

LOUIS PASTEUR

BY

S. J. HOLMES, Ph.D.



Pasteur has probably done more to preserve human and animal life than any other single human being. Every one knows of his work on hydrophobia; but not so many know that our whole theory of contagious disease is founded on his researches and that there has not yet been an end to the work he started. This book sets forth, briefly, and simply the chief discoveries of this great investigator, and shows how his life was one of incessant labour and ultimate triumph.

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LOUIS PASTEUR

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WITH ILLUSTRATIONS



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PREFACE

THIS small volume has been written for students and general readers who may desire to know something of the life and work of Pasteur, but who hesitate to undertake the perusal of more comprehensive biographies. In the preparation of this sketch I have been greatly indebted to the incomparable *Life of Pasteur* by Vallery-Radot, and I hope that what I have written may induce many of my readers to make the acquaintance of this larger work. I owe much also to the valuable *History of a Mind* by Émile Duclaux who was for several years one of Pasteur's ablest co-workers and hence exceptionally qualified for the task which he has so well accomplished. Among other useful sources of information especial mention may be made of Roux's *L'Œuvre médicale de Pasteur*, which, like the preceding works, was written on the basis of intimate personal knowledge.

The present book is the product of a long-felt admiration for Pasteur and his achievements. I do not pretend to have made any new contributions

to Pasteur's biography. It has been my aim to set forth, briefly and simply, the chief discoveries of this great investigator, to describe his methods of critical experimental enquiry, and to show how he was led on, step by step, from one field of research to another, making discoveries of the highest importance in every field he traversed. I have endeavored also to give an idea of Pasteur's personality and its relation to his scientific work. So remarkable and inspiring a career as that of Pasteur cannot be too widely known, and I make no apology, therefore, for adding to the number of books upon this great man.

I am indebted to Dr. T. D. Beckwith of the Department of Bacteriology of the University of California for reading the whole manuscript, and to Dr. J. H. Hildebrand, Professor of Chemistry in the same institution, for reading the chapters which deal with Pasteur's chemical researches.

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LOUIS PASTEUR

CHAPTER I

HOME LIFE, EARLY TRAINING AND AMBITIONS

IN the *London Times* for December 13, 1922, occurs this item: "M. Victor Berard, The President of the Senatorial Commission of France on Education, announces that the bells of Dôle will be rung for two minutes preceding five o'clock on the evening of December 27, and that all the bells of the Franche-Compté from the plain of the Saône to the crests of the Jura will reply to them. He suggests that during these two minutes all the bells should ring in unison to recall the great work which France has accomplished during the last hundred years." On this occasion the French people, who love to honor their great men, paused to celebrate by a beautiful and fitting ceremony, the hundredth anniversary of the birth of Louis Pasteur, who was born in the little village of Dôle, December 27, 1822.

Most biographies have something to say about parents and other ancestors if only to chronicle a few dry details of names and dates. The parents

of Louis Pasteur, however, were persons of very superior quality, although occupying an obscure station as did their families before them. The great-grandfather had actually been a serf of the soil who was given his freedom in 1763 for four pieces of gold. Thenceforth he followed the occupation of a tanner which continued to be a family trade during the two following generations. I have an especial admiration for the sturdy character of the father, Jean Joseph Pasteur, a serious, hard-working man, with only the merest rudiments of education, but with a great appreciation of learning, and willing to make many sacrifices so that his son might profit by the educational advantages which it had never been his own privilege to enjoy. Jean Joseph Pasteur had served in the armies of the great Napoleon during the war in Spain. The Third Regiment to which he belonged was especially noted for bravery, and along with many other survivors of this valiant group he was given the cross of the Legion of Honor at the hands of the Emperor. Through his substantial merit he had slowly risen through the ranks to the position of sergeant major. Throughout life Sergeant Pasteur cherished the intense devotion to Napoleon that was felt by so many of the common soldiers of the armies of

France. The downfall of Napoleon after the dazzling and brilliant victories that placed Europe under the feet of France affected him deeply. After his discharge from the Army in 1814 he returned to his humble family trade of tanner, resigning himself, with shattered hopes and wounded pride, to the new régime.

The life of the solitary and disappointed soldier was soon brightened by the acquaintance of a young girl, Jeanne Etiennette Roqui, whom he used to watch while she was working in a garden on the opposite bank of a small river that ran past the tannery. Feelings other than melancholy broodings began to arise in the breast of the "old soldier" as the villagers called him (he was only twenty-five), and he was married, after what preliminaries we do not know, to the young girl of the garden. The marriage proved to be happy. Madame Pasteur is described as kind hearted, vivacious, imaginative and enthusiastic,—qualities contrasting quite strongly with the reserve, caution and introspective bent of her husband. The first child died when only a few months old. Then came a daughter, and four years afterward their only son, Louis Pasteur. Two younger daughters completed the Pasteur family.

Soon after the birth of Louis Pasteur the family moved to the little village of Arbois which was destined to be their permanent home. Here the father established a tannery which yielded a very modest income. The parents were hard-working and frugal, but they gave their children such educational advantages as the village afforded. Louis went to the primary school and then to the little college of Arbois where he worked diligently enough, but without attaining any special distinction. The father wishing to improve upon his own limited education, worked along with his son, helping him as best he could with his lessons in the evening. A quiet, industrious, studious home, this maison Pasteur, devoted to the inculcation of sterling virtues of character,—a home in which the father and the mother, different as they were in temperament, were strongly attached to each other, and solicitous above all else for the welfare of their children. Jean Joseph Pasteur was ambitious that his son become a scholar. If only Louis could attain the station of professor in some small French college, what more in the way of worldly advancement could be desired? Doubtless the sturdy soldier used to meditate on his son's prospects during his Sunday walks which he was in the habit of

taking, always on the same road from Arbois to Besançon, after he had attired himself in his best clothes decorated with the white ribbon of the cross of the Legion of Honor.

In the college of Arbois Louis Pasteur awakened the interest of the head master, M. Romanet, who devoted especial attention to training the mind of his pupil. Pasteur's mind worked slowly, but very carefully, and he was exceedingly scrupulous in regard to the accuracy of his information. In this he resembled his father. Romanet perceived beneath the quiet demeanor of this industrious lad promises of future achievement which had not impressed other and less discerning instructors, and he encouraged Pasteur in the development of those habits of careful and accurate thinking which are commonly given little credit by teachers as compared with facility of learning and glibness of expression.

When Pasteur had finished his course in the little college of Arbois the question What next? began to agitate the family. Romanet had tried to persuade his pupil to look forward to going to the Ecole Normale at Paris, but this meant much additional preparation. The family was poor and could ill afford the expense of sending Louis to such

a distance and supporting him in Paris. Besides there was the fear in the hearts of the parents, who were loth to be separated from their son, that the temptations of the gay capital might overcome the effects of their careful training.

Through the influence of a family friend, young Pasteur secured the privilege of attending the preparatory school of M. Barbet who consented to receive him for reduced fees. This offer overcame the scruples of his parents, and accordingly Pasteur set out for Paris, accompanied by one of his young friends, Jules Vercel, whose society served to mitigate the dreariness of the long journey by stage coach. Young Pasteur, who was then sixteen years of age, was not happy in his new surroundings. Despite his heroic efforts to interest himself in study, he was seized by the peculiar malady of homesickness. Those who have suffered acutely from this affliction may understand something of the anguish of a young lad in a strange city separated from a family circle in which he had known only close and affectionate companionship. "If I could only get a whiff of the tannery yard," he said to Jules Vercel, "I should be cured." But his case went from bad to worse until M. Barbet, who feared that his pupil's health was becoming im-

paired, wrote to his father. One morning a messenger told the lad that some one wanted to see him in a nearby café. Louis entered and found his father who had come to bring him back home. As Stephen Paget remarks, this was his first and last failure.

After a few days of joy in the companionship of his family he took up some work again in the college of Arbois. For a time he became interested in art, and drew several portraits of friends and acquaintances, some of which have been said to possess real merit. Having obtained from the college of Arbois about all that this small institution afforded, it was deemed wise that he should go to the college of Besançon which was situated only about thirty miles from his home. Besides, the father visited Besançon occasionally in the course of his business and could look after him from time to time. If homesickness recurred while he was in the college of Besançon Pasteur never complained of it. Fortunately there were a few members of the faculty who were enthusiastic and capable teachers, and young Pasteur applied himself most diligently to work. "Dear sisters," he wrote, "let me tell you again, work hard; be loving companions. When one is used to work one can no longer

live without it. Besides it is upon that which everything in the world depends. With the aid of science one can rise above all competitors. But I hope that this advice is not needed and I am sure that you devote considerable time every day to learning your grammar. Love each other as I love you. I am looking forward to the happy day when I shall be admitted to the *École Normale*."

Pasteur's ambition to attend the *École Normale* now seemed nearer to realization, and he bent all his energies to qualify himself to enter that great school. His intellect was rapidly maturing, and in addition to performing his assigned scholastic tasks we find him reading books on philosophy, literature, and science in the endeavor to satisfy the hunger of his mind for knowledge and understanding. At Besançon he contracted a lasting friendship with a fellow student, Charles Chappuis, whose alert mind and wide intellectual interests afforded him both stimulus and diversion. The two read books together, and took long walks together in which they discussed all sorts of topics from the subtleties of theology to the peculiarities of chemical reactions. Such friendships are among the most valuable experiences of college life. The influence of a teacher, however great, can never take

the place of the wholesome effect of the close and sympathetic companionship of two young and eager minds.

Pasteur's scholastic work in the college of Besançon was creditable, but not brilliant. Twice he was second in his class, and once he took the first place in physics. He stood well in the estimation of his teachers and he was entrusted with giving some work to students in mathematics and physical science. After graduation he was eligible to take the examinations for the *École Normale*, but as he was only the fifteenth out of twenty-two candidates, he resolved to give himself another year of preparation. In 1842 we find him again at Paris at the Barbet Boarding School, no longer homesick, but full of energy, ambition and enthusiasm for his work. Only a third of the regular fees were required of him on account of his giving instruction in mathematics to some of the students from six to seven in the morning. In one of his frequent letters home he says, "I shall spend my Thursdays in a neighboring library with Chappuis. He has four hours to himself on that day. Sundays we walk and work together. I shall do some philosophy Sundays and perhaps also on Thursdays. Then I shall read some literary works. You

should see that this year I am no longer homesick."

During his year at Barbet's, Pasteur attended the lectures on chemistry which were being given at the Sorbonne by the celebrated chemist Dumas, who was destined to have a strong influence upon his future career. "You cannot imagine," Pasteur wrote, "the popularity of this course. The room is immense and always well filled. It is necessary to go a half hour ahead of time to secure a good place, just as in a theater. There is also much applause. There are always six or seven hundred persons." Dumas, noted for his important discoveries in chemistry, and the author of a series of standard works in this field, was one of the commanding figures of the science of his day. The lucidity and eloquence of his lectures aroused the enthusiasm of young Pasteur, who listened with rapt attention and admiration to the words of his instructor. Pasteur soon set his heart upon becoming a chemist, spoke of himself as a disciple of Dumas, and resolved to devote himself to research in his chosen field. In 1843 he realized his long cherished ambition of entering the *École Normale*. This time he was fourth in the list of entrants.

At the *École Normale* Pasteur plunged into work

with feverish energy. Grave, quiet, and retiring, he cared little for the usual sports and diversions of student life, and he looked forward to holidays chiefly as affording an opportunity to read in the library. His friend Chappuis would sometimes coax him for a walk when Pasteur would talk of tartaric acid, racemic acid, crystals, and other topics which had fascinated him and on which his mind continually brooded. He loved to expound subjects in which he was interested, and he found time to give some lessons in the school of M. Barbet in recognition of the kindness which the latter had shown him during his early struggles in Paris. "I am glad," his father wrote, "to see that you are giving lessons at M. Barbet's. He has done us so many favors that I am pleased to see you do something to prove your gratitude. Be therefore always obliging to him. Not only do you owe this to yourself, but you owe it also for the sake of others. It may make him act as he has to you toward other young men who perhaps without it would be handicapped in their future career."

Jean Joseph Pasteur was highly pleased with the progress of his son, but he was apprehensive that the work of the school would prove too taxing. "You know how much we are concerned about

your health," he wrote. "You are so lacking in moderation in your work. Have you not already injured your eyesight by your work at night? Having arrived where you are you should be quite happy and your ambition should be abundantly satisfied." Chappuis, to whom Pasteur's father had written, "Tell Louis not to work too hard," doubtless exercised a wholesome influence over the young student of science in his endeavor to lead him into a more nearly normal mode of life. Chappuis' interests were chiefly in philosophy and literature, but his active mind readily assimilated the subjects upon which his friend was fond of discoursing. Young Pasteur's mind was so full of his science and mathematics that he must find expression somehow. Realizing his father's educational shortcomings and his strong desire for knowledge, the son became the teacher of his father and he undertook to carry on a sort of course of instruction by correspondence. In his delicacy about assuming this rôle Louis wrote, "It is that you may be able to serve as teacher to Josephine that I am sending the work that you request." The father, who would sit up late at night over the work assigned by the son, was a willing and industrious pupil. "I have spent two days over trying to com-

prehend a problem," his father wrote, "which I afterwards found quite simple. When one must learn in order to teach it is no easy thing." But after a month he informed his son that "Josephine does not care to rack her brains, as she says. Nevertheless, I promise that her performances will please you by your next holidays."

There were several students in the *École Normale* who made better records than Pasteur. He was placed seventh when he passed the license examinations. Out of fourteen students who presented themselves for an examination for recruiting candidates for professors to teach in secondary schools Pasteur stood third of the four candidates who passed. Chappuis, always confident of his friend's superior merits, was wont to declare, "You will see what Pasteur will become." One of Pasteur's most distinguished teachers, the chemist Balard, who also appreciated his talents, made him a laboratory assistant, a post which gave him greater freedom and opportunity for carrying on his work in chemistry.

