# SCIENCE

VOL. LXXII FRIDAY, JULY 18, 1930 No. 1855



SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. MCKEEN CATTELL and published every Friday by

THE SCIENCE PRESS

New York City: Grand Central Terminal

Lancaster, Pa. Garrison, N. Y.

Annual Subscription, $6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

# PROMOTION OF MEDICINE AND PHARMACY[1]

**By Professor REID HUNT**

HARVARD MEDICAL SCHOOL

ONE of the duties of the president of this convention, as stated in the by-laws, is the presentation of an address "embodying such subjects as may seem to him suitable to the occasion."

Since many of those present are attending a meeting of the convention for the first time, it may be well to speak briefly of the purposes and history of this organization. It was founded in 1820 and has been in continuous existence ever since; the first sessions were held in the Senate Chamber of the Capitol. It is one of the oldest organizations in the United States, antedating by many years the American Medical Association, the American Pharmaceutical Association, the National Academy of Sciences, etc. It was founded by physicians; perhaps it would be more accurate to say that it was founded by a single physician, Lyman Spalding. Spalding was a man of rare vision; he was a pioneer in medical education and sanitation; he had an important part in the introduction of vaccination into the United States. His most important service, however, was the founding of the U. S. Pharmacopoeia, which is the oldest national pharmacopoeia of a modern type in the world. The U. S. P. was the first pharmacopoeia to adopt the recommendations of the Brussels Conference for the Unification of Potent Medicaments; it thus became the first national pharmacopoeia with an international character. It has also been translated into Chinese and Spanish; it is the official pharmacopoeia of Cuba.

This convention, which is incorporated under the laws of the District of Columbia, is different from most associations; the members are not here for any personal gain; all their activities are in the interest of the health of the people of the United States.

[1] Presidential address delivered at the 1930 U. S. Pharmacopoeial Convention, on Tuesday, May 13, in Washington, D. C.

The articles of incorporation state that the objects and business of this association are the promotion of medicine and pharmacy by selecting such materials as may be properly used as medicines and drugs, establishing formulas for their preparation and standards for identity, strength and purity.

Thus, provision for the selection of materials which may properly be used as medicines is the first duty of the convention.

So perhaps our function may be compared to that of those who are behind the lines of combatant troops: to select, standardize, properly label and pass forward the munitions which the actual fighters need. How important is the correct labeling of a drug may be indicated by the fact that one drug (epinephrin) was passed forward under thirty-five different names. The physician is constantly confronted with so many difficult problems that it is unfair both to him and the patient for such additional confusing factors to be introduced.

I think we must admit that those whose lives are spent in constant contact with the sick are in a better position to judge of what is and what is not useful than are those who can get such information only by gossip and hearsay. Hence, it has usually been the custom to place the major portion of the responsibility of determining what medicinal agents shall be admitted to the Pharmacopoeia upon the medical members of the convention, while much of the remainder of the revision work has been carried out by the pharmacists and chemists, who were invited by the physicians to join this organization in 1850.

This general principle was enunciated in 1820 by the founders of the U. S. P. in the following words: "It is the object of a pharmacopoeia to select from among substances which possess medicinal power, those, the utility of which is most fully established and best understood; and to form from them preparations and compositions, in which their powers may be exerted to the greatest advantage." Similar views had been expressed in the Pharmacopoeia of the Massachusetts Medical Society (1808)—the first civilian pharmacopoeia prepared in the United States, and which served as a model for the U. S. Pharmacopoeia. The authors of this work also had decided views as to the responsibilities of the two professions concerned with the preparation of a pharmacopoeia. They stated: "As it is the business of the physician to prescribe and of the apothecary to prepare medicines, the physicians as a body ought to point out those articles of medicine which they shall ordinarily employ, and the standard preparations of them." In later revisions reference was made to the "wants of the medical profession," the undesirability of "pandering to fashion," etc.

These principles were reaffirmed by the last convention when it stated that the object of the Pharmacopoeia is to provide standards for drugs and medicines of therapeutic usefulness or pharmaceutical necessity. In carrying out this program, fifteen subcommittees were elected; eleven of these consisted largely of pharmacists and chemists, whereas in four, medical representatives predominated. In the committee on scope (admissions and deletions) there were sixteen representatives of medicine and five of pharmacy.

This principle of "therapeutic usefulness or pharmaceutical necessity" has prevailed during much of the hundred and ten years of the existence of the Pharmacopoeia, but for a comparatively brief period "used" rather than "usefulness" seems to have governed the admissions. This led an eminent physician, for twenty years president of the convention, to state that there were preparations in the U. S. P. no more active or more useful than brick dust, and that brick dust would go into the Pharmacopoeia if there were a demand for it.

Such a view of the scope of the Pharmacopoeia has not been usual; it is inconsistent with the very purpose of the work as stated in the articles of incorporation; certainly medicine and pharmacy would not be promoted by the inclusion of worthless drugs. Physicians have frequently been thought to be rather indifferent to the Pharmacopoeia and perhaps for two or three decades they were: a physician engaged in a life-and-death struggle does not want his armamentarium cluttered up with brick dust and it has always been and always will be useless to expect his support for a work of that character.

