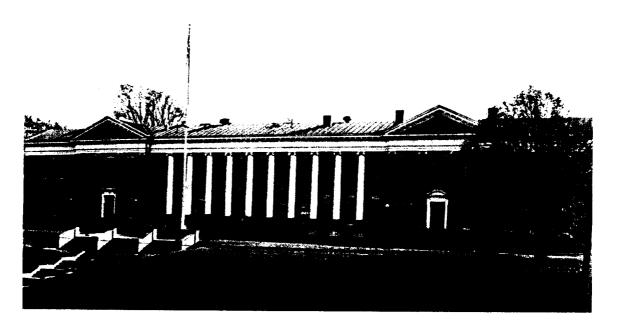


THE NEW AGE OF HEALTH LABORATORIES 1885–1915



This booklet, as well as the exhibit to which it relates, was prepared by James H. Cassedy.

The art work for both is by Daniel Carangi.

The Pasteur and Goldberger manuscripts displayed in the exhibit are from the collections of the National Library of Medicine, as are virtually all of the original monographs and reports and a major portion of the photographs.

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THE NEW AGE OF HEALTH LABORATORIES 1885–1915

AN EXHIBIT MAY-OCTOBER 1987

Marking the Centennial of the Founding of

The Pasteur Institute of Paris and

The National Institutes of Health

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The New Age of Health Laboratories 1885–1915

James H. Cassedy

Germs and the Creation of Laboratories

The bacteriological discoveries of the late nineteenth century represented a quantum leap in man's knowledge about diseases and life processes. This outpouring of new knowledge stirred up unprecedented excitement and hope among physicians and the general public alike. Scientists and health officials, meanwhile, recognizing that this wave of discovery could well be only the beginning, took advantage of the enthusiasm to push for improved facilities in which to extend their searches for the causative factors of diseases and for improved means of preventing or controlling the diseases. The result was a remarkable world-wide efflorescence of health-related laboratories, large and small, many of them university-related or governmentrun, but others independent.

Prior to 1880, research laboratories occupied highly anomalous positions in the medical world. Indeed, almost the only substantial health-related research establishments-one could not count most of the tiny medical school facilities for teaching elementary chemistry among them-were a small number of laboratories devoted to the study of physiology. The whole idea of bacteriological research, in fact, remained highly controversial, opposed by sanitarians who were seeking to improve health through environmental measures as well as by skeptics who remembered the many earlier failures of science to prove the germ theory of disease. During the last two decades of the nineteenth century, however, this opposition broke down before the cumulating weight of the new discoveries, and with it the importance of having good laboratory facilities for research was increasingly accepted.



R. Korh.

Robert Koch, 1843-1910

Among the projectors of the new laboratories were the earliest heralds and giants of the bacteriological age themselves—individuals such as Louis Pasteur in France and Robert Koch in Germany, who had worked out their convincing early proofs of the germ theory of disease with only the barest of research facilities. More often the projectors were students and disciples of the first pioneers along with investigators who from a distance had followed the early reports in scientific journals. Virtually all, in any case, shaped institutions that were predominantly concerned, at least in their early decades, with hygiene, microbiology, and the infectious diseases of mankind.

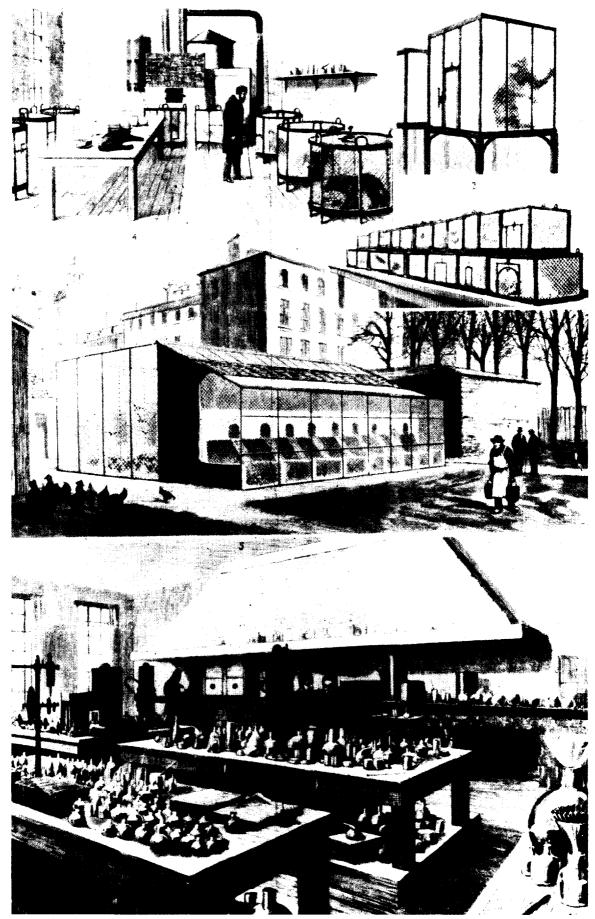
Relatively few of these new laboratories or institutes were devoted exclusively to research. In fact, scientists in some of them did practically none, but concerned themselves with such routine work as performing bacteriological diagnoses or producing and distributing vaccines or sera, both of which activities quickly became attractive sources of income. In many other laboratories, however, especially the larger establishments, research work was carried on along with one or more service activities.