About this time (1846) a new chemist was added to the faculty, a young man, August Laurent, already known for the originality and importance of his investigations. The theory of substitutions

which was then beginning to occupy the attention of chemists was Laurent's especial interest. It had been developed by Dumas, and it appealed strongly to the imagination of Pasteur. According to this theory, chemical changes may occur by the substitution of one atom or group of atoms in a molecule by another atom or group of atoms, while the rest of the molecule remains unchanged. Nowadays chemists can build up whole series of allied compounds by substituting one element or group for another, thereby building up compounds of greater and greater degrees of complexity. The possibilities of orderly constructive chemical transformation which the theory of substitutions suggests were clearly seen by Pasteur who recognized the great importance of this guiding principle in chemical research.

For his doctor's degree he prepared and defended two theses, one in chemistry entitled *Researches into the Saturation Capacity of Arsenious Acid. A Study of the Arsenates of Potash, Soda and Ammonia*; the other in physics entitled *A Study of Phenomena Relative to the Rotary Polarization of Liquids*. Both were dedicated to his parents. "Although we cannot judge your essays," wrote the father, "our satisfaction is no less great. But as

to the title of doctor I was far from expecting so much. My ambition would have been satisfied with the license to teach."

After the newly fledged doctor had spent a short vacation in the midst of his admiring family, who were perhaps somewhat over-awed by his academic distinction, he is back again in his laboratory in Paris. It is impossible for him now to keep away for long from his crucibles and retorts. "I am supremely happy," he writes soon after his return. "I shall soon publish a contribution on crystallography."

The Revolution of 1848 caused a temporary interruption of Pasteur's labors. A popular uprising had dethroned the citizen king, Louis Philippe, and proclaimed a Republic. Paris was in a turmoil. Pasteur, full of enthusiasm for the new republic, had joined the National Guard. The ideas of liberty, equality, and fraternity thrilled him as they thrilled so many others who thought they were witnessing the dawn of a new era for France. Pasteur writes, "There are great and sublime doctrines which are now being unfolded before our eyes. If it were required I should fight courageously for the sacred cause of the Republic." Seeing in the midst of a crowd a structure entitled

Autel de la Patrie upon which citizens were invited to place their donations to the popular cause, Pasteur hastens to the *École Normale*, gathers all his savings amounting to 150 francs and freely offers them in behalf of liberty. This sacrifice won the approval of his patriotic father, who with pardonable pride desired to have the gift recorded as coming from "the son of an old soldier of the Empire, Louis Pasteur of the *École Normale*."

After resuming his regular studies Pasteur received news of the death of his mother which left him for weeks unable to carry on his work. Home ties were always strong with Pasteur. Years afterward in the course of a celebration at Dôle when a memorial plate was being placed on the house where he was born, he exclaimed, "Oh, my father, my mother, dear departed ones who lived so humbly in this little house, it is to you that I owe everything. Your enthusiasms, my brave mother, you have passed them on to me. If I have always associated the greatness of science with the greatness of our country it is because I was imbued with the sentiments which you have inspired. And you, my dear father, whose life was as hard as your hard trade, you have shown what patience in long labors can accomplish. It is to you that I owe per-



FIG. I. PASTEUR AT THE AGE OF TWENTY-ONE

HOME LIFE AND EARLY TRAINING 19

sistence in daily tasks. Not only did you have the qualities of perseverance which make useful lives, but you have also the admiration for great men and great things. To look upward, to learn more and more, to seek always to rise,—these are the things which you taught me. I see you now, after your day of labor, reading in the evening some account of a battle from one of those books which recalled to you the glorious epoch of which you were the witness. In teaching me to read, your care was to teach me the greatness of France.”

CHAPTER II

EXPERIMENTS IN CHEMISTRY AND CRYSTALLIZATION

PASTEUR'S scientific career upon which we now find him fully embarked presents a remarkably consistent and logical development. As we follow it in the succeeding chapters we shall see how each step almost inevitably leads to the one which follows. Many scientists work in varied fields, but for the most part their versatility is the product of a variety of interests with no organic inter-relationship. With Pasteur a single thread may be discerned running through all his research. From the study of crystals he is led to attack the subject of fermentation, and then successively the problem of spontaneous generation, the maladies of wine and beer, the diseases of silk worms, the germ theory of disease of animals and men, and the production of vaccines for the prevention and cure of infectious diseases. Between the early studies of the crystalline form of the tartrates of potash and ammonia and his final great achievement in the conquest of hydrophobia occur a series

of steps, each leading on to the other in a perfectly natural sequence. There are perhaps few better illustrations of the unity of nature and hence the essential oneness of science than that which is afforded by Pasteur's work.

All along the road traversed by Pasteur we meet with discoveries of capital importance. During his generation Pasteur was the central figure in a great epoch in the history of biology and medicine. His life work was destined to be devoted to revealing the rôle in nature which is played by the microscopic forms of life. If he became a biologist after being a chemist, it was his work in chemistry that determined the living forms on which he worked and the kind of problems which he first endeavored to solve. In order to follow Pasteur's early studies it will therefore be desirable to say a few words about crystals which began to arouse his interest in the *École Normale*.

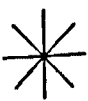
Many chemical substances, when they are recovered from the liquid in which they are dissolved, assume a perfectly definite crystalline form which is characteristic of their own particular kind of material. Thus common salt crystallizes in cubes, quartz in six sided prisms and the tartrates in eight sided prisms. The angles between the faces or


sides of the crystals have a remarkable constancy, regardless of whether the crystal is large or small. During the process of crystallization the molecules of the dissolved substance are added to the different faces of the crystal in definitely proportional amounts, thus preserving the general form of the whole. Crystals when broken may regenerate their normal form if they are placed in a solution of their own substance, material being added to the broken surface much more rapidly than elsewhere until the typical outline is restored.

Under conditions in which there is a limited supply of the dissolved material the substance for restoring the broken end of the crystal may even be obtained by dissolving away a certain amount of the substance from other parts of the surface; thus by taking material from one place and adding it to another a completely regenerated crystal of smaller size may finally be obtained. What forces regulate the behavior of chemical molecules while they are building themselves up into these beautiful and regular geometrical forms is a fascinating subject of speculation which has attracted many minds. That the process is dependent upon the chemical nature of the substances concerned seems evident from the constant and characteristic form which

many chemical compounds assume. Besides, similar compounds such as the salts of a given acid often have crystals of the same general shape.

As a rule, crystals are regular in form and may be divided by a plane into two symmetrical halves, but the crystals of some substances cannot be so divided; they appear to exhibit a certain degree of distortion, but they are distorted in a very definite way. Some are spoken of as right-handed and others as left-handed. Quartz has the peculiar property of crystallizing in both forms. Its right-handed and left-handed crystals are exactly alike except that the one is like the mirrored image of the other. They cannot be superposed; they are related much as our right and left hands.

The asymmetry of crystals is evinced not only by their form, but by their peculiar action on light. Light passing in a certain direction through Iceland spar or quartz, for instance, becomes polarized. Physicists have shown that light probably consists of very minute undulations or waves which are supposed to occur at right angles to the line of transmission although these waves may occur at various angles to each other, thus:  When a beam of light is passed through a polarizing prism it is found to be incapable of pass-

ing through a second prism held at right angles to the first one, although it can pass through the second prism when it is held parallel to the first. The ray has acquired the peculiar property of polarization in passing through the first prism. This is explained as due to the fact that the molecular structure of the crystal has reduced the undulations of the ray of light to one plane, thus:  The polarized beam can therefore pass through a second prism held in the same position as the first, but when it is placed at right angles to the first the light is quenched.

Some crystals have the property of twisting or rotating the plane of polarization of light which is passed through them. If I have two prisms of crystalline substance so arranged that the one cuts off the light transmitted by the other one, and if I place between them some substance which rotates the plane of polarized light passing through the first prism, it will be found that some of the light will now pass through the second. The plane of polarization has been changed and hence some light is able to get through the second prism. The amount of rotation can be determined by finding through how many degrees the second prism must be turned in order completely to cut off the light.

Some substances have been found to rotate the plane of polarized light to the right and others toward the left. Certain kinds of sugar (dextrose) twist the ray to the right and other kinds such as levulose twist it in the reverse direction, and the amount of these substances in a solution may be ascertained by means of the polariscope by measuring the amount of rotation which the light has undergone.

Is there any relationship between the asymmetry of crystals and the direction in which they rotate the plane of the polarized ray? The English astronomer and physicist, Sir John Herschel, suggested that such a relation might exist, but without submitting the question to the test of experiment. It was in regard to this question that Pasteur's researches on the tartrates are of special significance. It had been observed by Biot that the salts of tartaric acid when in solution rotate the plane of polarized light to the right, but that the so-called paratartrates had no effect on the polarized ray. Pasteur subjected the tartrates to a careful microscopic study and succeeded in observing the constant occurrence of small facets or surfaces which gave the crystals a slight asymmetry which had escaped previous observers. This asymmetry char-

acterized the tartrates of many substances, however different the form of their crystals might otherwise be. Pasteur then turned his attention to the paratartrates or racemates. These substances had been proven by chemical analysis to be of the same chemical composition as the tartrates. They had the same specific gravity and many other properties in common, and were held also to have

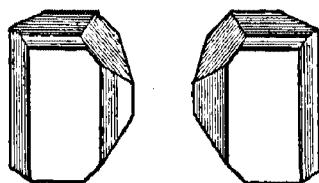


FIG. 2. RIGHT-HANDED AND LEFT-HANDED CRYSTALS OF TARTARIC ACID

the same crystalline form, differing only in their action on polarized light. By a careful study of the crystals of the paratartrates Pasteur observed that some of them were right-handed and others left-handed. He then carefully separated out these two types of crystals, dissolved them, and examined the solutions with a polariscope. To his great joy he found that the solution made from the right-handed crystals rotated the plane of polarization to the right, and the solution of the left-handed

ones rotated it to the left. The paratartrate was therefore a mixture of two substances, the right-handed one proving to be in no way different from ordinary tartrate. The paratartrates had no action on the polarized ray because the rotary power of one of the two ingredients neutralized that of the other.

This neat discovery aroused the enthusiasm of the chemists of the Ecole Normale. Balard told of it at the Institute de France where it awakened the interest of Dumas and Biot. The latter, then a man of seventy-four, was among the most prominent of French scientists. Distinguished both in astronomy and physics, and especially for his investigations on crystallography and the polarization of light, he was naturally impressed with Pasteur's observations. He had previously discovered the different rotary effect of different crystals of quartz, and when Balard told him of Pasteur's experiments, he remarked, "It would be desirable to examine closely this young man's results."

Pasteur wrote to Biot whom he did not know personally, but for whom he felt the admiration which he was accustomed to cherish toward distinguished investigators in science, requesting the pleasure of a visit in which he might exhibit his

discovery. He was received in Biot's laboratory. The old scientist insisted on furnishing his own materials for the demonstration, and Pasteur made the required solutions in his presence. In the words of Pasteur who has left us a description of this interview, "The solution was then placed in his laboratory and allowed slowly to evaporate; when thirty to forty grams of the crystals had separated, he again called me to the Collège de France to collect and distinguish by their crystallographic character the right and the left rotating crystals from one another, under his direct observation; he bade me repeat the declaration that the crystals which I had placed in his right hand would rotate the plane of polarization to the right, and the others would rotate it to the left.

"After this had been done, he declared that he himself would complete the experiments. He prepared the carefully weighed solutions and, when he was ready to make the observations in the polarizing apparatus, he called me again into his laboratory. He put first into the apparatus the most interesting solution, the one which should rotate toward the left. Without making a reading, but upon the instant, he noted a change in color in the two halves of the field of vision, and he recognized

an important leavorotation. Then the excited man seized my hand and said, 'My dear child, I have all my life so loved this science that I can hear my heart beat for joy.'” This seance was the beginning of a friendship between the old man of science and the younger one that lasted throughout the former's life.

The relation between crystalline form and rotary power discovered in the tartrates Pasteur was eager to test upon other materials in order to ascertain how generally this relationship might be found to occur. It was not easy to find many forms with asymmetrical crystals which proved at the same time to have the power of turning the plane of polarized light. Asparagin proved to be one of these, and was found to have the peculiar power of rotating the plane of polarization to the left in alkaline or neutral solutions, but to the right in acid solutions. Malic acid and its salts were found to have both right-handed and left-handed crystals, whose action on light was frequently the same as that of the tartrates, but it sometimes behaved in an apparently contradictory manner that Pasteur was unable to explain. It is now known that in dealing with the salts of aspartic and malic acids, Pasteur fell into certain errors of detail, which pre-

vented him from following out the clue to his original discovery. If he finally abandoned his tentative view that there might be a constant relation between crystalline form and rotary power, he held firm to the idea of molecular asymmetry as the basis for the action of dissolved substances on polarized light.

Here are two substances, identical in chemical composition, and in numerous physical properties, but having opposite effects on the polarized ray. How can such a relationship be explained? The molecules themselves, thought Pasteur, must have asymmetry, the one being, so to speak, the mirrored image of the other. This conception formed the foundation upon which was built one of the most important branches of chemical science, namely, stereo-chemistry, which is concerned with the relative arrangement in space of the constituent parts of the chemical molecule. Is it possible, asked Pasteur, to change one of these asymmetrical forms into the other? Paratartaric or racemic acid, which was a relatively rare form which had been obtained as a sort of by-product of the manufacture of tartaric acid, had suddenly ceased to appear where Pasteur had previously obtained it. In order to collect other samples, Pasteur visited

many chemical factories in Europe in search for this precious substance. He traveled from country to country, encouraged by reports of its presence in this place and that, only to find, upon investigation, that the reports were baseless. "I will go on for ten years if need be," he wrote; but while he found traces of paratartaric or racemic acid in several of the tartars he studied, it occurred only in quantities too small to be of practical service.

Then he set himself resolutely to work to prepare it artificially,—a feat which he believed impossible; but, after numerous experiments, he finally effected the transformation by keeping cinchonine tartrate for several hours at a high temperature. In June, 1853, he telegraphed to Biot, "I transformed tartaric into racemic acid; please inform MM. Dumas and Senarmont." For this discovery, the Paris Pharmaceutical Society awarded him a prize of 1500 francs. The Paris Academy of Sciences devoted a whole sitting to his discoveries, and after active efforts in his behalf by his friend, Biot, he was given the Red Ribbon of the Legion of Honor. "He had won it," says Vallery-Radot, "not in the same way as his father had, but he deserved it as fully."