That revision committees recognized the fallacy of basing admissions upon use is shown by the fact that, in the course of three decades, no fewer than 573 articles were dismissed from the U. S. P.; although the suggestions as to the preparations to be omitted originated for the most part with the physicians, the representatives of pharmacy, who outnumbered the physicians two to one, gladly acquiesced.

May not this return to the ideals of the fathers of the Pharmacopoeia be another recognition of how clearly the men of that day saw great general principles? Would not the founders of the Pharmacopoeia have been as surprised at some of the developments in regard to this work as the authors of the Constitution of the United States would have been at some of the amendments which have been added?

There never has been a time when there were not drugs in rather extensive use which were soon forgotten: the authors of the Pharmacopoeia of 1820 evidently had this in mind when they stated that, of the substances which possess medicinal value, only those

the utility of which is best established should be admitted to the Pharmacopoeia.

It would seem easier at present than ever before to adhere to these basic principles. Each of the professions chiefly interested in the Pharmacopoeia now has its own special book of standards into which preparations of more immediate interest to its members may be introduced: the National Formulary and "New and Nonofficial Remedies."

The National Formulary was founded by the American Pharmaceutical Association in 1888. The committee which prepared it stated that "it was not within the province of the committee to meddle with matters of which the medical practitioner is the proper and competent judge," and added that their object was to establish formulas for preparations which were used either by physicians or the laity and which were not in the Pharmacopoeia.

Thus these two works were designed for special purposes: the Pharmacopoeia as a book of standards for the drugs which the physician finds useful in the practice of medicine; the National Formulary as a standard for various preparations not in the Pharmacopoeia, but which the pharmacist is asked to supply. There seems to be little reason for confusing these functions, especially since the National Formulary has the same dignified standing under the national and state drug laws as has the Pharmacopoeia. The pharmaceutical profession also has a recipe book in which still more preparations, in which its members are especially interested, are described.

"New and Nonofficial Remedies," which is published annually, provides standards for drugs which seem to the physician to be promising and which are developed between the revisions of the Pharmacopoeia and the National Formulary.

It should also be recognized that each profession has its own peculiar interests: the need of the surgeon for drugs and supplies, while urgent, is limited to a comparatively few articles with which the pharmacist is directly concerned. Similarly, the modern drug-store has developed to meet a demand for many things in which the physician is not especially interested. May not this fact account partly, but only partly, for the feeling among some pharmacists that the medical profession does not give the support it might to professional pharmacy?

It is somewhat disconcerting, however, to find that a distinguished ex-president of the American Pharmaceutical Association (D. F. Jones), whose ideas of the relation of the professions of medicine and pharmacy to each other are so strikingly like those of the medical profession, has expressed the view that the Pharmacopoeia seems to have grown of less practical value to the professional pharmacist and the practicing physician. I think that it can be shown that, as regards the members of the medical profession, conditions are changing and that they are appreciating more and more the value of the Pharmacopoeia.

One reason why I speak with so much confidence of the interest, at the present time, of the medical profession in the U. S. P. and of their real and practical loyalty to the work, is based upon the little book, "Useful Drugs," issued by the American Medical Association—the largest association of physicians the world has ever known.

The drugs listed in this book, the eighth edition of which is now in preparation, are selected with but a single purpose: the welfare of the sick. There are no restrictions as to their source; the U. S. P., the National Formulary and the whole group of non-official and proprietary remedies can be drawn upon. The list represents the drugs which large numbers of physicians in active practice voted to be of prime importance, and a few vehicles and flavoring agents.

This list of drugs has been accepted by the national and state boards as the basis for examinations for license to practice and by the medical schools as the basis for the teaching of materia medica and therapeutics, and by leading hospitals as representing the most important drugs.

The number of drugs which it seemed necessary to include in this list may surprise many physicians—there are about 365 of them—more drugs than there are bones or muscles in the body; the drugs are more numerous than the diseases which a physician ever sees. The great war was waged with fewer munitions. And yet physicians are criticized for not prescribing more and still more drugs.

All but seventeen of the 365 preparations in "Useful Drugs" are in the present U. S. Pharmacopoeia.

The founders of the Pharmacopoeia stated in 1820: "The value of a pharmacopoeia depends upon the fidelity with which it conforms to the best state of medical knowledge of the day. Its usefulness depends upon the sanction it receives from the medical community and the public."

It may be that the adoption of the Pharmacopoeia as a legal standard, which necessitates the introduction of the most precise methods of analysis, has tended to diminish its usefulness to the practical pharmacist. But we can hardly begrudge this inconvenience when we think of what it means to the welfare of the people of the United States. These high standards also give the discriminating physician as well as the public greatly increased confidence in the U. S. P. drugs.