Pasteur and the Pasteur Institute, 1880-1915

Among the very first of the large health research institutes, and one that became a model for many others, was the institution built for and by Louis Pasteur in Paris. During the quarter-century prior to 1885, working much of the time in cramped laboratories at the Ecole Normale Superieure of Paris, Pasteur had earned the admiration of scientists everywhere with his investigations into crystallography and spontaneous generation; his applied researches bearing on the production of beer and wine and on the cultivation of silkworms; and his studies of the etiology and prevention of such animal diseases as anthrax, fowl cholera, and swine erysipelas.



Louis Pasteur, 1822-1895



Pasteur's early laboratory and animal cages at l'Ecole Normale

However, the great impetus to the creation of a Pasteur Institute came from Pasteur's researches, late in his career, on rabies, culminating with the daring and successful inoculation in July 1885 of the Alsatian boy, Joseph Meister, against the disease. This initial inoculation almost immediately precipitated a flood of rabies victims descending upon Pasteur's modest laboratory from all over Europe and the Americas in hope of obtaining treatment. News of these dramatic human and scientific developments was spread far and wide by a remarkable outpouring of stories, both in the popular press and in medical publications. While some of the accounts, both in France and abroad, were critical of Pasteur and the early inoculation processes, many others recognized the breakthrough that Pasteur had achieved. Most Frenchmen, for their part, still smarting from their crushing military defeat in the Franco-Prussian War of 1870, welcomed the discovery as a major boost to their national morale and prestige.

In the French Academie des Sciences, Pasteur's friends quickly moved to create a French center for manufacturing the rabies vaccine and performing inoculations, an institution that would also include spacious facilities for Pasteur's researches. In 1886 a committee organized a public subscription which rapidly attracted funds from all over France and many foreign countries. In 1887 a plot of land was purchased in Paris and construction on the first laboratory buildings was started. Finally, in late 1888, the Pasteur Institute was inaugurated in a ceremony attended by many scientists and dignitaries, headed by Mr. Sadi Carnot, President of France.

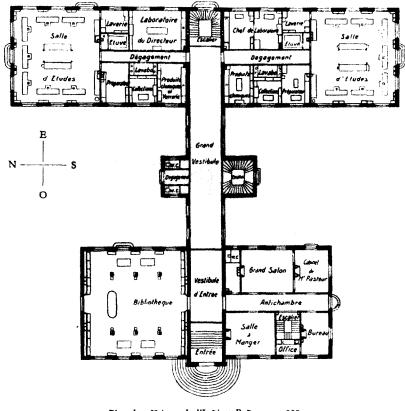
By the time his new Institute was ready for occupancy, Pasteur was tired, aging, and impaired by a second stroke. In his own words, he was a man "vanquished by time." He managed to continue some of his researches on rabies and to defend his work against

occasional detractors. However, much of his time was taken up with organizing the Institute and acknowledging the world's plaudits. He died in 1895 and was eventually interred in an impressive crypt on the grounds of the Institute.

During the following years, up to World War I, the Pasteur Institute flourished in the aura of the great man's name while nurturing and expanding on the research lines and interests he had started. Further physical growth quickly became necessary. Among the major early additions were the acquisition of extensive serum production facilities in the Paris suburbs, the building of a separate chemistry building in 1901 and, about the same time, the development and completion of a research hospital of 120 beds, primarily for infectious disease studies.