The work on molecular asymmetry, and its rela-

tion to light and crystalline form consumed about five years of very active investigation. During this time Pasteur had changed his position from the *École Normale*, first to Dijon, where he remained only a few months, and thence in 1849, to the University of Strasbourg, where he was made Professor of Chemistry. Half of the 1500 francs prize he received was spent in fitting up the chemical laboratory of that institution. Scientific laboratories at that time were rarely furnished with adequate equipment. Claude Bernard, who made epoch-making discoveries in physiology, worked in a sort of cellar in the *Collège de France*. Deville, one of the foremost organic chemists of his time, was limited to a miserable corner, and the room assigned to Dumas at the Sorbonne was so unwholesome that he supported a laboratory at his own expense outside the University. When Pasteur began as Professor at the *École Normale*, he had to utilize, as a laboratory, two attics close under the roof with no laboratory attendant or assistant of any kind. At a later period, he was given a small building in which he installed a drying oven under the staircase, which he could reach only by crawling on his knees.

Pasteur found Strasbourg a favorable place for

his work. He devoted much care to his lectures in chemistry, but he found a good deal of time to spend upon investigation. He was comfortably situated in the house of his old school friend, Bertin, the Professor of Physics, who would not hear of his going elsewhere. A letter from his father at this time contains the following remarks: "You tell us that you will not marry for a long time, and that you will take one of your sisters to live with you. I could wish it for you, and especially for them, for neither of them could wish for a greater good fortune. To serve you and to look after your health is what both of them would wish most of all."

But Pasteur had met the daughter of the Rector of the Academy at Strasbourg, M. Laurent. He had called upon the family soon after accepting his new position, and the charm of the quiet and united family circle and the attractions of Mlle. Marie, spurred him to a sudden resolve. We have little record of the association of Pasteur and Marie Laurent during the period immediately following their first acquaintance, but the mind of Pasteur, usually so cautious and deliberate, had no doubts about the young woman to whom he was so strongly attracted. There are some natures

whose nobility and sweetness of character are so transparent that they inspire, almost at once, a perfect confidence. Mere time, as an element in acquaintance and understanding, becomes an irrelevant detail. Only two weeks after Pasteur's arrival, he sent, in accordance with prevailing custom in such matters, the following communication to M. Laurent:

Monsieur, a request of high import for me and for your family will be made to you in the course of a few days, and I believe that it is my duty to put you in possession of the following facts, which may enable you to grant or refuse this request:

My father is a tanner in Arbois, a little village in the Jura. My sisters, in the care of the household and the business, take the place of my mother, whom we had the misfortune to lose during last May. My family is in a comfortable position, but without fortune. I estimate our possessions at not over 50,000 francs; and, as to myself, I have long since decided to leave to my sisters all that may fall to my lot. I have therefore no fortune. All that I possess is good health, good principles, and my position in the University. I graduated two years ago from the *École Normale* as an *Agrégé* in Physical Science. I took my doctor's degree eighteen months ago, and I have presented to the Academy of Sciences some

productions which have been very well received, especially the last. A very favorable report which I have the honor to send to you with this letter was made on this work.

Such, Monsieur, is my present position. As to the future, all that I can say is that unless my tastes completely change, I shall devote myself to researches in chemistry. I have the ambition to return to Paris when my scientific contributions shall have brought me some reputation. M. Biot has spoken to me several times about thinking seriously of the Institute. Within ten or fifteen years, perhaps, I may think of it if I continue to work assiduously. This is no more than a dream. It is not this that makes me love science for science's sake.

My father will come in person to Strasbourg to make this proposal of marriage. Accept, Monsieur, the assurance of my profound respect and devotion.

I was twenty-six years old on the 27th of last December.

Somewhat more cautious than Pasteur, Laurent deferred for a few weeks his reply to this request. At last, a favorable answer came. The marriage took place on May 29th, 1849. Like that of Pasteur's father and mother, it proved a happy one. "All the qualities I could desire in a wife," Pasteur writes to Chappuis, "I find in her. . . . But I do

not think I exaggerate at all and my sister, Josephine, is entirely of my opinion."

The compounds whose solutions had been found to exercise a rotary power on the plane of polarized light, had, up to that time, proved to be organic compounds,—that is, compounds formed through the agency of living organisms. Pasteur was led to the view that molecular asymmetry is a peculiarity of the compounds formed through the agency of life, and that it represents a fundamental difference between the products of living and non-living matter. At that time, chemists had been able to produce artificially many of the chemical substances formed by living beings. Beginning with the synthesis of urea from its elements by Wöhler in 1822, organic chemists had formed in the laboratory one organic compound after another, using the simpler ones as bases or steps from which to build up substances of greater and greater complexity. Dessaignes, an able chemist of Vendôme, had transformed the optically inactive maleic acid to malic acid and then to aspartic acid. As the latter acid had been found to have the power of rotating the ray of polarized light, the question arose as to whether an optically inactive substance had been changed into an optically active one.

Pasteur went to Vendome, obtained a sample of the aspartic acid made by Dessaignes, and found, as he had anticipated, that it possessed no rotary power. The malic acid, which was made from the aspartic acid was also optically inactive. Pasteur concluded that there were four kinds of compounds of identical composition, the symmetrical, the right-handed, the left-handed and those arising from the combination of right-handed and left-handed forms. The artificial products were believed to differ from the natural ones in being optically inactive. As Pasteur says, "We recognize that when natural organic bodies arise under the influence of vegetable life, they are usually asymmetric in opposition to minerals and synthetical bodies. The elementary constituents of all living matter will assume one or the other of the opposite asymmetries, according as the mysterious life force, which causes asymmetry in natural bodies, acts in one direction or the other."

The barrier, which Pasteur attempted to erect between the products of the living and the non-living, like so many others that have been erected, has now broken down. The optically inactive malic acid, which Pasteur derived from asparagin, was subsequently shown by Bremer to be a com-

bination of right-handed and left-handed acids. But, although errors of detail in this difficult field of research led Pasteur to an untenable deduction, his general conception of molecular asymmetry has proven to be a most fruitful one. Professor G. M. Richardson, credits Pasteur with the first suggestion that led to the development of stereo-chemistry. As Duclaux has stated in his admirable work on Pasteur's discoveries, "Our knowledge has been very much extended since Pasteur did his work, but there has been no change in its source; and in its immense development, it remains faithful to this parent idea of Pasteur that all difference in the grouping of the atoms of a molecule must be expressed externally in some way."

One of Pasteur's observations is of especial importance, not merely for its scientific interest, but for its possible influence on the course of his future studies. It had been observed by manufacturers that calcium tartrate, when contaminated by a small amount of albuminous matter, undergoes a process of fermentation, giving rise to a variety of products. Pasteur endeavored to find if other tartrates would behave in a similar manner. Taking a solution of pure right-handed or dextro-ammonium tartrate, he placed in it a small amount

of albuminous material. Like the calcium salt, it was found to ferment. He tried the same experiment with ammonium paratartrate which, it will be remembered, is a mixture of right-handed and left-handed tartrates. This solution, at first optically inactive, was found, as fermentation went on, to rotate the polarized ray more and more to the left. When the fermentation stopped, the right-handed tartrate had disappeared; only the left-handed tartrate remained. The fluid, originally clear, was now clouded, owing, as was shown by the microscope, to the presence of minute living organisms. The microscopic forms of life selected as food the one asymmetrical tartrate, and left the other, thereby suggesting a peculiar asymmetry of their own protoplasm, which made it possible for it to act chemically on but one of the two constituents of the solution.

Doubtless this discovery confirmed Pasteur in his views regarding the asymmetry of the compounds that are immediately concerned with vital activity. What is of especial importance for his future career is that it took him across the boundary that separated chemistry and biology. Henceforth, it was the micro-organisms which were to form the chief object of his research.

CHAPTER III

THE WORLD OF MICROSCOPIC LIFE

AT this stage of our history it may be advantageous to consider briefly some of the peculiarities of the minute organisms to whose study Pasteur was destined to devote the remainder of his life. Readers who are familiar with microscopic organisms and their ways will probably prefer to omit the perusal of this chapter. In fact, they are advised to do so. I am throwing this chapter in for the benefit of those,—and my experience as a teacher of biology has shown them to be very numerous,—who have never been introduced to this vast and important assemblage of living beings which have remained so long unknown because they happen to be so very small in size. But they make up for their smallness by their prodigious numbers, their variety, their rapidity of multiplication and the magnitude of their mass effects.

Science has proven that microscopic organisms play a very important rôle in nature which was entirely unsuspected a century ago. We may

imagine the eager curiosity with which the old Dutch investigator, Anton van Leeuwenhoek, examined for the first time the minute creatures which were revealed by his hand-made microscopes. Leeuwenhoek lived in the seventeenth and eighteenth centuries (1632-1723) at a time when the compound microscope was just coming into use and was being applied by Malpighi, Grew and others to reveal the finer structure of animals and plants. He had used his microscopes to observe the stings of bees, the scales of butterflies' wings, and other favorite objects of the amateur microscopist, but one day he chanced to examine some drops of stagnant rain-water when, greatly to his surprise, he found them swarming with a variety of minute living creatures, swimming about in all directions in the most lively manner. It was like the revelation of the fauna of a new continent, except that the animals were much more strange and different from what we are familiar with than any animals we should be apt to find in an unexplored part of the world. Leeuwenhoek sent many notes describing these new and strange creatures to the Royal Society at London which published them in the early volumes of its transactions. Wonderful revelations these! Inevitably they aroused

widespread interest, and attracted other observers to turn their attention to this newly-opened field.

Knowledge of the world of minute organisms progressed rapidly. Great improvements effected in the compound microscope made it possible to learn much concerning the structure of these small living creatures and to bring into view forms of life whose minute size had rendered them invisible with the cruder instruments of the older observers. Leeuwenhoek described the creatures he observed as "animalcules," or little animals, and little animals many of them are; but many others turned out to be minute plants. In these low forms, however, the plant and animal kingdoms draw nearer together as if converging toward a common root, and there are many forms about which it is very difficult to decide to which kingdom they belong.

A much greater insight into the nature and relationships of these forms followed the establishment of the cell theory which was originally promulgated in 1838 and 1839. According to this theory the bodies of higher animals and plants are made up of living units, the cells, which may be compared to the bricks which are used in the construction of a house. The small living forms studied by the

older observers formed a most varied assemblage. Many of them proved to be the minute representatives of higher groups of animals, such as worms and crustaceans. Others, such as the wheel animalcules, belong to groups of many-celled forms characterized by their small size. But a large proportion of this minute world is found to be composed of organisms consisting of a single cell, the one-celled animals being known as the Protozoa, and the one-celled plants as the Protophyta.

The Protozoa form an extensive group, including many thousand known species of the greatest diversity of form, size, and behavior. The majority live in water, but some, like the soil *Amœbæ*, live in earth; others are found in decaying organic matter; some species live in the tissues of plants, and many kinds are parasitic within the bodies of animals. In the sea they are represented by very numerous forms, many of which are furnished with beautiful silicious or calcareous skeletons and coverings, whose accumulation at the bottom of the ocean is responsible for the formation of chalk, many limestones, and other rocky deposits. Together with the unicellular plants of the sea, which are able to build up their living substance out of the salts dissolved in the water, they afford the

food supply of over 99 percent of the animal life of the ocean. The smaller animals, as well as some of the larger ones, feed on them directly and serve in turn as food for fishes and other larger forms. The support of practically all the life in the open sea from the jellyfish to the whales is afforded, in the last analysis, by those minute forms of plant-life which have the property of utilizing as food the mineral substances found in the water in which they are suspended.

The Protozoa, like the primitive plants, commonly multiply by dividing. An individual simply constricts into two parts and each assumes the form of the whole organism. As each two becomes four in the same manner and each four becomes eight, and so on in geometrical progression, and as the divisions frequently follow within the limits of a few hours, it is easy to see that in a short time enormous numbers might arise from a single individual. Many species, especially those that live in fresh water or decaying organic matter, are able at times to assume a spherical form and secrete a covering or cyst of resistant material within which they are able to tide over unfavorable conditions of life. Within these cysts they may undergo prolonged drying after which, if placed in water, they

may subsequently emerge and begin the usual course of their lives. A few forms have been kept for several years in the encysted state and subsequently revived. Some of the soil *Amoebæ* when in these cysts are able to withstand several minutes of boiling without being killed.

The ability of many Protozoa to withstand drought while in the encysted state greatly favors their wide dissemination. These cysts may be blown in the dust of the air like the spores of mold. If we make an infusion by boiling some animal or vegetable material and then set it aside for a few days exposed to the air, we shall probably find it to be teeming not only with bacteria but with several species of Protozoa. Or if I soak a bit of dried hay in water for a few days and then examine it with the microscope, I would probably observe a veritable menagerie of small animal forms of the most diverse kind. I well remember when as a boy after becoming the proud possessor of a compound microscope I used to make up all sorts of decoctions, malodorous and otherwise, and examine them for the living creatures that somehow mysteriously came to develop in them. This world of life with its rolling ciliated infusorians, swiftly darting flagellates, and sluggish slowly-crawling *Amoebæ*,

although composed only of forms well known to science, was to my un instructed vision as new and fascinating as it doubtless was to Leeuwenhoek, the Columbus of this new world.

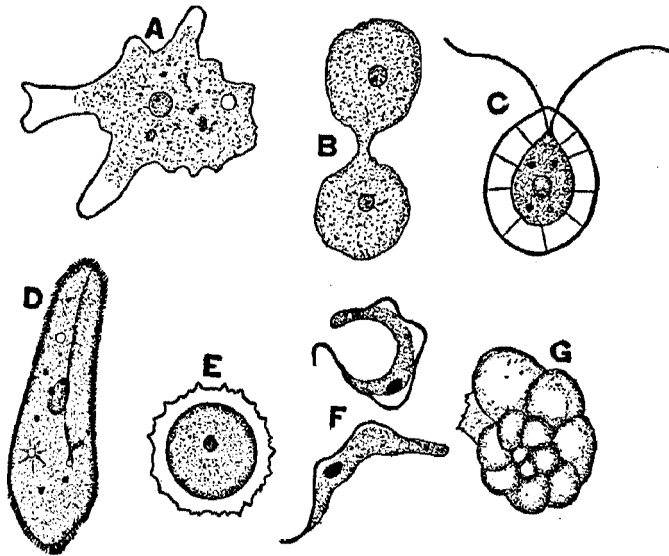


FIG. 3. FORMS OF PROTOZOA. A, Amœba; B, Amœba dividing; C, a flagellate, Hæmatococcus; D, an infusorian, Paramecium; E, an infusorian cyst; F, trypanosomes; G, a foraminiferan.