Possibly the asserted decline in the usefulness of the Pharmacopoeia to the pharmacist is more apparent than real; it may be a matter of dilution. An ob-

server can not but note the number of drug-stores and pharmacists in the United States, as compared with the number in some foreign countries; it is authoritatively stated, for example, that there are approximately 57,000 drug-stores in the United States, one to less than three physicians. In proportion to the population, the United States has six times as many drug-stores as has Germany.

The physicians have few professional interests aside from the care of the sick; they outnumber the pharmacists by almost two to one; is it not logical to let them determine what shall be included in the work which they themselves established? Of course, physicians at times have been woefully blind—blind for centuries—to the virtue of a drug, but have their colleagues in other fields seen more clearly? Certainly, in one of the most frequently cited cases of this kind, the physicians saw more clearly than did their critics. A recent writer states, as have earlier writers: "In 1880 a British Medical Commission learnedly reported that cocain had no medical value, being at best merely a poor substitute for caffein." No references are given as to where this commission reported, or who composed it. But, in any case, it seems to be forgotten that the really important use of cocain is as a local anesthetic and that this action was not recognized until 1884. Among the uses proposed for cocain before 1884 were the following: insanity, epilepsy, cachexia, bodily and mental exhaustion, melancholia, neurasthenia, hysteria, etc. It was also proposed to give it to soldiers and sailors to appease hunger and thirst and to relieve fatigue. The thought of cocainized armies and navies is rather appalling—our Army and Navy have had sufficient troubles with individual cases of cocain addiction. May not the "British Medical Commission" (whoever composed it), which is said to have reported adversely on the internal use of cocain, have been rather wise in their day and generation?

An examination of the preparations in "Useful Drugs" also shows that there are not as violent and as radical changes in the physician's use of drugs as many seem to believe. More than half of the preparations in "Useful Drugs" were in the Pharmacopoeia of the Massachusetts Medical Society of 1808. It is almost startling to find so many of the standard remedies of to-day in this 122-year-old book. The salts of iron, mercury, silver, copper, arsenic, antimony and zinc were there, as were also opium, digitalis, cinchona, ipecac, aloe, rhubarb, senna, chenopodium, sulphur and many others. Ordinary ether and the spirit of ether were there, although the most important action of ether—the production of general anesthesia—was not recognized until thirty-eight years later.

Chairman Cook has recently pointed out that, of the 305 individual therapeutical agents in the latest revision of the U. S. P., 114 were official in the U. S. P. of 1820—another illustration of how wisely our earlier predecessors selected the articles for the Pharmacopoeia.

Progress in drug as in other forms of therapeutics often seems very slow, and every one is painfully conscious of the great gaps to be filled. But, looked at from a broader point of view, the progress has been very encouraging. The drugs in the first edition of the U. S. Pharmacopoeia represented the achievements of mankind in this field in all the ages; some of the most important drugs (opium and its preparations, metallic mercury, etc.) were in the pharmacopoeia of Dioscorides of A. D. 77. The additional drugs in the tenth revision represent the advances in a single century.

This convention is the only representative organization in a great country devoted to the scientific consideration of drugs; it is the only place where pharmacists, chemists and physicians come together. Would it not be proper to consider briefly means by which new therapeutic agents may be added to what are already available? Every such addition increases the usefulness of the professions to the public and adds to the standing of both physicians and pharmacists in the community.

I may call your attention again to the wording of our articles of incorporation: the "encouragement and promotion of the science and art of medicine and pharmacy by selecting by research and experiment and other proper methods—such materials as may properly be used as medicine."

What was the source of the medicines in the U. S. Pharmacopoeia at present? How were their medicinal properties discovered? I mentioned how, speaking in very general terms, the drugs of outstanding, universally recognized value—the sort of drugs which led Sydenham to make his famous remark that without opium few would care to be physicians—fall into two groups: those which were available when the first Pharmacopoeia was published and the additional ones to be found in the tenth revision. A physician might hesitate if he were forced to choose between the drugs in the 1820 Pharmacopoeia and the new drugs discovered in the last 110 years. Again speaking in general terms, the drugs of the first period resulted from empiricism, those of the latter period from pharmacological experimentation; the drugs of the former period were for the most part available as such in nature, whereas among those of the latter group there are a large number of synthetic drugs. The plant world will doubtless still yield valuable therapeutic agents; the possibilities of the animal

world are by no means exhausted, but after all there is a limit to what can be expected from these sources. But the field of synthetic organic chemistry has no limits. Already some of our most valuable drugs have come from that field.