Meanwhile, continued scientific excellence was achieved, during that period and beyond, under two eminent directors, Emile Duclaux from 1895 to 1904 and Emile Roux from 1904 to 1933; both men had been close disciples and associates of Pasteur. Roux, along with Alexandre Yersin, Louis Martin, and other disciples, in the early 1890s made the Institute one of the chief centers of research on the etiology of diphtheria and of the introduction and production of antitoxin against that disease. And as time went by, the Institute's staff scientists launched equally important investigations of other diseases.

Apart from the regular staff, from an early date distinguished outside scientists were invited to use the facilities. As early as 1888 Pasteur himself made room for the Russian scientist Elie Metchnikoff as a laboratory chief. Remaining in Paris up until his death in 1916, the latter found the Institute to be a congenial site for much of his research into the mechanisms of immunology. Similarly, other "independent spirits" of science were offered facilities, including men of the stature of the French



Plan du 1er étage de l'Institut Pasteur en 1888.

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Pasteur Institute. Layout of one floor



Emile Duclaux, Pasteur's successor as Director of the Pasteur Institute.



Medallion struck for Pasteur's 70th birthday, 1892.



An early inoculation of diphtheria antitoxin, 1895

Emile Roux, assisted by Drs. Laveran, Metchnikoff, and Yersin, with students of the Pasteur Institute's first microbiology course

PREMIER COURS DE MICROBIE TECHNIQUE



L'enseignement de microbie technique (microbio-logie) fut inauguré le 15 Mars 1889. Ce cours fut créé par le Docteur Roux avec Yersin comme préparateur. Ce cours de perfectionnement microbiologique a

été complété par un enseignement sérologique. Il est suivi chaque année par une centaine d'étu-diants venant de France et du monde entier.

1 - THIROLOIX 2 - Dr BATTLE 3 - Dr ARCHINARD 4 - Dr RÉMOND 5 - Dr PRÉEL 6 - HALLION

7 - ETLINGER 8 - Dr. LORIS MELIKOFF 9 - MARQUESY 10 - OUSTANIOL 11 - Dr. LEVITSKY 12 - REPIN

13 - Dr LAVERAN 14 - Dr ROUX 15 - Dr METCHNIKOFF 16 - Dr YERSIN 17 - Dr SCHLEMMER 18 - Dr SUZANNE

military physician Alphonse Laveran, who as early as 1880 had discovered the causative organism of malaria.

The Pasteur Institute became, along with Koch's Institute in Berlin, one of the two principal early centers in the world for teaching the new techniques of microbiological research as well as for disseminating information about the modes of producing vaccines and sera. Formal classes in biochemistry (Duclaux) and microbiology (Roux) were begun early in 1889. They soon attracted students from numerous countries, while many other scientists came to the Institute for shorter periods of observation. At the same time, places as teaching or research assistants were found on the Institute staff for a succession of junior scientists, some of whom subsequently achieved great renown. Particularly prominent were several who ultimately left the parent Pasteur Institute to form or help staff similar laboratories or Pasteur institutes in other cities, among them Jules Bordet in Brussels, Albert Calmette in Saigon and later Lille, Charles

Nicolle in Tunis, and Alexandre Yersin in Nhatrang and Hanoi.

Elsewhere, other important laboratories and health research institutes were being founded with the Pasteur Institute as a principal source of inspiration if not as an actual model. Among these, the Russian Institute for Experimental Medicine opened in St. Petersburg in 1890, the British Institute of Preventive Medicine (later changed to the Lister Institute) in 1891, and Shibasaburo Kitasato's Institute for Infectious Diseases in Japan in 1892. In Germany, meanwhile, Robert Koch had made his great bacteriological contributions of the 1880s in the laboratories of the Imperial Health Office and the University of Berlin. Only in 1891 did he finally obtain his own magnificent facilities, the Institut fur Infectionskrankenheiten. Moreover, within a few years several of Koch's outstanding students and assistants had become heads of institutes, prominent among them Kitasato, Emil von Behring, and Paul Ehrlich.