The subject of protozoölogy, which deals with these one-celled animals, has now become one of the most important branches of biology. Not the least of the rôles played by these organisms is that

of parasites within the bodies of higher animals. Some Protozoa in fact live within the bodies of other Protozoa, and there are even protozoan parasites of protozoan parasites.

One of the primary divisions of this group, the Sporozoa, is composed entirely of forms parasitic in other animals. Hundreds of different species inhabit the alimentary canal and other organs of insects, crustaceans, and worms. It is a protozoan of this group that causes *pébrine*, the destructive disease of silkworms which was studied by Pasteur. One whole subdivision of the Sporozoa, the Hemosporidia, is peculiar in living within the red blood cells of vertebrate animals; examples of this subdivision are furnished by the plasmodium causing malaria in man and the parasite causing Texas fever in cattle, a highly malignant disease, transmitted from one animal to another by the bites of the wood-tick.

The amoebas causing amoebic dysentery, the flagellates causing various intestinal diseases, the trypanosomes giving rise to the fatal sleeping-sickness in Africa, are a few of the many Protozoa that cause trouble in the human body. The species afflicting the lower animals are much more numerous and are found in the bodies of almost all ani-

mals down to and including the Protozoa themselves.

It is with the minute forms of plant life that the researches of Pasteur were mainly concerned, and the importance of these greatly exceeds that of the Protozoa, great as this may be. There can be no doubt that in the absence of these primitive plants, all higher life on the globe would be impossible. Like the Protozoa, the Protophyta or one-celled plants, belong to many groups. There are the minute green algae, which are common inhabitants of both fresh and salt water, the more primitive blue-green algae, the diatoms with their beautifully sculptured silicious shells, the desmids, and the many other forms which we cannot even mention in this cursory sketch.

One group of primitive fungi, the yeast plants, are, however, of more than usual interest to us in this history on account of their relation to the problem of fermentation studied by Pasteur. Mankind has made use of yeasts from the earliest times without suspecting that their activity is due to the life of minute plants. Examination of actively fermenting beer or wine, and especially the growth that often appears floating upon the surface, reveals multitudes of spherical or oval bodies which

may be seen to put out buds which slowly increase in size and finally constrict off as new yeast cells.



FIG. 4. CELLS OF
YEAST

Showing bud-
ding and in
one case four
spores.

Sometimes the substance of the yeast cells breaks up within the cell wall into (usually four) rounded bodies called spores, and these bodies, which are more resistant to drought and other destructive influences than the yeast plants themselves, may give rise to new individuals. There are many

kinds of yeast plants, each producing its own peculiar kind of fermentation. The importance of yeasts in making bread, alcoholic beverages, and other products of industry has greatly stimulated the study of their different varieties and modes of life.

The most important of all one-celled forms of plant life are unquestionably the bacteria. These are also the simplest and most primitive of all living organisms. Their discovery dates back to our industrious old Dutch observer, Leeuwenhoek, who in 1683 in one of his notes to the Royal Society describes and figures several very small creatures that undoubtedly belong to this group. Although countless in the number of their species, the bacteria present little variety of external form as compared with the Protozoa. A very common

type is the rod-shaped form called bacilli (Latin: bacillus—rod); then there are the spherical cocci, and the spiral bacteria (the spirilli and spirochetes) and sometimes forms of peculiar shape. Bacteria have no clearly-defined nucleus and they present but little differentiation of internal structure, although their very small size would probably pre-

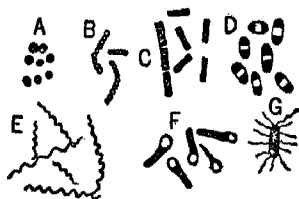


FIG. 5. FORMS OF BACTERIA. *A*, staphylococci; *B*, streptococci; *C*, bacilli of anthrax; *D*, bacilli of the plague; *E*, *Spirocheta pallida*; *F*, tetanus bacilli showing spores in one end; *G*, the typhoid bacillus.

clude us from observing it even were it present. Sometimes there are whip-like appendages or flagella, which are employed in locomotion, although many forms move about actively without possessing any external appendages at all.

All the bacteria are invisible to the naked eye. It is impossible to specify their minimum size; even with the most powerful microscopes there are forms which can barely be seen, and it is practically certain there are others which are too minute to be

seen at all. Some of the ultramicroscopic forms pass through filters (the so-called filterable viruses) and their existence is inferred only by the effects which they produce.

Like most other unicellular organisms, bacteria multiply by fission. At times some species such as the hay bacillus and bacilli of tetanus and anthrax may form spores which are very resistant to heat, dryness, and destructive chemicals. The fact that as spores some bacteria may withstand boiling even for several hours, proved to be a very troublesome circumstance in the controversy over the spontaneous generation of life as we shall see in a later chapter.

Under favorable conditions the multiplication of bacteria may proceed with great rapidity. Since divisions in some cases may follow one another every twenty or thirty minutes, the number arising from a single individual in the course of a few days is enormous. Cohn estimates that if a bacterium divides once in an hour it would produce over three and one-half million descendants at the end of twenty-four hours. Assuming its size to be that of a *Bacillus proteus*, which is about $\frac{1}{500}$ of a millimeter long by $\frac{1}{1000}$ of a millimeter thick, the volume of this mass of bacteria after twenty-

four hours would be about a fortieth of a cubic millimeter; after two days the volume would be about a half liter or about one pint; and after four and a half days, however, the volume would more than equal that of the water of the entire Pacific Ocean!

The food material utilized by bacteria varies with different species. A few forms are able to build up their living substance out of purely mineral constituents. One of the sulphur bacteria can subsist on a bill of fare made up as follows:

Ammonium sulphate	1 gram
Potassium phosphate	1 gram
Magnesium carbonate	1 gram
Water	1 liter

Here we have the food supply reduced to perhaps its simplest possible terms. Most kinds of bacteria, however, demand some organic matter. A great many species live upon compounds furnished by the dead bodies of plants and animals whose decomposition is brought about by the activity of these minute forms. The large number of parasitic bacteria which subsist within the bodies of plants and animals are still more specialized in

their food requirements. Different forms vary in their reactions to oxygen, some requiring this gas, while others (the anaërobes) will not grow if free oxygen is present.

Bacteria differ not only as to the substances which they take in but also as to the substances which they give out. Just as our own bodies give off carbon dioxide and other products of excretion, so do the bacteria get rid of various substances characteristic of different varieties. It is chiefly with respect to the materials which the bacteria eliminate that many of the characteristic effects of their growth and activity are brought about. The rôle of bacteria in ripening cheese, curing tobacco, and many other industrial processes is due to the products of metabolism of certain species employed for these purposes. One very important effect of bacteria in relation to agriculture, depends upon the property possessed by a few species of converting the free nitrogen of the air into a form which may be used as food for higher plants. Some of these bacteria live within the roots of leguminous plants, such as beans, clover, alfalfa, vetches, etc., and consequently crops of these plants are grown in order to increase the supply of available nitrogen in the soil.

The study of bacteria involves the use of an especially refined technique. It is a study full of pitfalls, and in which many errors have been made in the past. One great difficulty arises from the fact that it is often very difficult to isolate particular kinds and to keep them free from admixture with foreign species. Even with the most careful treatment our cans of fruit and vegetables sometimes spoil, and the investigator occasionally finds his material contaminated after all possible precautions had been taken to prevent the entrance of outside germs. Perhaps the difficulty in keeping material free from outside bacteria can best be realized by watching the dust particles revealed by a beam of light entering a room. For each particle that we can see there are many others too small to be seen, and even the smallest visible particle would appear under a powerful microscope to be quite a large object many thousand times the size of a bacterium. The floating matter of the air, as has been shown by the extensive studies of the great English physicist, John Tyndall, is widely distributed even in the air at great heights. It is responsible for the blueness of the sky and the redness of the sunset. A beam of light is visible only on account of the dust particles in its course. And

these are present even in ordinary air in astonishingly large numbers.

It is no wonder then, even if only an occasional dust particle contains a bacterium, that it is so difficult to keep out all of these intruders. The bacteriologist who wishes to have air admitted to his materials employs plugs of cotton wool which allow air to enter, but filter out all solid particles. Bacteria may be grown in many kinds of media, some species in one medium and others in other media; a few forms cannot be cultured artificially at all. A very convenient and much employed method of culture is partly to fill a test-tube with the culture medium, plug it with cotton wool, sterilize it by heating, and then to introduce from the point of a needle a minute amount of material containing bacteria. The growth of the colony may often be followed by observing the clouded area in the culture medium. Colonies may be transplanted from one tube to another and kept going for an indefinite time.

The varied applications and refinements of the technique of bacteriology would require a volume to describe. Perfection of technique has been brought about as bacteriology has progressed and become applied to different fields. Undoubtedly

the enormous development of bacteriology is one of the most striking features in the history of the nineteenth century, a history especially noteworthy

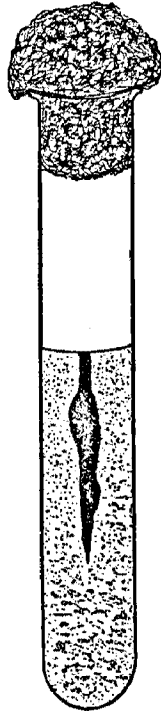


FIG. 6. A TEST TUBE PLUGGED WITH COTTON AND SHOWING A BACTERIAL COLONY GROWING IN THE CULTURE MEDIUM

for the advance of science. For over a century and a half following their discovery by Leeuwenhoek, the great importance of bacteria was practically

unknown. They were among the many other interesting and curious forms of minute life whose study occupied the attention of a few naturalists. Now there are departments of bacteriology with their several courses in most universities and medical schools. Government bureaus, agricultural experiment stations, institutes for medical research, and many private industrial firms are carrying on investigations in this field. A small army of investigators devote themselves to such subjects as the bacteriology of milk, the bacteriology of water, soil bacteriology, dairy bacteriology, and the bacteriology of sewage, to say nothing of the bacteriology of plant and animal diseases. Almost all of the enormous development of bacteriology with its numerous ramifications has taken place in the last fifty years. What strides may be made in the next half century we can only vaguely conjecture.

I have said a little concerning the relation of bacteria to disease. This topic, which is of the greatest importance for our human welfare, will occupy us more or less in the succeeding pages. There is one fact in regard to bacteria, however, which is of fundamental significance in relation to disease as well as to other practical aspects of bacteriology, and which has come to be established

only after a great deal of careful and critical work. This is the specificity of these low forms of life. Each kind of micro-organism breeds true to type, maintaining, even amid considerable changes in the course of its life cycle, certain structural features characteristic of its species as well as its own peculiar physiological activities. Several of the older observers had very incorrect views concerning the relationships and transformations of these primitive forms of life. Thanks to the refinements and perfection of bacteriological technique the older errors have been corrected. The most primitive organisms fall into species just as the higher animals and plants do. There is a certain amount of variation or deviation from the type, to be sure, but this is quite analogous to, and probably no more extensive than the variability observed in higher organisms. The more we know of primitive forms the more closely are they found to resemble the highly developed types with which we are familiar. Life is very much the same sort of thing wherever we find it.

CHAPTER IV

STUDIES IN FERMENTATION

PASTEUR had scarcely more than entered upon the study of fermentation at Strasbourg when he was appointed Professor and Dean of the Faculty of Science at Lille. The faculty at Lille had just been reorganized, and one of the innovations made in the course of instruction was to grant to students for a small fee the privilege of entering scientific laboratories and carrying on experiments. This improvement in education was warmly approved by Pasteur. In his opening address as Dean he spoke of the advantages of laboratory instruction in the following terms: "Where will you find in your families a young man whose curiosity and interest are not awakened as soon as you put into his hands a potato with which he will make sugar, with this sugar alcohol, with this alcohol ether and vinegar? Who would not be happy to tell to his family in the evening that he was about to make an electric telegraph?"

"And, gentlemen, be convinced of this, such

studies are not readily forgotten, if they ever are. It is almost as if, in order to teach the geography of a country, one causes a student to travel in it. That geography is preserved in the memory because one has seen and been in contact with the places. Similarly, your sons will never forget what is contained in the air we breathe when they have analyzed it, when in their hands and under their eyes the admirable properties of its elements have been revealed."

The relative merits of studies in pure and in applied science have been the subject of no end of learned disquisitions. Lille is in the center of an industrial region and its inhabitants looked to the University for scientific information of a practical kind. The words which Pasteur addressed to the public on the appropriate occasion of his installation are well worthy of quotation. "Without theory practice is but routine engendered by habit. Theory only is able to cause the spirit of invention to arise and develop. It is important that you, above all, should not share the opinion of those narrow spirits who disdain everything in science that has no immediate application. You may recall the charming response of Franklin when he took part in the first demonstration of a purely

scientific discovery. When he was asked, 'What is the use of it?' he replied, 'What is the use of a baby?' Yes, gentlemen, what is the use of a baby? And yet at this age of tender infancy there are already unknown germs of the talents by which you are distinguished. In your infants in arms, in the little ones whom a breath would overthrow, there are magistrates, scientists, heroes as valiant as those who, at this time, are covering themselves with glory under the walls of Sebastopol. Similarly, gentlemen, theoretical discovery has only the merit of existence. It awakens hope; that is all. But let it be cultivated, let it grow, and you will see what it will become." One sentence of this address stands out as expressing a truth of which his own career was destined to form a striking illustration. Speaking of the rôle of good fortune in discovery, Pasteur says, "In the field of observation chance favors only the mind which is prepared."

Pasteur's duties at Lille as teacher and dean were discharged with that energy and capacity which he applied to all the tasks that fell to his lot. He did much to improve and enliven laboratory instruction. He took his students to visit the factories in neighboring towns. And he frequently

devoted the services of his laboratories to the solution of the practical problems that presented themselves in the industries of the surrounding region.