Some of the saddest pages in the history of mankind are connected with the failure of physicians to see the therapeutic possibilities in well-known chemicals. Take for example an incident, typical of many, which occurred at the Massachusetts General Hospital about 1821, as described by J. C. Warren: a patient with a dislocation of the hip was given powerful purgatives, a hot bath and then tartar emetic to produce deadly sickness; a vein was opened and blood drawn as rapidly and in as large quantities as possible (the "unholy trinity of bleeding, purging and puking"). Then pulleys were attached to the limbs and power traction exerted for an hour, with occasional intermissions to permit a slight recovery from the pain; but the dislocation was not reduced. A contemporary writer compared the procedure to the execution of a would-be assassin of a king of France: four powerful young horses, attached to the limbs of the criminal, pulled for fifty minutes before the man was torn asunder. Stories are told of how the cords to the pulleys broke and had to be repaired while the patient waited—stories strangely reminiscent of the breaking and repairing of the hangman's rope. The records of successful operations in those days usually closed with the words, "the patient was untied and returned to bed." But these methods were considered by the surgeons of Dr. Warren's time, and earlier, as very humane; Percival Pott remarked in 1779 that the mere relation of the methods used in earlier times was sufficient to shock any humane man. The descriptions of the machines, or, as they were called, "engines" of earlier days strongly suggest that they were transferred from the torture chamber to the clinic; or were they taken from the clinic to the torture chamber? There were stories of thumbs and even arms being torn off by these efficient "engines." Yet patients preferred even this kind of treatment to no treatment.

A drug by the use of which the vomiting and purging and bleeding and the pain in such cases could have been prevented had already been known for nearly three hundred years; Dr. Warren knew it in 1805; he and Dr. Jackson had described its preparation and properties for the Massachusetts Pharmacopoeia of 1808; it was in the first U. S. Pharmacopoeia. For a quarter of a century before the ether day of October 16, 1846, it had been in the very hospital in which Dr. Warren operated; the pharmacist knew it well, for he made it himself and often supplied it to the hospital students for their—politely called—"ether frolics." It was a well-known drug at the time of the American Revolution and during the Napoleonic wars, when a single surgeon sometimes did two hundred amputations in a day. Why this three hundred years' delay? Because the physicians of those days were convinced that they knew enough to state positively that such results as were caused by ether would never be obtained with any drug, and because they had not yet learned to appreciate the value of experiments on animals.

Many analogous scenes could be regalled: patients with lockjaw; blisters produced from ear to ear in the vain effort to secure relaxation of the jaw; teeth broken so that a few drops of water or milk could be given. Or consider the scenes in the tetanus hospital at Gettysburg: sentries removed far from the hospital so that the sound of their footsteps would not throw the inmates into spasms, or the night when a wind arose and rattled the windows and the wounded soldiers passed the night in one painful convulsion after another. Contrast this scene with one in a German military hospital in 1915. Again patients with lockjaw; unable to swallow; excruciatingly painful cramps, intense cyanosis. A small amount of a solution was injected into a vein: in two minutes the convulsions ceased, pain disappeared; the patients were soon eating, drinking, reading, playing cards, laughing. Or consider a scene at the Massachusetts General Hospital: a child in strychnine convulsions; life maintained by artificial respiration. A few drops of a solution injected into the spinal canal: instant recovery; in a few minutes, child interested in toys; no return of the convulsions.

And the drug in these cases was Epsom salt, well known to the medical profession since 1694 and, of course, in all the older Pharmacopoeias. But no one seemed interested until 1905 in determining what this drug would do when injected into an animal or a man.

Just one more such picture: "There was one poor man in the wards suffering dreadfully from angina pectoris; he used to have an attack every night and for two hours the unfortunate man would sit on the edge of his bed and could not move forward, backward, or to one side, with his face pale and sweat pouring off it, in perfect agony." Three or four drops of a drug were inhaled. The impossible happened: "instant and complete relief" in this most painful condition. And the drug, amyl nitrite, had been well known to chemists for twenty-three years.

The same story with acetanilid and similar drugs: relief may be obtained anywhere in the world for a few cents, which fifty years ago was beyond the reach of any potentate or Croesus. The bromides which in 1853 first brought relief to one of the longest

known and most distressing diseases, chloral hydrate, cocain, phenol and many other drugs were well known to chemists long before they were to physicians. Arsphenamine, introduced into medicine in 1910, is, from the chemist's point of view, only a slight modification of the arseno-benzene known since 1875, but it required the genius of the pharmacologist Ehrlich to see how the comparatively simple process of the introduction of hydroxyl and amino groups into this old and uninteresting compound would result in a drug which has so changed the outlook in syphilis and other serious diseases.

The discovery of the anesthetic action of ether has been described as "the most important event in surgical, and one of the most important events in human history." You remember Weir Mitchell's lines:

> Whatever triumphs still shall hold the mind,
> Whatever gift shall yet enrich mankind,
> Ah! here no hour shall strike through all the years,
> No hour as sweet, as when hope, doubt and fears,
> 'Mid deepening stillness, watched one eager brain,
> With God-like will, decree the Death of Pain.