Robert Koch's Institut fur Infectionskrankenheiten, in Berlin

Americans and the Growth of Health Laboratories

It is hardly surprising, given the country's historic lag in education, science, and other areas of learning, that the United States failed to produce a Pasteur, Koch, Lister, or other giant figure in the early decades of the bacteriological revolution. Nevertheless, many Americans were anxious to make up such deficiencies as rapidly as possible. Despite the well-entrenched anticontagionist beliefs that had prevailed here throughout much of the nineteenth century, Americans proved as receptive as individuals in other nations to the new discoveries. Since before the Civil War, American scientists who were accomplished in microscopy-Joseph Leidy, John Riddell, John C. Dalton, Jeffries Wyman, and othershad been viewing algae, infusoria, animalcules, and other minute organisms through highpowered lenses, but they lacked the techniques necessary either to cultivate such organisms in the laboratory or to connect them positively with given diseases. When the Europeans, during the 1870s and 1880s, began to publish their successes in these areas, a new generation of American physicians quickly demonstrated

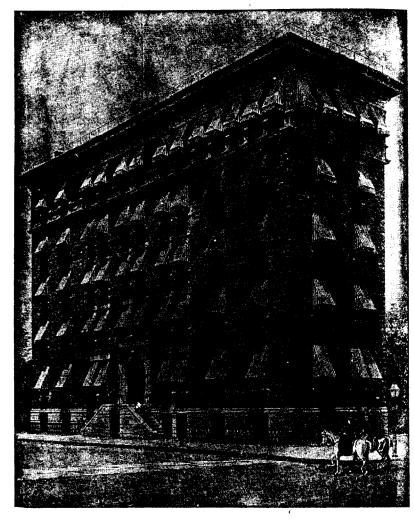
its eagerness to learn about and perhaps duplicate and extend those findings. A few of these individuals—notably George Stemberg and Theobald Smith—virtually taught themselves the principles of bacteriology without leaving the United States, and then went on to make outstanding original contributions in the field. Others, however, in increasingly large numbers, opted to cross the Atlantic to meet the European investigators in their laboratories and to learn from them the exacting techniques of the new science.

While some of them ultimately went to the British Institute and other laboratories as they were founded, for much of this pre-World War I period scientists of all nations made the Koch and Pasteur laboratories their destinations of choice. German educational, scientific, and medical institutions, of course, were already at a high level of prestige worldwide. Now large additional numbers of Americans and other foreigners were attracted to Koch's laboratories, where they enrolled in courses of study or made arrangements to do research.





Two of America's pioneer microbiologists: at left, William H. Park, N.Y. City Health Department; at right, Theobald Smith, U.S. Bureau of Animal Industry



THE NEW YORK

PASTEUR INSTITUTE BUILDING

Where the Diphtheria Antitoxic Serum and other Biological Products are Prepared. (New York Biological and Vaccinal Institute.)

One of several American serum centers named after Pasteur



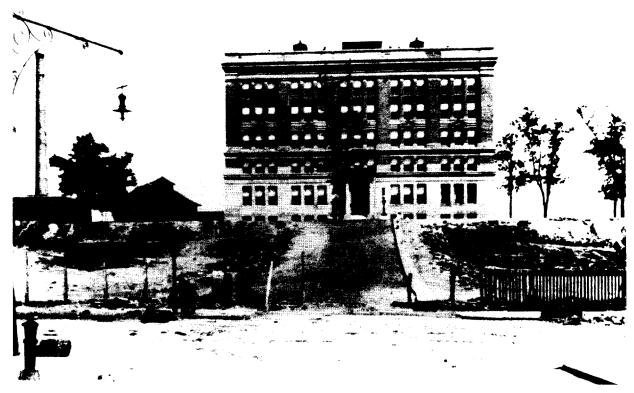
THE CARNEGIE LABORATORY

And Go Last Twenty-sixth St., New York

This early New York laboratory was the gift of steel magnate Andrew Carnegie

American awareness of and connections with Pasteur and his laboratories expanded greatly with the early 1880s, when reports in the periodical literature alerted the medical and scientific community to the progress of the rabies researches. Popular interest intensified somewhat later, in mid-1885, immediately following Pasteur's first human inoculation against rabies. Later the same year, the wellpublicized trip to Paris of a group of Newark children to receive inoculations, a trip sponsored by the New York Herald, brought this enthusiasm to its peak. Beginning about this same time but continuing for over a decade, American physicians and health officers were drawn to Paris to observe Pasteur's methods of treating rabies and to bring back samples of the serum used. A few Americans, during the mid-1880s, sent contributions of money for the Pasteur Institute building fund. And, after completion of the Institute, some Americans began enrolling in the courses conducted by Roux and Duclaux, while others came for varying periods of research on immunology or some particular disease organism.