Although fully aware of the importance of the search for knowledge regardless of its practical applications, Pasteur was not one of those who disdained to spend his time upon matters of practical economy. In fact, a considerable part of his researches has been devoted to economic problems. The maladies of wine and beer, the production of vinegar, the diseases of silkworms, and the epidemics of fowl cholera, swine plague, and splenic fever in sheep and cattle, are all matters whose economic importance had much to do with enlisting his interest. He was ever ready to respond when the industries of his country called upon science for help. That a problem is an economic one does not detract in the least from the scientific importance of its solution. If it may be said in behalf of pure science that it leads to valuable practical results, it may also be said that investigations carried on with purely practical aims frequently yield discoveries of the greatest theoretical import. In most of the researches of Pasteur theoretical and practical considerations were very closely related. The solution of the practical problems

which he attacked involved the answer to theoretical questions. Whether we are studying the souring of milk, the fermentation of sugar, the maladies of beer and wine, or the diseases of animals and men, the thing of fundamental importance to get at is the cause of the phenomenon we are dealing with. We may learn much *about* all these things by observation and the collation of facts; but if we wish to get at the root of the matter we must discover causes. Knowledge of the widest general import frequently comes from getting at the real root of particular problems. When we thoroughly understand the reasons for lactic acid or alcoholic fermentation our knowledge is of great service in understanding fermentation in general, and the demonstration of the cause of one infectious disease opens the way to the discovery of the causes of many others. If Pasteur occupied himself with particular economic problems such as how to keep wines from spoiling and silkworms from dying of a destructive epidemic, he solved his problems in such a way that by getting at the real causes in these particular cases he threw a flood of light upon related phenomena that has illuminated whole new fields of enquiry.

It was a combination of theoretical and practical

considerations that determined Pasteur's point of attack upon the subject of fermentation at Lille. His observations on the relation of the molecular asymmetry of the tartrates to fermentation and the fact that this fermentation was accompanied by the appearance of multitudes of minute organisms impressed him profoundly. The thought that fermentation is essentially a vital phenomenon and not a mere chemical transformation due to decomposing substances became more deeply impressed upon his mind as he continued to investigate the subject. It was one of those "preconceived ideas" which he frequently alluded to as guides to the investigator in the discovery of truth. In his case it was an idea that was ever-present during the years which he devoted to the study of fermentation.

When Pasteur began his studies on fermentation the prevalent ideas on the subject were very obscure. One peculiar feature of the chemical transformations occurring in a fermenting body is that they may be set up in the same kind of material by transferring to it a small part of the fermenting substance. The Swedish chemist Stahl held that fermentation is the result of a peculiar "internal movement" which may be communicated from one

substance to another. Through the labors of Lavoisier, Gay-Lussac, Thenard, and others, a good deal had been learned of the chemical changes that occur during the fermentation of sugar into alcohol and the transformation of the latter into vinegar. The part played by yeast in converting sugar into alcohol and carbon dioxide seemed quite mysterious. An important step was taken when Cagniard-Latour showed that yeast consisted of small oval or rounded bodies which had the power of growth and multiplication by budding and fission. This observer and the German biologist Schwann held that fermentation is produced by the growth and activities of these small organisms, and Schwann gave reasons for believing that these organisms are of vegetable origin. But the chemists, as a rule, were averse to attributing fermentation to the influence of living forms; they sought for a purely chemical explanation of the process and regarded the association of fermentation with the mysterious vital activities of the living organism as a backward step calculated to obscure rather than to elucidate the phenomenon.

The illustrious Liebig who called attention to the fact that sugar can be caused to undergo alcoholic fermentation by adding to it almost any decom-

possible nitrogenous compound, held that it was the death and decay of the yeast which causes the breakdown of the molecules of sugar, fermentation being a consequence of death and decomposition rather than of life. "In what respect," argues Liebig, "does the explanation of fermentation appear more clear to you when you have introduced a living organism? What if they are everywhere present? But you see yourself that there are none in the putrefactions. Let us admit, if you will, although this appears very extraordinary, that the meat and the sugar are destroyed by different agencies. But the sugar may undergo various fermentations very similar to alcoholic fermentation and even accompanying it; lactic fermentation, butyric fermentation, etc. Do you find in these fermentations anything that resembles yeast? Do not these behave absolutely like the putrefaction of meat? Your explanation limps and encounters obstacles at every step. For me, on the contrary, these transformations present a common character, that is, of taking place in the presence of organic matter in course of decomposition. One may start a lactic or a butyric fermentation by means of old cheese or rotten meat. For alcoholic fermentation, Colin showed in 1828 that one may bring it about

by means of a number of organized nitrogenous substances, different from the yeast of beer, provided that they are in a state of decomposition. It is these dead substances which are the ferments. I do not forget, moreover, the experiments of Thenard on the almost constant production of yeast in fermenting fluids. . . . But this yeast does not embarrass me; it enters my system. If you admit that it lives you also admit that it dies. Then it is in dying that it acts, as a consequence of the decomposition that it undergoes at this time, and of this Thenard furnishes us the proof."

This passage read in the light of our present information is most instructive in reflecting the most advanced knowledge of its day. That it contains a number of errors both in statement of fact and in conclusions was made apparent by the later observations of Pasteur. Liebig held that albuminous substances in a state of decomposition imparted a sort of "molecular movement" whose influence is to break up sugar into alcohol and carbon dioxide, or in the case of putrefaction, to effect destructive changes that give rise to other products. This view was defended by Liebig with energy and ability and it became the most widely accepted doctrine of the time.

Pasteur, as we have seen, had been brought, through his studies of molecular asymmetry, into contact with the problems of fermentation. Molecular asymmetry as revealed by its rotary effect upon light, he looked upon as a characteristic of the products of life. His observation that the right-handed tartrate of ammonia would ferment while the life-handed one would not, suggested a relation between the asymmetry of the tartrate and the asymmetry of some of the compounds of the living substance of the yeast plant which has been compared to the relation of a lock and key. In regard to the agents causing the decomposition of organic products a number of pertinent questions suggested themselves to his fertile mind. Are fermentations in general caused by living organisms, or may they be provoked by various kinds of albuminous matter? Is putrefaction due to living germs, or does it occur in material that is quite free from them as stated by Liebig? Is each kind of decomposition produced by a specific organism? In what relation does the yeast plant stand to the decomposition with which it is associated? Is fermentation due to the life of the yeast plant or is it a result of death and decomposition? Here are several questions which have a close relation to the

views of Pasteur in regard to molecular asymmetry and life. Moreover, fermentation being a method of splitting up organic compounds is a valuable instrument for studying the relationship of the asymmetry of an organic compound and the asymmetry of its derivatives if they possess any. In fermentation Pasteur surmised there might be furnished the clue to many problems not only in chemistry, but also in biology, if only the confusion and obscurity surrounding the subject could be dispelled.

Pasteur's early studies were made on lactic acid fermentation, the process which is responsible for the souring of milk. His memoir on the subject, though short, is very noteworthy, not only in establishing for the first time some important facts, but in containing the expression of several of the leading ideas which guided him throughout his future investigations. Pasteur observed that the little gray patches which appeared on the bottom and sides of the vessels of fermenting fluid were composed chiefly of minute organisms, much smaller than yeast plants, and that these organisms increased in number as fermentation proceeded. Are they the agents that cause the souring of milk, as yeast plants produce alcohol from sugar? Pasteur

made up a medium composed of a solution of sugar to which was added a small amount of chalk and the boiled and filtered extract of the yeast of beer to furnish the albuminous material needed for carrying on fermentation. In this mixture he placed some of the gray material composed mostly of the small organisms just mentioned, and set the fluid in a warm place. The next day revealed an active fermentation. The liquid originally clear was now turbid or clouded. Bubbles of gas, which proved to be carbon dioxide together with variable amounts of hydrogen, rose to the surface and escaped. The chalk, which had settled on the bottom, disappeared. After fermentation had ceased, the fluid, when evaporated down, gave a residue chiefly of lactate of lime. The sugar had been transformed into carbon dioxide and lactic acid, and the latter had combined with the chalk (which is carbonate of lime) and crystallized out. Here was revealed a process very similar throughout to alcoholic fermentation; with the same materials which would form alcohol upon the addition of ordinary yeast; we obtain quite different products solely by the substitution of a different ferment.

Lactic acid fermentation, like alcoholic fermentation, was found by Pasteur to arise in suitable

material to which its special ferment had not been added. Both kinds of fermentation often occur in the same material in which bits of cheese or other decomposable substances are placed or which have simply been exposed to the air. Still other kinds of fermentations might occur, the products obtained varying greatly according to circumstances and often for reasons that appear quite accidental or capricious. Pasteur recognized in these varied phenomena the influence of mixtures of different organisms which might have been introduced in different proportions from the floating matter of the air or from the rotten cheese or meat used to start up the fermentation. He observed in such cases yeast plants along with the organisms found in lactic acid fermentation, and also other organisms, some of which were bacteria, while others were forms that he referred to as "infusoria."

"We may compare," Pasteur says, "what goes on in fermentation with what is produced in a field in which one sows no seed. One soon sees it inhabited by diverse plants and insects which are mutually destructive." Pure fermentations were found to contain predominantly but one characteristic kind of organism, while the mixed fermentations contained two or more kinds in variable propor-

tions. "The purity of a ferment," observes Pasteur, "its homogeneity, its free development without any restraint with the aid of a nutriment appropriate to its peculiar nature form one of the essential conditions of good fermentation." One may obtain mixed fermentations of a given material at will by sowing in it diverse kinds of organisms.

Lactic acid fermentation, then, is not a process occurring independently of minute organisms, as stated by Liebig. Pasteur had discovered that it was due not to yeast plants, but to bacteria which had not been noticed by previous observers. A knowledge of the cause of this kind of fermentation gave the key to its control. The memoir on lactic acid fermentation showed the conditions under which the small bacteria concerned could best be grown and kept reasonably free from contamination. The mind of Pasteur was naturally led on to the general conclusion that the different kinds of fermentation in nature have each its own peculiar organisms whose nutrient needs and metabolic products determine the characteristic chemical substances arising from their activity.

The illuminating investigation of lactic acid fermentation was followed two years later by a memoir on alcoholic fermentation. Pasteur showed

that in the fermentation of sugar, other substances besides alcohol and carbon dioxide, namely glycerin and succinic acid, were regularly formed in small amounts, and that these substances were formed at the expense of sugar. The alcoholic fermentation of sugar cannot be adequately represented by the simple equation in which chemists were accustomed to express it. It is a complex, many-sided process in which sugar yields several products, among which, as Pasteur proved, is the cellulose constituting the substance of the cell wall of the yeast plant. This suggested the intimate rôle played by the life of the yeast cell in the process of fermentation. Pasteur held that this process was dependent on the vital activity instead of the death of the organisms found in fermenting matter, and he sought to ascertain the rôle of the nitrogenous matter which must be added to dissolved sugar if it is to transform into alcohol. The chemists held that it acted through its decomposition or merely by its presence. Pasteur, on the other hand, believed that it served simply as food for the yeast plants which, in common with all living creatures, require nitrogenous matter for building up their living substance. But the question was how to put the matter to the test?

It occurred to Pasteur to see if yeast plants could derive their nitrogen from simple inorganic salts instead of albuminous matter of uncertain composition. Accordingly, he made up media consisting of sugar, water, ammonium salts, phosphates, and a few other inorganic ingredients to which he added a minute amount of yeast. After experimenting for some time he succeeded in making up solutions in which yeast plants would grow and which would undergo at the same time a typical alcoholic fermentation. The yeast plants require several substances as food, but organic nitrogenous material was proven unnecessary both for fermentation and for the growth of the yeast cells. The theories of Liebig and other chemists were dealt a severe blow. Brought to the test of experiment they were found wanting. On the other hand, it became more apparent that it was owing to the growth and activity of microscopic organisms that fermentations were brought about.¹

¹ Although Liebig was in error in attributing ordinary fermentation to decomposing nitrogenous substances, there is an element of truth in his chemical theory. It has long been known that enzymes of organic origin produce fermentation. Micro-organisms may effect the decomposition of surrounding substances by giving rise to enzymes. In fact an enzyme has been extracted from ordinary yeast that has the property of converting sugar into alcohol and carbon dioxide. Fer-

Pasteur's position was strengthened, also, by the study of other ferments. It was found that, after lactic acid fermentation had ceased, the lactate of lime was capable of undergoing fermentation in turn if a drop of material were added which is undergoing butyric fermentation. Butyric acid is the acid that makes its appearance in rancid butter. Upon searching for the organisms in material undergoing butyric acid fermentation, Pasteur was surprised to find active rod-like bodies which he classed as vibrios and which he believed, on account of their activity, to belong to the animal kingdom. In this Pasteur was misled by the imperfect knowledge of his day, for it is now well known that many one-celled plants, and especially bacteria, move about in a most lively manner. During his examination of these so-called vibrios Pasteur made an interesting observation that led him eventually to further generalizations on the nature of fermentation. Taking a drop of the fermenting solution, he placed it on a glass slide, covered it with a thin glass cover-slip, and proceeded to study it under the microscope. The organisms at first active

mentation is not a vital process in quite the sense that Pasteur thought it was, although it remains true that living organisms play an essential rôle in ordinary fermentations. They produce the enzymes that do the work.

throughout the fluid were found to become immobile near the edges. This is quite the reverse of what often happens with other forms, because it is near the edge that there is the most abundant supply of oxygen. Can it possibly be that oxygen, the great supporter of life, checks the movements of these forms? Ready as always to put his ideas to the test of experiment Pasteur passed a current of air through a flask of liquid containing active vibrios, thus supplying the material with an abundance of oxygen. The activities of the vibrios ceased, and the butyric acid fermentation that was going on was brought to a close. Pasteur was thus led to the conception of anaërobic life, or life without free oxygen, and the organisms which developed best in a medium devoid of oxygen and whose activities are checked in the presence of this substance he called anaërobes.

The nature of the changes undergone by a decomposing substance may be determined, therefore, by the amount of oxygen with which it is supplied. If it contains a variety of micro-organisms, then, under conditions of free supply of air, certain organisms that require oxygen will develop and produce their characteristic effects. If, on the other hand, the oxygen supply is limited, the anaërobic

forms will thrive and produce different effects. Frequently one change follows another, the ordinary aërobic organisms using up the available oxygen in the material, and thus creating a condition in which the anaërobes may take their turn.