But the introduction of ether had no effect upon the mortality of operations at the Massachusetts General Hospital. About two decades later, however, the number of operations began to increase at a rapid rate and there was a wonderful reduction in mortality. Operations scarcely dreamed of before were performed almost daily. A new drug, which was destined soon to have a greater influence upon medicine than ether, had been placed in the hands of the surgeon. And where had it been found? At a sewage disposal plant in Scotland. Lister thought that the carbolic acid which checked the putrefaction of sewage might check the putrefaction in wounds. This soon led to aseptic surgery, and another new era in medicine had begun. A medical orator stated: "Hand-in-hand, equal benefactors, anesthesia and asepsis march calm and triumphant"—but this impressive procession did not start for three hundred years after the discovery of ether and about fifty years after the discovery of carbolic acid.

Anesthesia and asepsis came when the medical profession had demonstrated to their own satisfaction that these were impossible.

How needlessly pessimistic have physicians been at times in regard to the discovery of new drugs is shown by that often quoted, or misquoted, but apparently not often read, essay on "Self-Limited Diseases" by Jacob Bigelow, one of the authors of the first edition of the U. S. Pharmacopoeia. Bigelow, writing in 1835, placed epilepsy and angina pectoris among the "self-limited diseases" in the sense that, as he says, the paroxysms of these "can neither be foreseen, prevented, nor, as far as we know, materially abridged in their duration."

How easily satisfied was Bigelow with the results from now almost discarded drugs is shown by his remark: "Thirty years ago, we might have added gout to the opprobrious list under consideration"; but states that gout might now be withdrawn from the list since colchicum and veratrum and abstinence from alcohol had so markedly lessened the frequency and violence of the attacks. The bromides, which are certainly far more efficacious in epilepsy than are colchicum and veratrum in gout, were well known to chemists when Bigelow wrote the above; amyl nitrite was discovered soon afterwards. Bigelow also made the remark, which seems never to be quoted: "In regard to the diseases which have been called self-limited, I would not be understood to deny that remedies capable of removing them may exist. I would only assert that they have not yet been proved to exist." However, in some mysterious way, this article, or the interpretation placed upon it, seems to have convinced the medical profession for generations that it is useless to look for new drugs of value. This attitude is strikingly evident in the dozen or more ether day addresses.

For many years ether day was celebrated with solemn pomp at the Massachusetts General Hospital; this was stated to be a day on which the adherents and friends of the hospital were accustomed to "take account of stock and to ask for such visions of the future as may guide it fruitfully." It might have been more appropriate to have observed the day as one of humiliation and repentance for the needless agonies inflicted in the three hundred years which elapsed between the discovery of ether and its application. But not one of the distinguished speakers seemed to have grasped the real meaning of the discovery: how it was possible to obtain with an ancient drug results which science and religion alike had taught to be impossible.

Nor was attention ever called to the fact that there were known in 1846 a number of drugs besides ether with which surgical anesthesia could have been discovered; nitrous oxide, ethylene, chloroform, ethyl chloride and bromide and acetylene were all well-known chemicals at that time.

The subject of surgical anesthesia was often treated as if it were a closed chapter; but steady progress is being made, as shown by the recent introduction or reintroduction of ethylene, and of various new local anesthetics, as well as of new general anesthetics. But the question should be seriously considered if man has even got on the right track in regard to general anesthesia. The effective anesthetic dose of the present general anesthetics is more than 50 per cent. of the

fatal dose—a smaller margin of safety than with any other class of important drugs. The essential action of anesthetics seems to be the blocking of the passage of impulses to the brain at certain synapses; impulses coming from the brain to peripheral organs may be blocked by drugs in a thousandth or even millionth of the fatal dose.

Another slogan which has done much to retard rational therapeutics is the "healing power of nature." Nature is certainly not very active in healing cancer, syphilis, tetanus, amebic dysentery, yaws, diabetes, myxedema, hookworm and many other diseases, many of which may now be relieved or cured by drugs. There is truth in Benjamin Rush's famous remark that nature should be turned out of doors and efficient art substituted for her.

Not only can the introduction of almost every modern drug into medicine be traced straight back to pharmacological experiments, but the rational use of some of the older remedies is almost wholly dependent upon such experiments. Even the underlying pathological conditions have often been elucidated by such work. To-morrow will be the twenty-fourth anniversary of the presentation to a medical association meeting in this hotel of a paper by two modest pharmacologists (the late Professor Cushny, and Edmunds, whom we have with us to-day) in which an explanation was offered for the first time of the condition (auricular fibrillation) in which digitalis produces its most spectacular results.

These pharmacologists were also largely responsible for the introduction into medicine of physiological standardization. Other pharmacologists, especially Hatcher and Eggleston, developed the subject farther and have done much to place digitalis therapy upon a firm foundation. Still, some of the latest model medical schools do not see any use in pharmacology; the faculties of the old proprietary medical schools often consisted of men of greater vision.