Besides the training they received in Europe, the Americans came back filled with ideas for their own new laboratories and research institutions. In several cities, groups drew up plans for American Pasteur institutes that were to be principally devoted to producing anti-rabies serum, selling it, and administering it to patients; at least three such institutions were actually formed, in New York. Chicago, and Ann Arbor. Pharmaceutical firms also began expanding their laboratory facilities during this period in order to take advantage of the large new market for sera and vaccines. Much more important scientifically at this time, however, were the numerous research and public health laboratories that came into being.



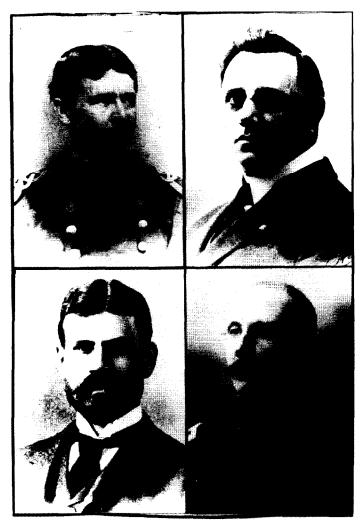
Founders Hall, Rockefeller Institute for Medical Research, 1906

Several of the earliest laboratories were developed in or attached to academic institutions. Following the creation in 1884 of the pioneering Carnegie Laboratory at the Bellevue Hospital Medical College, substantial bacteriological or hygienic laboratories were founded at New York University (1886), the University of Michigan (1889), the University of Pennsylvania (1889), and the Johns Hopkins Medical School (1893). Meanwhile, laboratories that were established between 1886 and 1893 by the Massachusetts State Board of Health and the health departments of Providence and New York City provided many of the earliest demonstrations of the significance of bacteriology for practical public health work.

These pioneer facilities were soon duplicated in other American universities and in other

state and city health departments. Few if any, however, offered such rich opportunities for research as those provided at the Rockefeller Institute for Medical Research, founded in 1901. Certainly, when that Institute acquired its research hospital in 1910, it became the first of the American health-research institutes to match the Pasteur and Koch institutes at all closely in size and scientific stature.

Still another important source of research support and activity was the Federal government. Several different governmental agencies began, during the 1880s and 1890s, to establish health-related laboratories or to promote research. The short-lived National Board of Health had no laboratories of its own but did award funds for sanitary research. In the Department of Agriculture, the work of the



The Reed Board, which in 1900–1901, solved the century-old problem of the cause of yellow fever. Dr. Waiter Reed left, top,: Dr. Aristides Agramonte, Dr. Jesse W. Lazear who lost his life as a result of the experiments; and Dr. Lens Carroll.

Leading participants in the Army's famous yellow fever experiments in Cuba

Bureau of Chemistry, under Harvey Wiley, was mainly devoted to routine laboratory analyses, but the Bureau of Animal Industry provided scientists of the caliber of Theobald Smith, Daniel Salmon, and Emil A. de Schweinitz with excellent opportunities for original research. The Army Medical Museum also took on a research mission. Its earliest facilities, modest though they were, nonetheless made possible much of the microbiological research of

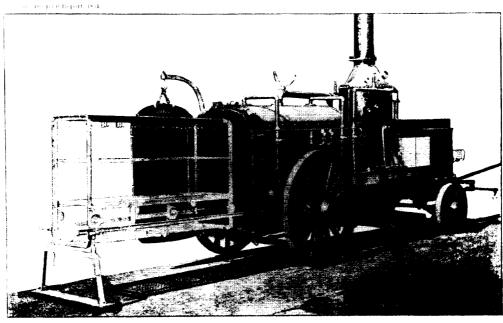
several outstanding investigators, notably Joseph J. Woodward and George M. Sternberg. After 1893, however, the establishment of the Army Medical School and creation of additional laboratories transformed the Museum into an increasingly productive scientific institution, one which supported the bacteriological and parasitological research not only of Walter Reed but of a steadily growing coterie of other capable army medical scientists.