Some organisms, as Pasteur found in the case of common yeast of beer and wine and some species of molds, may live either with or without free oxygen. In any case they need oxygen for their life, and if they cannot secure it directly they take it out of some of the compounds in which it is chemically combined. Pasteur found that the ordinary yeast of beer, if given abundant oxygen, would grow rapidly, but would produce very little alcohol. If its supply of oxygen were limited, it would ferment much more of the sugar into alcohol and carbon dioxide. By being forced to wrest away its oxygen from sugar it becomes thereby a ferment. Fermentation depends, therefore, in his view, on the capacity of an organism to live without air.

What is called putrefaction was proven by Pasteur to be essentially like the phenomena which had been described as fermentations, only it is produced, as a rule, by different kinds of organisms and gives rise to different products. What we com-

monly designate as putrefaction is simply fermentation which generates substances having a bad smell. Commonly, but not necessarily, putrefactions are caused by anaërobic bacteria.

The result of Pasteur's numerous labors on fermentation was to bring order out of chaos. No longer were the phenomena obscure or mysterious. Fermentation was shown to be associated with the functioning of minute living organisms instead of with the decomposition of dead nitrogenous matter. Different kinds of organisms were proven to cause each its own peculiar kind of fermentation in a given substance such as sugar. The products of one ferment, it was shown, might be split up again by another kind of an organism. The influence of these living ferments was shown to be specific or limited to certain kinds of transformation. The loose ideas which then prevailed concerning the ready transformation of one type into another were proven to be based on faulty observation or inconclusive experiments. We now know that microorganisms produce their own kind as faithfully as do cabbages or turnips, and a transformation of a bacterium into a yeast plant, or an infusorian would nowadays be no more expected than the conversion of a cow into a horse, or a maple into an oak tree.

The great progress that has been made in our knowledge of fermentation is based on the sound foundations laid down by Pasteur. Brewers are as careful of their special varieties of yeast as stock-raisers are of their breeds of cattle. Poor yeasts produce undesirable fermentations. Many of the impurities of "home brew" and the various alcoholic liquors that are now secretly made and peddled are due to the influence of micro-organisms which regular manufacturers had learned how to exclude. The doctrine of the constancy of specific types has proven to be a guide of great value in the solution of problems of fermentation both theoretical and practical. We shall see further indications of its far-reaching import when we come to consider its relation to infectious disease.

It was when Pasteur was in the midst of his studies of fermentation that he had an opportunity to join the Faculty of the *École Normale* of Paris. He decided to accept the new position, and in 1857 we find him installed as a professor in the institution which it was once his dream to be able to attend. Although his duties in the school were many, he made a laboratory out of the attic which we have previously mentioned and began work on the fermentation of alcohol. During a part of the

summer the heat of the attic made it impossible to work there. "I see with regret," he wrote to Chappuis, "the longest days of the year lost for my work. Nevertheless I am growing used to my garret and I shall find it hard to leave it. I hope to enlarge it during the next holidays."

During the year 1859 he was studying fermentation. In the latter part of the year he met with a great sorrow, for he had lost his eldest daughter who had died of typhoid fever in September. He wrote his father, "I am unable at present to think of anything except my little girl, so good, so full of life, so happy in living, whom the fatal year that has just passed has taken from us. In a little time she would have become such a loving companion for her mother, for me, and for us all . . . but I beg pardon, my dear father, for recalling to you these sad memories. She is happy. Let us care for those who remain and make ourselves keep from them, as much as in our power, the bitterness of this life."

CHAPTER V

CONTROVERSIES OVER SPONTANEOUS GENERATION

PASTEUR'S studies on fermentation inevitably brought him face to face with the problem of the origin of those minute forms of life through whose activity the process of fermentation is caused. The minute organisms found in decaying substances were regarded by many scientists as arising, by a process of spontaneous generation, out of organic matter in a state of dissolution. Pasteur, who had traced specific kinds of fermentation to specific organisms, and had shown that these organisms reproduced their own kind true to type, and moreover possessed extraordinary powers of dissemination through the atmosphere, was very skeptical in regard to their alleged origin, *de novo*, out of organic matter. Realizing the futility of the metaphysical discussions and *a priori* arguments on the subject, which had been so frequently indulged in, and convinced that it is only by careful and critical experimentation that the question could finally be

settled, he resolved to devote himself to the task. In January, 1860, he wrote to his friend, Chappuis, "I am doing my best with these studies on fermentation, which have a great interest on account of their relation to the impenetrable mystery of life and death. I hope to make soon a decisive step by solving, without the least confusion, the celebrated question of spontaneous generation. Already I could speak, but I want to perform still more experiments. There is so much passion and so much obscurity on both sides, that it will require nothing less than the cogency of an arithmetical demonstration to convince my adversaries of my conclusions. I intend to accomplish even that."

Biot, who had followed Pasteur's career, with a sort of fatherly interest, endeavored to dissuade him from an investigation which he believed would prove fruitless. Dumas, less decided in his remonstrance, remarked that he "would counsel no one to occupy himself too long with such a subject." But Pasteur, who doubtless had a clearer vision in this field than either of his elder counselors, perceived that the problem of spontaneous generation lay, as it were, across his path. To attack it, was the next logical step in his scientific career.

The belief in the spontaneous origin of living

forms is a very old one. Formerly, caterpillars were supposed to arise spontaneously from leaves; and frogs, fishes, and eels were said to be produced from mud and ooze. Virgil has described how bees arise from the carcass of a dead bull, and Van Helmont, although a scientist of eminence, tells us that mice may be engendered by putting some dirty linen in a container along with a few grains of wheat.

The first to perform real experiments in regard to the origin of living things was Francesco Redi, physician to the Grand Dukes of Tuscany. Reflecting on the origin of the maggots observed in decaying meats, he set himself to trace their source. Noticing that blowflies frequently hovered about, and often alighted on, decaying meat, he thought that these flies might possibly be responsible, in some way, for the appearance of the maggots. Accordingly, he placed pieces of meat in jars covered with gauze to exclude the flies. Although the meat so protected was found to putrefy, no maggots made their appearance. Moreover, Redi observed that the flies laid eggs, and that from these eggs small maggots arose which grew rapidly as they devoured the decaying flesh. By many observations and experiments, Redi conclusively showed

that maggots do not arise spontaneously, but develop from eggs laid by flies.

Other naturalists extended these observations and experiments, and finally banished from science the notion that such creatures as worms, insects, fishes or frogs arise spontaneously. Closer investigation of the life history of these forms revealed the fact that they arise from eggs of members of their own species. To-day nothing could seem more incredible to a trained biologist than that an angleworm or an insect should arise by a process of spontaneous generation. He would as soon expect that a Westminster Abbey should suddenly build itself out of the paving stones of the street.

With our present knowledge, we easily perceive that the older notions of spontaneous generation were exceedingly crude. In the light of the scientific knowledge that accumulated during the seventeenth and eighteenth centuries, it was impossible for them long to persist. But when the compound microscope revealed myriads of minute living creatures in a drop of stagnant water, the question of spontaneous generation presented itself anew. That these strange simple organisms might arise by a transformation of organic matter was a conclusion

that did not appear to be unreasonable. It was observed that they made their appearance in infusions previously boiled, and exposed to the air. As boiling was held to kill all living matter, it was inferred that the organisms appearing in boiled infusions must have arisen by spontaneous generation. Moreover, these minute organisms seemed so very different from higher forms of life, and as very little was known of their life history, their spontaneous origin was all the more readily accepted. The Irish priest, Needham, had heated flasks of organic infusions, corked them up while hot, and found, in the course of a few days, that the liquid became turbid from the multitude of minute organisms which were engendered within it. The origin of these living forms was attributed to a "vegetative force" operating on the organic substances of the infusion.

These experiments aroused the interest of another priest, the sagacious Abbé Spallanzani, who attacked the subject by somewhat more rigorous methods. He made infusions in flasks whose contents were thoroughly boiled. Being suspicious of corks, he sealed his flasks by drawing out their necks and fusing them, thus absolutely excluding all air, and hence any germs which might be car-

ried by it. His flasks, unlike those of Needham, remained clear for a long time, and showed no trace of living organisms. Spallanzani concluded that organisms appearing in boiled infusions do not arise spontaneously, but are brought in from the atmosphere. Needham objected that the heat used by Spallanzani altered the vegetative force of the infusions, and that boiling drove off the air necessary to produce life. The controversy came to no decisive issue, and parties to both sides of the question continued their discussions.

Schulze, in 1836, conceived the idea of supplying boiled infusions with air which had been drawn through sulphuric acid in order to rid it of any living germs which it might possibly carry. Infusions supplied with air in this way remained several months free from decay. Schwann, in the following year (1837) varied the experiment by supplying his infusions with air which had been passed through a heated tube. As these infusions remained free from organic life, he concluded that it is not air that causes life to develop, but something in the air which is destroyed by heat. In 1854, Schroeder and Dusch obtained the same results by drawing into their infusions air which had simply been filtered through a plug of cotton wool. Thus

originated a method which is now an every-day procedure in every bacteriological laboratory.

These experiments, which were distinctly unfavorable to the theory of spontaneous generation, were not permitted to go unchallenged. Their most noteworthy opponent was Prof. F. A. Pouchet, Director of the Museum of Natural History at Rouen, a man celebrated as a naturalist and of high standing among the scientists of his country. In 1859, Pouchet published a large work entitled "Hétérogénie" in which the experiments of his opponents are subjected to a searching criticism, and in which many new experiments are described which, in the opinion of the author, prove conclusively that life develops in boiled infusions under conditions which completely exclude the entrance of germs from the outside. Pouchet threw himself into this work with much vigor and enthusiasm. He repeated the experiments of Schulze and Schwann, and obtained living organisms where they had obtained none. If germs exist in the air in the abundance which would be necessary to produce the effects ascribed to them, Pouchet maintains, the air would be quite obscured. The extensive researches of Pouchet, carried on with the appearance at least of careful control, and set forth in a

confident and impressive manner, tended to make opinion more favorable to the theory of the spontaneous origin of life.

Naturally, these researches were closely followed by Pasteur. Although their results were contrary to his own experience and the conclusions to which he was led, he refrained from any discussion of the subject until he had carried out many investigations of his own. No one was better prepared than he to realize the difficulties that beset the investigator in this field. Even with the most scrupulous care, one may, quite unsuspectingly, make little slips that entirely vitiate his results. Pasteur strongly suspected the adequacy of the technique employed by Pouchet, and he set himself to repeat the experiments of his opponent and to devise others which would afford a conclusive answer to the much controverted question with which he was grappling. Pouchet affirmed that suitable infusions supplied with oxygen would develop living organisms when every care was taken to exclude outside germs. Pasteur, on the contrary, found, in agreement with Schulze, that if air were drawn through a heated tube before supplying the infusions, no life would develop.

One type of experiment which is particularly

significant was the following: Pasteur placed infusions of many different organic substances in glass flasks whose neck was drawn out into a long curved tube. After thorough boiling, the air which was sucked in to take the place of the condensed steam after the liquid gradually cooled, would deposit

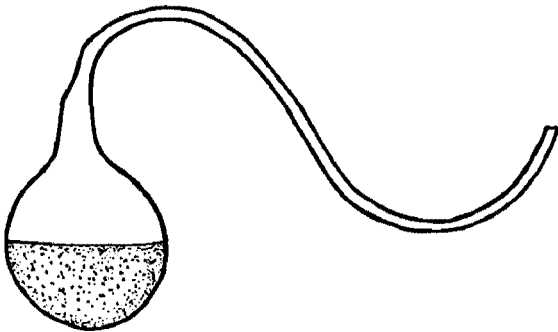


FIG. 7. FLASK WITH CURVED NECK USED FOR KEEPING BOILED INFUSIONS SUPPLIED WITH AIR FREE FROM GERMS

nearly all its floating matter along the sides of the tube. Although supplied with air, the contents of the flask were found to remain for a long time perfectly clear and free from decay. If now the flasks were tilted so that some of their contents came in contact with the walls of the tube, putrefaction would invariably be set up. The material in the flask was able to develop life. The only thing lacking was not air but something which was caught

in the long narrow neck. When this was added, living forms appeared in abundance. What was this something?

Pasteur affirmed that it was germs floating in the air, and he set himself to demonstrate that germs actually do float in the air. To show this, he caused air to be drawn through a tube, plugged with gun cotton to act as a sort of filter. After a given volume of air had been drawn through the tube, the gun cotton was dissolved in alcohol and ether. A residue was deposited which, under the microscope, was seen to be composed of many kinds of particles, among which were bodies indistinguishable from the spores of mold, the cysts of infusorians, and various kinds of bacteria. That the cotton actually contained the germs of organisms was shown by another experiment. Taking a flask of sterile infusions, Pasteur, under precautions to keep out the entrance of matter from the outside, placed a small bit of the cotton in the neck but without allowing it to come into contact with the liquid; then the neck of the flask was sealed. So long as the cotton remained in the neck of the flask, the liquid kept clear. After fifteen days, or a month or longer, the flask was tilted so as to bring the liquid in contact with the cotton. Soon the

liquid became turbid, and teeming with living organisms. "What reply," asks Pasteur, "do you make to this experiment? Will you claim that the cotton, being an organic substance, generates life?" Even this possibility was met. Pasteur replaced the cotton by the purely mineral fiber of asbestos, and obtained precisely the same results. These

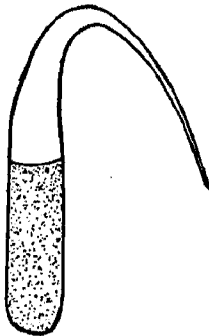


FIG. 8. FLASK WITH SEALED NECK PARTLY FILLED WITH BOILED INFUSION

were crucial and clear-cut experiments and their answer was decisive.

Pasteur's instinct for thoroughness led him to make a detailed study of the atmosphere of different localities, in order to ascertain whether or not it possessed uniformly the same power of generating life. In this investigation, he used small straight-necked flasks (Fig. 8), partly filled with an infu-

sion, and after bringing the contents to a boil, he sealed the necks by fusing the glass with a blow pipe while the steam was escaping. He then carried these flasks to where he wished to study the atmosphere, sterilized the necks, snipped them off with sterilized pincers, thereby allowing the air to rush into the flasks; then he re-sealed them. As a rule, some flasks remained clear, and others not, depending upon whether or not germs happened to be present in the sample of intruding air. Of the ten flasks opened in the calm air of the cellar under the observatory at Paris, only one showed any signs of contamination. Of the eleven flasks opened in the yard of the same institution, all gave evidences of the development of life.