But it is not necessary to pursue this aspect of the subject farther; you would not be here if you did not have faith in drugs. But what are the possibilities of adding to the list of valuable drugs? Never in the history of the world have the possibilities been so great. When ether, chloroform, chloral hydrate, amyl nitrite, phenol, etc., were introduced into medicine, the number of synthetic organic chemicals was very few; they were numbered in hundreds, or at most in a very few thousands. A year of two ago the organic chemists had already carefully described the physical and chemical properties, method of synthesis, etc., of 258,000 organic compounds; about twenty new ones are being added to the list every day and, if there were a demand for them, they could be increased a hundred fold. Perhaps the pharmacologist would feel that a fair amount of knowledge is available as to the possible therapeutic value of two or three thousand of these; he can find casual references to some of the physiological effects of three or four thousand more, but, even with these, he is prepared for such surprises as occurred in connection with cocain, acetanilid, phenol, simple derivatives of arsenobenzene, etc.

Little indeed is being done to test these new compounds for possible medicinal value; at the present rate of progress it would require not only decades but centuries, perhaps a millennium, for the medical profession to examine what the chemists already have to offer.

No one doubts that an exact knowledge of the cause of disease may be of great value in its prevention or cure. But, in this topsy-turvy world, progress has not proceeded in a logical way. Some of the formerly most deadly diseases (smallpox and yellow fever) were the first to be effectually controlled, although even their causes are still unknown. More progress was made in the cure of malaria and syphilis long before their cause was discovered than in such diseases as pneumonia and tuberculosis, concerning which there is a large amount of exact knowledge. Only the most imperfect knowledge as to pathogenic bacteria was available when Lister revolutionized surgery and medicine by the use of phenol.

Empiricism gave us some drugs and poisons with a highly specific action: quinine and emetine ferret out and, under favorable conditions, destroy, the organisms of malaria and amebic dysentery; atropin paralyzes the ending of parasympathetic nerves; epinephrin stimulates the endings of the sympathetic; cocaine paralyzes the endings of sensory nerves, etc.

Pharmacology is duplicating these achievements of nature: malaria, amebic dysentery, syphilis, yaws, etc., yield to synthetic drugs.

There are many considerations which should tend to encourage the hope that a diligent and really intelligent study of the chemotherapy of cancer, for example, might lead to a cure before the cause is discovered. The highly selective action of drugs upon certain tissues is very suggestive; it was almost startling, for example, to have seen many cases in which methyl alcohol had destroyed a few cells in the retina and caused complete blindness, without there being the slightest indication of injury to other organs or tissues. May there not be in the vast number of known but untested compounds some which may have a similar effect upon the cancer cells? A person thinks again of the number of drugs known before 1846 with which anesthesia might have been produced.

Haphazard, random experiments in such a field avail no more than would similar experiments have

helped Ehrlich in his search for arsphenamine. Ehrlich's knowledge of chemistry and pharmacology was so enormous that he could quickly eliminate many compounds from further consideration; he would draw a circle and, after a few experiments, divide it into two and remark that only the compounds in one half of the circle seemed promising; later he would again draw a line and study the compounds in only one quarter, and so on.

Somewhat similar methods can and have succeeded in other fields of pharmacology, as well as in the chemistry of dyes. Ehrlich early recognized in cocain a group which he called an anaesthiophore group, analogous to the chromophore group of the dye chemist; the recognition of such groups has been the basis of the development of other local anesthetics.

The pharmacologist can already predict with a high degree of certainty what chemical compounds will have a "muscarine" or a "curare" or a "stimulating" or a "paralyzing" nicotin-like action. The central atom in such compounds may be nitrogen, sulphur, arsenic, etc.; but if certain side chains are present, the pharmacologist can be certain that the compound as a whole will have one or other of the above actions.

Time does not permit of more than the briefest possible consideration of the means by which work in this field can be speeded up. A comparison of the tenth with the fifth revision of the U. S. Pharmacopoeia indicates the progress made in fifty years. Among the important therapeutic agents added in this period are the arsphenamines, cocain and all other local anesthetics, every effective hypnotic, every analgesic (acetanilid, cinchophen, etc.), the salicylates, the nitrites, bromides, the antitoxins, nearly all the antiseptics, etc. Nobody questions for a minute the great value of these drugs. It is also evident that the United States has scarcely made a single really original contribution to this list. The great majority of these drugs were discovered in Germany and most of them in the pharmacological and other laboratories of the German universities or in special research institutes. At the present time, there is scarcely a university pharmacological laboratory in the United States the equal of a number in Germany forty or even fifty years ago.

There is no institute in the United States comparable to the one founded for Ehrlich at Frankfort in Germany. The contributions of Ehrlich to serum therapy had been so important that it was proposed to call the Frankfort institute a serum institute. Ehrlich, however, insisted that it be called an institute for experimental therapeutics and at the first opportunity practically abandoned work with serums and returned to pharmacology, to which he had already made important contributions. Just twenty-eight years ago, Ehrlich expressed the view that the "future of medicine lay in pharmacology." He was convinced, however, that the ideals of the pharmacologists had been unnecessarily low and chose to limit his work largely to one field of pharmacology which he later called chemotherapy. But the methods he pursued were the same as those he had used in his pioneer work on analgesic drugs, the therapeutic use of dyes and his fundamental work on cocain. (It may be remarked parenthetically that Ehrlich's famous side-chain theory originated from this cocain work; recently published letters of Ehrlich show the impatience he felt with what he called the stupid people who never realized that his conception of side-chains was wholly that of the organic chemist.) Ehrlich was able to make rapid progress in this field owing to his extraordinary knowledge of organic chemistry and his encyclopedic knowledge of pharmacology, and also his complete freedom in research.