The Hygienic Laboratory

The Hygienic Laboratory, forerunner of the present National Institutes of Health, was among the very first of the American health laboratories to be established. However, for its first dozen or so years, it remained small and unpretentious. The facility was set up in 1887 in a single room of the United States Marine Hospital on Staten Island and was moved in 1891 to space in the headquarters building of the Marine Hospital Service, in Washington. The first Director of the Laboratory, Dr. Joseph J. Kinyoun, a recently appointed medical officer in the Service, had taken courses in bacteriology at New York's Carnegie Laboratory in 1885 under an excellent American preceptor, Herman Biggs, and he may also have had training in European laboratories about the same time. In any case, in order to make the Laboratory more effective, he made a number of trips during the 1890s to both the Koch and Pasteur institutes to study new

bacteriological discoveries and techniques.

During the early Kinyoun years the Hygienic Laboratory was literally a one-man operation. Even after 1890 it often had no more than one or two medical officers temporarily assigned at any one time to share the scientific work. Kinyoun himself became an excellent, if overworked, laboratory diagnostician whose services were increasingly called upon by personnel at the various marine hospitals and quarantine stations. During the great cholera and yellow fever scares of the 1890s, he was from time to time pulled out of his laboratory for periods of special duty as quarantine inspector at New York or other ports. Nevertheless, he found some time for research. He confirmed the etiology of cholera, anthrax, tuberculosis, and other diseases; he was one of the first in the United States to prepare and standardize diphtheria antitoxin; and he made exhaustive and important original studies



FORTABLE STEAM DISINFECTOR, WINYOUN-FRANCIS PATTERN, DESIGNED FOR U. S. MARINE-MUSPITAL SERVICE. PREADY FOR SERVICE

Disinfection apparatus designed by Joseph Kinyoun, 1893-1894





The first three directors of the Hygienic Laboratory: left to right, Joseph J. Kinyoun, Milton J. Rosenau, John F. Anderson





Advisory Council, Hygienic Laboratory, May 1906, and personnel of the Hygienic Laboratory.

1st ROW (left to right): Drs. John F. Urie, U.S. Navy; Milton J. Rosenau, Director, Hygienic Laboratory; William H. Welch, Johns Hopkins University; Surgeon General Walter Wyman; Drs. Victor C. Vaughan, University of Michigan; Frank E. Westbrook, University of Minnesota; A.D. Melvin, Chief, Bureau of Animal Industry, Department of Agriculture.

2nd ROW: Drs. William T. Sedgwick, Massachusetts Institute of Technology; Reid Hunt, Chief Division of Pharmacology; John F. Anderson, Assistant Director, Hygienic Laboratory; Major Walter D. McCaw, U.S. Army;

Drs. Charles Wardell Stiles, Chief, Division of Zoology; Joseph H. Kastle, Chief, Division of Chemistry; John W. Kerr.

3rd ROW: Laboratory Attendant William Lindgren; Stenographer E.B.K. Foltz; Clerk David G. Willets; Pharmacist F.J. Herty; Dr. Joseph Goldberger.

of the germicidal effect of various disinfectants, as well as developing equipment for the large-scale disinfection operations of the Marine Hospital Service.

However, it remained for others to build up the tiny Hygienic Laboratory into a firstclass health research establishment. Kinyoun's successor, Milton J. Rosenau, accomplished much of this transformation during his ten years as Director, from 1899-1909, while John F. Anderson continued the process during the years up to 1915. Among the key initial steps taken were the creation of separate divisions of chemistry, zoology, bacteriology and pathology, and pharmacology; the recruiting of able scientists to staff them; and the naming of a high-caliber advisory council under William H. Welch. Another important initiative was the launching by Rosenau in 1902 of a course of instruction in pathology and bacteriology for medical officers of the now-renamed Public Health and Marine Hospital Service. That course served the immediate added function of providing the Hygienic Laboratory's permanent scientific staff with competent assistants and even collaborators, sometimes for extended periods. It also served as a direct impetus for the creation and staffing of laboratories in the various hospitals operated by the Service around the United States. Some of these quickly proved their value both in initiating occasional independent local investigations and in facilitating and assisting studies organized by scientists of the laboratory in Washington.

