching would find out the truth, and by its skillful and scientific use bless mankind, and crown their lives with happiness and honor.