During his vacation in 1860 Pasteur decided to experiment with the pure air of the Alps. On September 20th of that year we find him ascending the Montanvert, near Chamounix, with a mule laden with cases of flasks. In his first experiment, being unable to close the necks of his flasks until he returned to the inn where he was stopping, he found that nearly all of his infusions became contaminated. His next experiment was carried out on the Mer de Glace glacier. After sterilizing the neck of each flask he raised the flask high above his

head to avoid the entrance of germs from his clothes and broke the neck with a sterilized forceps and quickly re-sealed it. Of the 20 flasks so treated only one gave signs of life. By these and other experiments Pasteur showed that air is by no means uniform in its power to generate life in infusions. Where the air is pure and relatively free from floating matter it rarely gives rise to living forms. It is therefore not air that generates life, but something in the air, as Pasteur repeatedly affirmed.

The publication of these results stirred Pouchet and his colleagues to renewed efforts in support of their cause. They had affirmed that air taken from anywhere would give rise to life when brought into contact with a proper sterile solution of organic material. They resolved to meet Pasteur on his own ground, and accordingly they also set out for the Alps with a supply of flasks. A party of three investigators, Pouchet, Joly, and Musset, made a somewhat perilous journey to a height considerably above the Montanvert, for they must outdo Pasteur in the excess of their precautions to obtain pure mountain air. Their flasks which had been partly filled with a boiled infusion of hay (a noteworthy point as we shall see later) were opened

and sealed again with the most careful precautions. In a few days the investigators were rewarded by finding all of their flasks turbid and teeming with life. Even the purest air of the mountains, Pouchet triumphantly claimed, is capable of generating life in putrescible material.

Here we have a most curious situation! Different investigators of high standing and unquestioned integrity performing what they deemed to be the same experiment under as nearly as possible the same conditions arrive at diametrically opposite results. What is the explanation? Who is right? Did Pouchet and his adherents commit some experimental error which allowed germs to gain entrance without their knowledge into their infusions?

In order to resolve this apparent deadlock Joly and Musset made the fair and reasonable proposal that the Academy of Sciences appoint a commission, before whom both parties to the controversy should repeat their experiments. Pasteur, convinced of the truth of his position, readily acceded to this proposal. The Academy therefore appointed five men, Flourens, Dumas, Brongniart, Milne-Edwards, and Balard. Pasteur wished the discussion to occur as soon as possible, but his opponents plead for delay on account of the cool-

ness of the weather. But when warm weather came they refused to comply with the conditions laid down by the Commission, which presented a report favorable to Pasteur.

The heterogenesisists still continued the discussion, and it was a number of years before the question was cleared up to the satisfaction of the most competent judges. In the light of what is now known it is not improbable that Pasteur's opponents would have been able to repeat their experiments before the Commission of the Academy with the results which they had predicted, and Pasteur, although right in his fundamental contention, would probably have been unable to refute them. Truth is sometimes very elusive, and nowhere more so than in this field. The positive results obtained by Pouchet and his co-workers under conditions in which Pasteur was unable to obtain any traces of life were probably not due, as Pasteur thought, to faulty technique, but to a fact then unknown to both parties, i.e., that certain forms of life may resist prolonged boiling without being killed. This is demonstrably true of the spores of the hay bacillus, and it is significant that Pouchet worked with infusions of hay, while Pasteur employed a decoction of yeast and various other infusions.

The controversy was somewhat analogous to the celebrated discussion of the color of the two sides of the shield.

This fact was brought out only several years later in the course of a discussion with the celebrated English champion of the doctrine of spontaneous generation, Doctor Charlton Bastian. Bastian, who was well known in medical circles in England, had written a large, two-volume work entitled "The Beginnings of Life," in which he brought forward much experimental evidence for the spontaneous origin of living organisms, and contended that many of the low forms of life passed readily into species of a quite different character. Although his work is full of wrong conclusions based on inaccurate observations, Bastian performed several experiments which have been the means of materially advancing our knowledge of the propagation of minute forms of life. Bastian claimed that urine boiled to free it from germs, then rendered alkaline by a solution of boiled potash and set aside to incubate, became swarming with bacteria in nine or ten hours. It is not germs, he claimed, that give rise to the bacteria, but the alkali which supplies a condition necessary for spontaneous generation.

The experiment was repeated by Pasteur who confirmed Bastian's observations, although he sought to explain them in a different manner. It cost Pasteur and his co-workers, Joubert and Chamberland, much work to get at the real solution of the difficulty. Chamberland showed that in an acid medium some germs may be heated to the boiling point, but will remain inert until the medium is rendered alkaline when they again develop. Again, germs, such as the spores of the hay bacillus, may endure a temperature in an alkaline medium several degrees higher than in a neutral or acid medium. By heating to 115° or 120° C., the materials used by Bastian it was found that all bacterial development in alkaline urine was effectually checked. Nowadays a practice is made of heating to 120° C. materials which it is important to thoroughly sterilize. As Duclaux remarks, "Bastian rendered a service to science; he lashed it on its weak side, but he compelled it to advance."

The interest aroused by these controversies and the importance of the question involved drew several investigators into the field. Many facts of importance in regard to the vitality of germs under different conditions were brought out as a result

of efforts to arrive at a definite settlement of the problem. It was found that in a dried condition germs may resist degrees of heat considerably above the boiling point. Bacteria may lodge upon the sides of glass vessels or the necks of glass retorts and remain there in a living condition while the fluid contents have been subjected to boiling. As Duclaux observes, "The heating to 120° C. of a flask half full of liquid may sterilize only the moistened part, allowing life to persist in the regions which are not in contact with the liquid. In order to destroy everything, it is necessary to subject the dry walls to 180° C. Hence the utility of flaming all the receptacles used in microbiology, and behold once more a practice arising, like the autoclave, from the laboratory of Pasteur, and which, along with it, established a good technique and made the future secure."

As knowledge of micro-organisms became more extensive and precise, the position of the opponents of spontaneous generation grew steadily in strength. In England the problem was investigated with great ability and manipulative skill by the physicist, John Tyndall, who approached the problem by a route very different from that of Pasteur. Tyndall was led to it from his investigations of the way in

which light is affected by minute particles in the air and other media which it traverses. The blueness of the sky and the blue color of the sea and the water of deep lakes he explained as due to minute particles held in suspension which, on account of their very small size, reflect chiefly only the shortest light waves of the visible spectrum, or those near the violet end. It was necessary for him in the course of his experiments to obtain air free from floating matter. Light passing through ordinary air reveals its course by being reflected from a multitude of minute particles. Tyndall showed that a beam of light sent through air free from floating particles is absolutely invisible. I have often noticed in the shade of the dense redwood forests of northern California how beams of light reveal their path, high up among the trees, by delicate hazy streaks in the exceptionally pure air of that region. Even there the air is charged with floating matter. Of what does it consist?

Tyndall studied the question in samples of the air of London by an ingenious method. A coil of platinum wire which could be heated to redness by an electric current was enclosed in a glass vessel into which air could pass only by going through a dense plug of cotton. A beam of light passing

through the vessel could be traced by the illuminated motes in the air. After the platinum coil had been heated to redness for some time the course of the beam was no longer visible. The floating matter had been burned; it was therefore organic matter. The same result was also obtained by passing air through the flame of an alcohol lamp. Examination of floating matter in several places has shown that it contains as a rule only a small proportion of inorganic dust. The more persistent floating matter is composed mostly of organic material which when dried and finely divided is very light and readily wafted to great heights by even a very gentle breeze.

Occasionally inorganic particles, if very small and of light material, may be carried to great distances in the air. Several years ago after the eruption of the great volcano of Krakatao, it was estimated that the dust was carried several times around the world in the higher levels of the atmosphere, causing the striking red sunsets which were observed for several weeks after that event.

Tyndall found that passing air through sulphuric acid as Schulze had done failed to make it "optically pure." Some of the motes in the bubbles failed to come into contact with the liquid and

passed through unaffected. Such air he showed was occasionally able to develop organic life in sterilized infusions, but for reasons quite different from those given by Pouchet.

Is there any relation between the optical purity

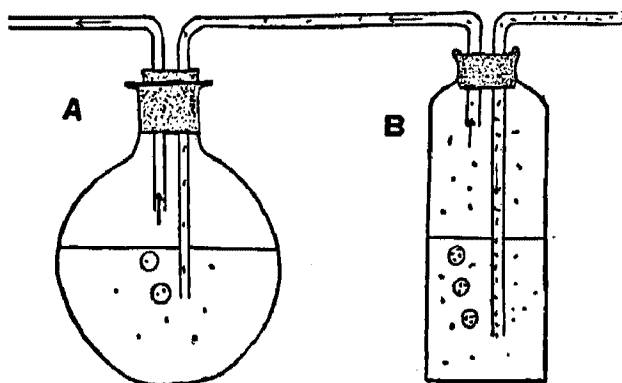


FIG. 9. APPARATUS DESIGNED TO FREE AIR FROM GERMS BY DRAWING IT THROUGH SULPHURIC ACID CONTAINED IN B

Air sucked through in the direction of the arrows causes it to bubble through the acid, but some of the germs, represented by dots, may escape coming into contact with the fluid and pass into the infusion in the flask A.

of the air and its power of causing putrefaction? Tyndall attacked this problem with his usual thoroughness and skill. Like Pasteur he experimented with sealed flasks containing infusions which were opened and closed again in different kinds of air. He also experimented upon the air in his favorite

vacation ground in the Alps with results corroborating those obtained by Pasteur. Many experiments were carried on with an apparatus constructed as follows: A case with glass front and a glass window in either side (Fig. 10) is provided with a bottom having holes in which glass test tubes are fixed, air tight, with their open upper ends in the chamber. Through the top is a funnel tube passing through an India rubber disc. This tube is movable and is used for filling the tubes with liquid. Two tubes are fitted for admitting air, but they are bent several times to intercept any floating matter that might be carried by the slow exchange of air between the inside and the outside of the chamber. The inside of the chamber is coated with glycerine to catch any floating motes which come in contact with it.

A powerful beam of light sent through the glass windows revealed the existence of floating particles in its course. After a time the beam became less and less visible as the motes in the air settled to the bottom or were caught by the coating of glycerine on the top and sides. In three days the beam within the box was quite invisible, but before it entered the box and after it emerged its track was "vivid in the air."

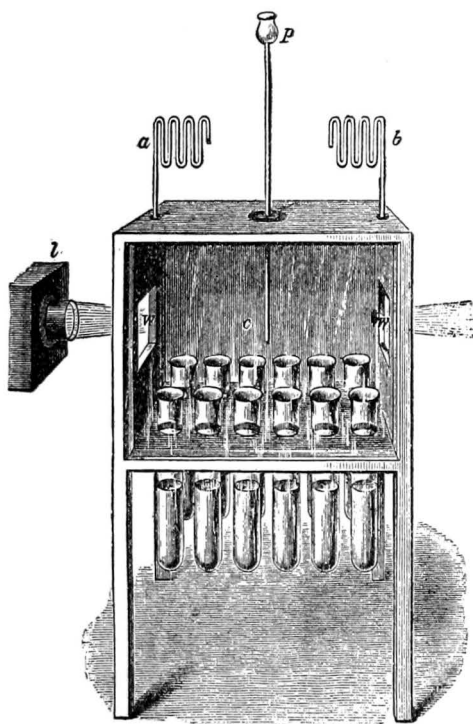


FIG. 10. APPARATUS DESIGNED BY TYNDALL FOR FREEING AIR FROM FLOATING MATTER

a and *b* curved tubes for admitting air; *p*, tube used for filling the test tubes in the bottom. *l*, source of light passing through the windows, *W* and *W*.

Various infusions were poured through the funnel tube into the test tubes and brought to a boil by a burner placed below them. Similar sets of tubes, filled with the same material, were boiled for the same length of time and exposed to ordinary air as a control experiment. In the one case the tubes were protected from floating matter, in the other they were exposed to it. Otherwise the conditions in the two sets were the same.

Hundreds of experiments were tried with all sorts of substances; urine, infusions of beef, haddock, sole, codfish, hare, grouse, liver, oysters, turnips, hay, and many other materials in varying degrees of strength. Tyndall was nothing if not thorough. And what was the outcome? "There is no shade of uncertainty," says Tyndall, "in any of the results. In every instances we have within the chamber perfect limpidity and sweetness—without the chamber, putridity and its characteristic smells. In no instance is the least countenance lent to the notion that an infusion deprived by heat of its inherent life, and placed in contact with air cleansed of its visibly suspended matter, has any power whatever to generate life anew."

The hay infusion employed had been heated to 120° C. for four hours as the spores of the hay

bacillus were proven to be exceptionally resistant to heat, especially in an alkaline medium, but all of Tyndall's protected tubes "remained for more than three months as clear and healthy as they were on the day the infusion was poured into them."

That several kinds of micro-organisms remain alive in boiling water is a fact that has proven a fertile source of error in experiments on spontaneous generation. It was but natural that in the earlier experiments on this subject it was generally assumed that boiling must be fatal to all living substance. Gradually it became manifest that different species vary greatly in their power to resist destruction by heat. The bacteria causing the souring of milk, for instance, are easily killed, and in Pasteurizing milk it is only necessary to heat it to about 60° C. Other organisms in milk are not killed by this temperature, and some of these may cause milk to putrefy without becoming sour. Only a few forms can withstand boiling, and they do so commonly in the form of spores. Their protection by a resistant coating which prevents their protoplasm from being softened is probably one reason for the high resistance of the spores of several forms. For a similar reason a high resistance to

heat is shown by the seeds of several plants. Seeds, like the germs of micro-organisms to which they are analogous, vary greatly in their resistance to heat. Most of them are destroyed by temperatures far below the boiling point; some, like mustard seed, may withstand a few seconds exposure to boiling water. A few kinds of seeds have been found to resist boiling for several hours without destroying their power of germination.