Beginning in 1902, Congress assigned the Laboratory the large new function of testing and regulating all vaccines and other biological products sold in interstate commerce, including inspection of the laboratories that manufactured them. At that time three such products—diphtheria and tetanus antitoxins and smallpox vaccine—were on the market. This testing work, together with the other new activities and enlarged staff, made an increase of space imperative. Congress finally

recognized this need and authorized a new building specifically for the Laboratory. Completed in 1902, the structure still did not include space for some essential work, and it continued for some time to lack such key elements as a research hospital and an adequate animal facility. Nevertheless, with its added resources, the new building did constitute a large step toward achieving research respectability, toward the attainment of the standard established by the Pasteur Institute for twentieth century health laboratories.

The Hygienic Laboratory's extensive pre-World War I growth coincided with the period of American history often known as the Progressive era. In fact, the very existence of the Laboratory, as well as its lines of work, reflected many of the dominant beliefs, values, and objectives of that era: the expansion of government authority and activity generally; the reining in and regulation of big business; a new insistence on efficiency, expertise, and scientific knowledge in society and government; the conservation of all of the nation's valuable resources-not only its forests and minerals but its human health, vitality, and well-being. A large proportion of the Laboratory staff's time and energies, therefore, went into applied researches of immediate relevance to given sanitary or public health concerns. Many of these activities involved long-term field work, for which the laboratories and personnel of marine hospitals or quarantine stations often provided routine servicing, though the central Laboratory remained as the backup and coordinating facility.

Among the earliest of these studies, and one which attracted enormous public as well as scientific interest, was the investigation of Charles Wardell Stiles, Chief of the Laboratory's Division of Zoology, into the etiology and distribution of hookworm disease. Stiles determined, among other things, that this condition was endemic throughout many areas of the South, and as such was a primary factor in the chronic backwardness and desti-

Uncle Sam, Doctor. By Frank G. Carpenter.

HEALTH OF THE PEOPLE.

HOW THE NATIONAL GOVERNMENT WATCHES OVER IT.

From Our Own Correspondent

ASBINGTON (D.C.)-Monkeys which have the mescales, gainea pigs with the diphtherm and rabbits with exploid tever-these are some of the things to be seen in the areat experiment station which Uncle San; has established on the banks of the Potomac to keep disease away from his children. It is now ten years since a national bureau of public bealth was founded. The institution has proven to be of enormous value, and there is a possibility that it will some day be made a Cabinet department with a secretary at its head. As it is now, the bureau is controlled by the Secretary of the Treasury. Its superintendent is Surveyor-General Wyman, whose life has been spent in fighting the great diseases which affect the nation. It is to him that we owe the movement now being made against tuberculosis, pellagra and typhoid fever, the government regulations as to the sale of viruses and toxins, and also the establishment of the hygienic laboratory whose work I describe farther on in this letter.

capital: Our government institution, known as the In the Guinea Pig Pens hygienic laboratory, is backed by the nation, and it gets its appropriations from Congress. It is connected with the national bureau of health, and it has so grown that it is now one of the most important of the government undertakings

The hygienic laboratory consists of several large buildings which are devoted to research work. It contains chemical and other laboratories specially fitted up rooms in which germs and microbes of all kinds are reared, rooms for the testing of diseases through a study of animals which have been infected with them and all the machinery for modern medical investigation. It would take many columns to give a record of the various kinds of work now going on and a description of what has already been accomplished. In this letter I can mention only a few of the problems which are now being studied and some of the methods by which the scientists arrive at their conclusions.

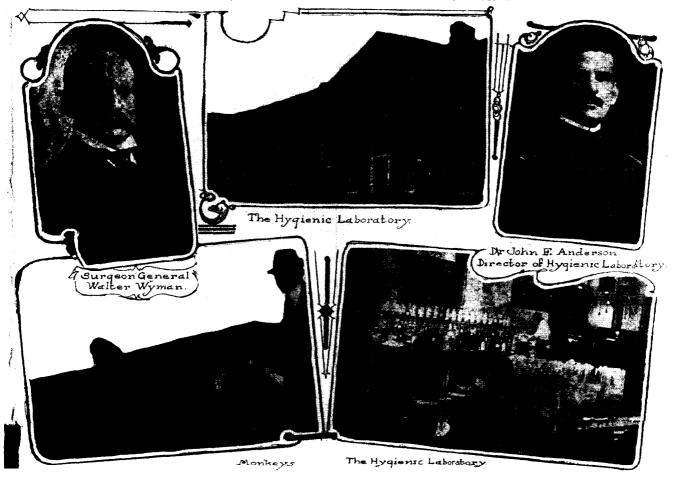
Uncle Sam's Medical Zoo.