It is not unusual in the United States for considerable sums of money to be made available for the discovery, for example, of a cure for cancer, an improved drug for syphilis, etc. Such gifts come from the heart rather than from the head. I saw such an experiment tried in Ehrlich's Institute. Ehrlich had accepted funds for a study of the therapy of cancer; the work began with enthusiasm, but after two or three years the workers were so discouraged that they placed a sign over their door: "Abandon hope, all ye who enter here"; and Ehrlich frequently warned, "Never, never accept money for one specific purpose." The history of arsphenamine was entirely different; the real beginnings of that work were so obscure and so unrelated to either syphilis or arsphenamine that they were never published, but the course can still be followed in the early laboratory note-books. First a purely theoretical study of the relation of the vinyl linkage in the quinine molecule to toxicity; there was no thought at that time of any possible relation of these compounds to pneumonia, but years later it was found that one of these came nearer to being of use in this disease than any previously known drug. The effects of the quinine compounds were studied upon various protozoa and then upon the organisms of sleeping sickness, but without encouraging results. Then pentavalent arsenic compounds were studied in connection with sleeping sickness, then various trivalent arsenic compounds, then arseno compounds. Finally, the arseno compounds were studied in connection with experimental syphilis of the rabbit, and the result was arsphenamine. Had Ehrlich been limited to a study of the compounds of quinine or sleeping sickness, or of any one group of arsenic compounds, arsphenamine might never have been discovered.

You remember how Woehler tried to make ammo-

nium cyanate and obtained urea, an observation which broke down the distinction between compounds formed as the result of so-called vital forces and ordinary carbon compounds, and how the experience of Woehler was compared to that of Saul, who was said to have gone forth to seek his father's asses and discovered a kingdom.

Conditions have never been as favorable for the development of such work in the United States as at present. Organic chemicals which a few years ago were imported from Germany in gram lots are now obtainable in tank cars. There are hundreds of chemists eager to cooperate with the medical profession in the investigation of these compounds for possible medicinal value. But not only are there at present few facilities for such work, but it is difficult for manufacturers to obtain trustworthy data even as to the possible poisonous properties of their products.

Within the last year or two funds aggregating nearly a million dollars have been available for research in pharmacology, some of which had very important bearings upon the treatment of disease and the public health, but great difficulty was found in finding laboratories equipped for such work; in many cases none was found.

Of course, we all appreciate what some American manufacturers are doing in this field; how, for example, they have completely relieved the humiliating situation in which the United States found itself at the beginning of the World War when no local anesthetics or modern arsenicals and few hypnotics were available. And American laboratory workers and physicians deeply appreciate the many courtesies and assistance which these firms are always ready to give. But, with a few notable exceptions, distinctly new fields have seldom been opened. The chances of making the books balance in work of this kind are small and not infrequently new drugs are placed on the market with the frank admission that there has been pressure from the sales department.

Pioneering work in this field has usually been done, as it should be done, in endowed institutions and has been pursued largely as a branch of pure science just as was the work which has led to the applications of electricity. It is just this pioneering work which at present is so much neglected in our universities and research institutions.

Perhaps some of those who have made large fortunes in the drug or chemical industry would be glad of an opportunity to aid in the founding of an institute analogous to that at Frankfort, the purpose of which was stated to be the study of therapeutics and which, under Ehrlich's direction, was devoted chiefly to the study of drugs. Recently, according to press reports, several million dollars acquired in the drug business were willed to a university; the undergraduate students are reported to be busy arguing whether this should be used for the promotion of athletics or for building more dormitories. Professor Lusk recently remarked: "We are building great comfortable homes for the students in our colleges; we are planning pent-house apartments for the internes in our hospitals. But who is concerned with the material welfare of the professor? The answer is, virtually no one. No pent-house apartments are thought of for him." But after all it matters little about the professors who are already in the work; they could not get out if they would. It is discouraging, however, to see almost every year brilliant and enthusiastic young men and women who are eager to undertake such studies but who soon learn that few institutions offer reasonably good facilities for such work and that the outlook for the future is very dubious in comparison with the opportunities in clinical work, not only as regards facilities, but also for advancement.