One of the interesting features of the laboratory is its study of human discuses through animals of one kind or other. Indeed, in one respect the institution might be called "Uncle Sam's Medical Zoo," for it has hand in order that it may investigate through them the nosed and studied.

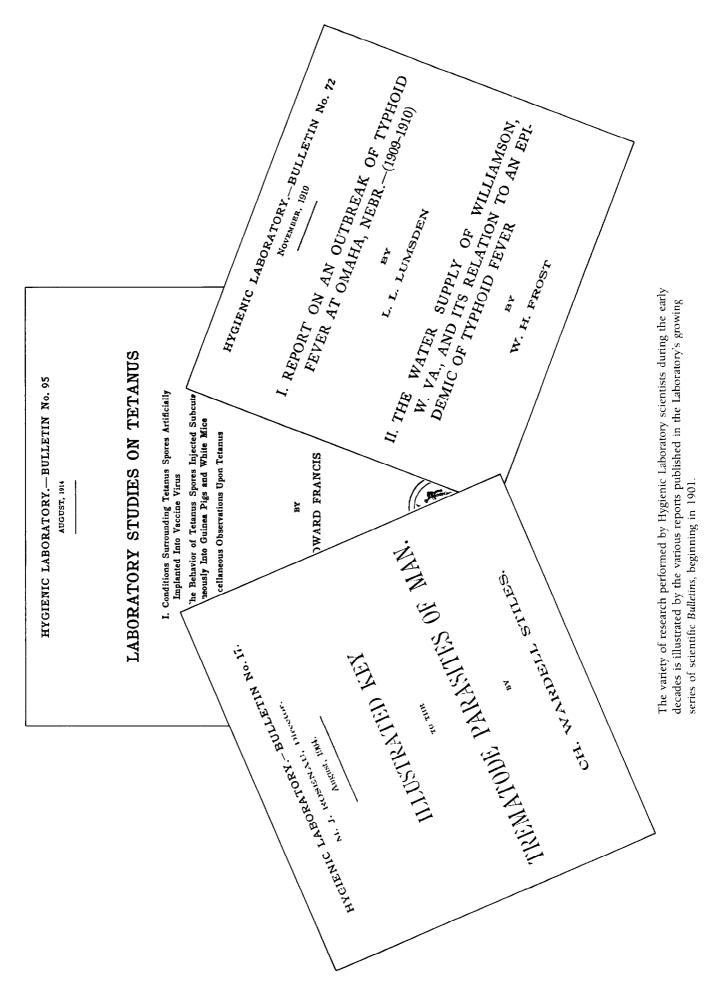
In another part of this same house is when I is call the guinea-pig stock yards. This is concerned of many little pens occupied by guinea page. A made and four females are allotted to each pen. They have to idly, and there are enough of them to keep apoint state or more of these little animals which the labor boy

consumes every year.

In another place there are rabbits, some of the solids: gray and others as white as the engine close of a rain-There are also dainty mice of the color of show, which scamper and play about the little houses in which they are penned. Each kind of animal has lite own place in the research work, and many of those which have been kept here have been of service in the remarkable discoveries made by this laboratory as to human diseases. All of these animals are carefully treated. They have well ventilated houses heated by steam, and the best of food that can be obtained. During my stay I saw them feeding the monkeys. The little animals were given bananas, bread, nuts and such other things as they specially like. The guinea pigs are kept fat on guinea-pig dainties and the rabbits rejoice in green lettuce and cabbage. The animals are kept in perfect health and as far as possible in good spirits in order colonies of animals which the government keeps on that the diseases given to them may be directly diag-



1911 press account of the work of the Hygienic Laboratory





Rocky Mountain Laboratory, Hamilton, Montana, 1910. Temporary site of the Hygienic Laboratory's early studies of Rocky Mountain spotted fever.

Front cover illustrations:

Top: L'Institut Pasteur, Paris

Artist's rendering, ca. 1889

Bottom: U.S. Hygienic Laboratory

Washington, ca. 1910

Back cover illustration:

Zeiss microscope purchased 1887 for the United States Hygienic Laboratory and used by the Laboratory's first Director, Dr. Joseph J. Kinyoun.



U.S. Department of Health and Human Resources—Public Health Service—National Institutes of Health