It is difficult to avoid the conviction that when the historian of the future discusses the present status of medical research in the United States, when he notes what the study of drugs has already meant to the human race and when he thinks of the quarter of a million or more untested preparations on the chemists' shelves, the present will seem one of the darkest periods in medicine; he may even find a parallel between the attitude of some of those now responsible for the trend of medical research and the complacency of Percival Pott who in 1779 thanked God that his contemporaries (who had ether but did not use it) were not cruel like their predecessors.

I can not conclude these remarks without again expressing my appreciation of the honor of being selected president of this organization. The contact with the officers of the convention and the members of the revision committee has been most pleasant, inspiring and profitable. As an *ex officio* member of the board of trustees, I have been privileged to see something of the business side of the work. No organization could have been more faithfully served. It has had the services of a wise and experienced chairman; those of two faithful and resourceful secretaries; a treasurer who not only looked after the financial problems with the greatest care, but who was always ready to help in a most practical way in any problem which arose; the modest, tactful, fair and broad-minded chairman of the revision committee.

The memory of the association with these and the other members of the board of trustees is one which I shall always treasure.

The convention has suffered severe losses by death,

including three vice-presidents and the secretary of the board of trustees.

It is a sad commentary upon the rate at which we live that it is impossible to do more than merely mention the names of men who devoted a lifetime to the problems in which we are so much interested—such men, for example, as the versatile and lovable Dr. Whelpley, and the charming and scholarly Dr. Power, who achieved preeminence in two countries by his important contribution to the knowledge of plant chemistry.

I can only ask the secretary of the convention to announce the names of the officials of the present convention who have passed away, and, in accordance with custom, ask you to stand for a few moments in honor of the dead.

# OBITUARY

## RALPH HAMILTON CURTISS

THE death of Dr. Ralph H. Curtiss, professor of astronomy and director of the Astronomical Observatories of the University of Michigan, which occurred on Christmas Day, 1929, brought grief to a wide circle of friends to whom he was endeared by the kindly and lovable traits of his character. To the world of science and to the university which he had served so faithfully and ably his loss is a grievous one. Both by his own researches and through the inspiration and wise counsel generously given to his students and coworkers, he has contributed notably to the advancement of astronomy. It is one of the tragedies of his untimely death that he was about to see the realization of the project for a new and larger observatory in a more suitable location for which he had planned and worked unceasingly. During his last illness the land for the observatory site was purchased, and it is to be hoped that the new edifice will be constructed in accordance with his plans as a fitting tribute to his memory.

Ralph Hamilton Curtiss was born at Derby, Connecticut, February 8, 1880, of Puritan parents, Hamilton Burton and Emily Wheeler Curtiss. The early training in this Puritan home, ordered in accordance with the fine traditions of the stock, left a lasting imprint upon his character and was reflected in many of the outstanding qualities which characterized his life —a high sense of duty and justice, untiring devotion to his work and a deep appreciation and love of scholarly attainments. In 1892 the family moved to Redlands, California, where young Curtiss received his elementary education, graduating from the local high school at the age of sixteen, with high honors.

After a year spent in working and saving to provide funds for his college education, he enrolled in the fall of 1897 as an undergraduate at the University of California, where for the next four years he not only maintained a high scholastic record, but entered enthusiastically into the many activities of student life. He was a good "mixer," popular in his fraternity, Delta Tau Delta, and in fact with all his associates, both students and faculty. To his genial and lovable traits was added the rare talent of a musician. He was a member of the University Glee Club and played the violin with unusual skill. Early in his academic career Curtiss was attracted especially to the science of physics largely through the influence and inspiration of the late Professor E. P. Lewis. Later he was drawn to astronomy by another great and inspiring teacher, Professor A. O. Leuschner, and he seems to have decided as early as his junior year to become an astronomer. Recognition of the excellence of his work as a student came through election to Phi Beta Kappa in his junior year, and of his standing in astronomy by his appointment the following year as an assistant in the Students' Observatory.

Early in 1901, with the requirements for graduation practically completed at the middle of his senior year, Curtiss was sent as a member of the Lick Observatory expedition to Padang, Sumatra, to observe the total solar eclipse of May 17–18. The degree of bachelor of science was conferred upon him by the University of California in 1901 during his absence on eclipse duties. There followed three years of graduate study in astronomy at Berkeley and Mount Hamilton, during which time he held one of the Lick Observatory fellowships. His work in this period laid the broad foundation for the future brilliant and successful career in his chosen field. He was equally conversant with the theoretical and the observational side, whether the subject lay in the older field of astronomy or in that of astrophysics. Keen and active of mind, skilful in the manipulation of instruments, untiring in his devotion to work, he was recognized by the members of both departments as a man of outstanding ability and scholarly attainments. At the Lick Observatory he made an extended spectrographic study of the Cepheid variable W. Sagittarii. In the course of this work he showed that low dispersion could be applied successfully to the determination of the radial velocities of stars of the later spectral classes through the use of a method which he developed for the measurement and reduction of the spectrograms. This method, to which he gave the name of "zero standard," satisfactorily eliminates the errors arising from uncertainties in the adopted wavelengths of the lines produced by the effect of blends,