Another very deceptive circumstance consists in the relation of the development of some germs to oxygen. In some cases infusions have been boiled and found to remain clear so long as they were kept from the air. When supplied with oxygen, under the most careful precautions to prevent contamination, they were nevertheless found to develop life. Here seems to be the kind of proof required for the theory of the spontaneous origin of life. More searching investigation, however, solved the problem in a different way. It was shown that the germs in question were not killed by boiling, but remained alive, though inactive, in the sealed tubes because they required oxygen for their development. When this was supplied under conditions that kept out any germs from the outside, life developed in the infusion. By bringing the infusion

to a temperature several degrees above the boiling point no life developed even with an abundant supply of oxygen. It was not the germs alone that were required as Pasteur at first thought, nor oxygen alone as the champions of spontaneous generation thought, but germs plus oxygen as Pasteur later came to discover.

I have been able to give but a brief sketch of the numerous experiments which the battle over spontaneous generation called forth. Few problems in science have proven so baffling. The difficulties and the pitfalls besetting the investigators of this question have led many into errors, and Pasteur himself was not entirely free from them. But the conquest of the difficulties has added much to our knowledge of the world of microscopic life. Today the scientific world is convinced that spontaneous generation, in the sense in which it was formerly believed, does not occur. That it has not occurred, or may not occur under precisely the right conditions, the cautious scientist would not assert. How the gap between the inorganic and the organic was bridged is a problem still far from solution.

The more we know of minute organisms the more their propagation is found to resemble that of

higher plants and animals. Their species breed as true as those of sheep or cattle. Their form may vary in different parts of their life cycle, but we often meet with profound changes of form in the life history of highly organized creatures. So far as our experience goes it corroborates the truth of the dictum, "Omne vivum e vivo,"—all life from antecedent life. And not only this, but it may be said that all life comes from antecedent life of approximately the same kind. The establishment of this doctrine for minute forms of life in the sense that it holds true for higher forms is an achievement of far-reaching importance in many relations. Pasteur was early convinced of its truth. He did more than any one else to establish it. And this principle served him as a most valuable guide in grappling with the problems with which he was destined to be occupied during the remainder of his life.

CHAPTER VI

THE DISEASES OF WINE AND VINEGAR

THE years devoted to the problem of spontaneous generation were years of growing fame. The controversies in which Pasteur engaged attracted the attention not only of the scientific world, but of the wide circle of people who were naturally curious in regard to the beginnings of life. A lecture on spontaneous generation delivered by Pasteur on August 7, 1864, drew a large and eager audience in which were such celebrities as George Sand, Duruy, Alexandre Dumas and the Princess Mathilde. The subject was discussed in the popular press and became a favorite topic of chatter in polite society.

As always occurs with great scientific issues there were many people whose chief concern with the question was over its possible bearing on religion. Spontaneous generation was regarded by some as tending toward atheism, while the opposed view was considered to be more in accord with the traditional account of creation as narrated in Genesis. Pasteur's work was, therefore, quite

orthodox in its supposed theological bearings. For this reason it was received with favor by some and suspicion by others. Pasteur felt called upon to declare, "This is not a matter of religion, philosophy, atheism, materialism, or spiritualism. I might even add that as a scientist these things do not concern me. It is a question of fact; I took it up without preconceived ideas, and if experiment convinced me that way I was as ready to maintain the existence of spontaneous generation as I am now persuaded that those who affirm it are blindfolded."

The purely scientific attitude of mind is hard for many persons to appreciate. The true scientist endeavors to exclude all kinds of bias which may obscure his vision of the truth, to follow humbly, without regard to preference or desire, wherever evidence may lead, regardless of consequences to his preconceived opinions. To close his eyes to evidence against his cherished convictions is, from the point of view of the seeker after truth, not only unwise, but immoral. But how often do we sin against the cause of truth, preferring to adhere to our opinions, rather than to bring them to the test, and to give them up if the balance of evidence turns against them!

In the realm of scientific fact Pasteur endeavored to maintain an open mind, and to be always ready to acknowledge error and to retrace his steps when he found himself on a wrong track. This trait is essential to a man of science, who is, so to speak, a professional seeker after truth. In the ordinary walks of life people may be unreasonable, pig-headed and intolerant in regard to matters of opinion without exciting much comment,—in fact this is to be expected. But even in ordinary life, matters of great importance may hinge upon the correctness of our judgments, and we may pay dearly for our disregard of the principles of right thinking. And there is no lot nor occupation in which adherence to these principles will not materially add to the effectiveness of our lives.

Although Pasteur endeavored never to allow his mind to be swayed by prejudice or inclination, his work was far from being carried on in a cold and dispassionate spirit. Few men worked under greater emotional stress. Of an intense nature, fired by a lofty enthusiasm for discovery, ambitious to throw light on fundamental problems in his fields of research, inspired by a vision of the far-reaching importance of his investigations, and conscious that he was opening the door to discoveries

of highest value to mankind, Pasteur threw himself into his work with feverish energy and entire absorption. Readily aroused by opposition he exhibited a vigorous pugnacity in controversy that is attributable less to irritability of temper than to the intense seriousness of his concern with the problems before his mind.

His family life was a singularly happy one. Fortunately, Madame Pasteur could appreciate her husband's scientific work and ambitions, and she betrayed no jealousy on account of his extreme devotion to his tasks. If she suffered an occasional pang, as doubtless she must have done, she loyally concealed it under a guise of cheerfulness and encouragement. In 1884 she wrote to one of her children, "Your father, always much preoccupied, talks little, sleeps little, rises at dawn, and, in a word, continues the life which I began with him thirty-five years ago to-day."

One of Pasteur's characteristics, which offers the strongest testimony as to his sterling qualities, was his capacity for making true and devoted friends. Men were drawn to him not only by his ability and achievements, but on account of personal traits that inspired their respect and affection. It was Pasteur's privilege to number among

his close friends such men as Balard, Dumas, Biot, Deville, Senarmont, and Claude Bernard, and it was his pride to have drawn around him as pupils and assistants men such as Roux, Joubert, Chamberland and Duclaux, who have made themselves famous by researches in fields opened up by his labors. When these men speak or write of their master it is in a tone which reveals the great admiration and devotion with which he inspired them.

Pasteur's essay on organized corpuscles existing in the atmosphere gained the prize which the Academy of Sciences offered for the best experimental investigation of the question of spontaneous generation. Several of his scientific friends endeavored to have Pasteur made a member of the Academy. As this learned body is one of limited membership, a new member is elected only when a vacancy arises through the death or resignation of one of its number. In 1857 a vacancy arose in the section in mineralogy and Pasteur was urged to present himself as a candidate on the basis of his researches on crystallography, for which he had already received the Rumford medal from the Royal Society of London. Although ardently supported by Biot, who had been his steadfast friend ever since his demonstration of right-handed and

left-handed tartrates, and in spite of a most flattering account of his work by the mineralogist, Senarmont, Pasteur received only sixteen votes, thirty being required for election. Again in 1861 he stood for election, this time in botany on account of his researches on minute forms of plant life. Championed by Balard and again by Biot he obtained 24 votes and failed again. The fact that he was a professional botanist doubtless counted against him. Moquin-Tandon, who was urged by Balard to support Pasteur, replied, "Let us go to Pasteur's and if you find a botanical work in his library, I shall put him on the list." It would not be surprising if the quest should have been unsuccessful. In 1862, through the death of his friend, Senarmont, a vacancy was again created in the section on mineralogy, and this time Pasteur was elected.

The battles over spontaneous generation had taught Pasteur many things which he was able to turn to good account in his efforts to solve several practical problems which now engaged his attention. Nearly a year was devoted to studying the manufacture of vinegar and in endeavoring to obviate several of the difficulties and mishaps that beset the makers of this useful article. Vinegar,

as is well known, is derived from the fermentation of alcohol. Wine, cider, and other liquids containing not too high a percentage of alcohol, turn sour under the proper conditions, owing to the transformation of alcohol into acetic acid. The city of Orleans in France was a great center for the manufacture of vinegar and those engaged in this occupation frequently suffered great losses, because the fermentations failed, for some unknown reason, to proceed in the proper way. Ordinarily in the half-filled casks of partly ripened vinegar and wine which were used, a thin film developed on the surface which the manufacturers knew, from experience, was important for the proper fermentation of the underlying liquid. When the film sank, or became dislodged, fermentation was checked. It was known that the film required air for its development, although it was not known why. Pasteur, in making a microscopic examination of this film, found it to consist of minute organisms, about twice as long as wide and $\frac{1}{400}$ of a millimeter in length. He called this form *Mycoderma aceti*, and he showed that it had the property of taking oxygen from the air and oxydizing the material below. One gram of these minute organisms was proven to be capable of transforming ten thousand

times its weight of alcohol into acetic acid in five days.

It is now known that several species of micro-organism may ferment alcohol into vinegar, but for the most part they closely resemble each other and may readily be distinguished from other organisms that are frequently associated with them. The vinegar-producing organisms multiply at an almost incredible rate. So long as alcohol is present they transform it to acetic acid, but when their preferred food is exhausted they may attack the acetic acid itself and transform it into carbon dioxide and water. Vinegar exposed to the air often, therefore, becomes weaker and its acid may in time entirely disappear. Not only wine should be shielded from air to keep it from turning sour, but vinegar should be similarly protected to keep it from growing weak. Pasteur found that if vinegar is heated, thus killing its organic life, it may be kept clear and pure for a long time.

Pasteur's studies introduced several improvements in the methods of producing vinegar which were the means of saving millions of francs to the manufacturers. In a lecture before the Chamber of Commerce at Orleans, which was largely attended by vinegar makers, doctors, and students, he gave

a general summary of his investigations. He told his audience of the work of the minute organisms that are responsible for fermentation, the conditions necessary for their life, the real reasons for the procedures followed in vinegar-making, the sources of failure so frequently encountered in this industry, and the means by which these failures may be avoided. "Nothing," he said in concluding his lecture, "is more agreeable to men devoted to a scientific career, than to increase the number of discoveries, but when the practical utility of their observations is demonstrated by practical utility their joy is complete." To Pasteur it was a great satisfaction to grapple with a troublesome problem and after mastering it, to set forth his discoveries before his grateful hearers.

Pasteur's studies on vinegar afforded a natural introduction to his investigations of the maladies of wines. Wine-making has always been one of the important industries of France, and French wines enjoyed a reputation which caused them to be sought after all over the world. But the wine industry had come to suffer from several diseases which occasioned much financial loss. Even the best of wines sometimes went bad, and wine-makers were quite in the dark as to the causes of

their misfortunes and the methods by which they might be avoided. From England a business man wrote to Pasteur, "In France people are astonished that trade in French wines has not been more extensive in England since the commercial treaty. The reason is quite simple. At first we received these wines with eagerness. But we soon had the sad experience that the business led to great losses and to much embarrassment on account of the maladies to which they are subject."

The Emperor Napoleon III, who had followed Pasteur's career with interest and appreciation, called upon him for aid in this emergency. Pasteur entered upon this investigation with his accustomed energy. The volume of *Studies on Wine* (Études sur le Vin), which is the product of his labors, was dedicated to his royal patron in the following terms:

Sire, Your Majesty, concerned with reason over the prejudice against the trade in French wines which has caused the alterations to which they are subject has deigned to invite me, now two years ago, to seek the causes of the diseases of wines and the means of preventing them. Since the day on which I was honored by this important mission I have not ceased to devote myself entirely to this work.

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If time, the necessary and infallible judge of all the productions of science, confirms, as I hope, the exactitude of my work, I shall have received, Sire, the satisfaction, the most enviable for a scientist, of having performed a useful service to my country in responding to the desire of the Emperor.

I am, Sire, with the most profound respect, the very humble and faithful servant and subject of Your Majesty.

L. PASTEUR.

French wines suffered from several different diseases, more or less characteristic of wines of different kinds and localities. Sometimes they become acid; again they may become turbid, generate gas, and acquire a flat taste. Such wines were spoken of as turned (*ourné*). This change was particularly apt to occur after the warm months of summer. One malady which was very troublesome was the development of bitterness (*l'amertume*) which was prone to attack all red wines and especially those of Burgundy. Again, wines may become ropy, as occurred in the wines of Champagne. Pasteur's first procedure was to subject wines suffering from these several diseases to a microscopic examination. He found that each disease was accompanied by characteristic organisms differing from those producing normal vinous

fermentation. The acid wines contained an abundance of the *Mycoderma aceti*. In the "turned" wines there were slender filaments resembling those found in the fermentations that form lactic acid. Bitter wines were found to contain larger filaments

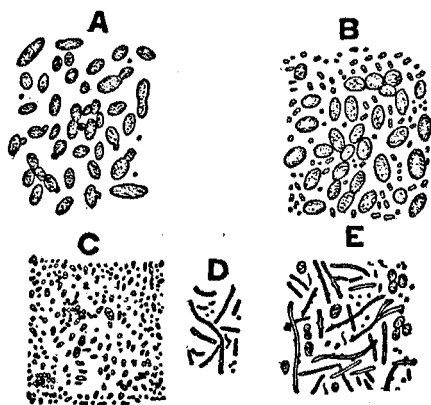


FIG. II. ORGANISMS FOUND IN DISEASED WINE

A, Cells of normal vinous fermentation; B, acid wine in early stage of deterioration; C, a later stage of the same malady; D, rosy wine (*maladie de la graisse*); E, bitter wine (*maladie de l'amertume*).

which were sometimes branched. As the diseased condition became more pronounced the characteristic organisms became more abundant.

And the remedy? It was very simple. At first Pasteur tried antiseptics but without much success. Then he tried heat. After considerable experimentation he found that heating wine to about 55° C.

sufficed to kill all of these troublesome living ferments. There was a natural prejudice against heating wines, but the treatment in no wise injured their flavor nor interfered with the slow process of ageing which Pasteur showed was due largely to oxidation. Once the cause of the trouble was known the remedy, as in so many other cases, was much more readily thought of.

A Commission was formed to try out the results of the new treatment. Five hundred liters of wine, placed aboard an outgoing vessel at Brest, were divided into two parts, one half being heated, and the other half left in the usual manner. After the return of the vessel from a ten months' cruise the heated wine was found to be in excellent flavor, while the non-heated wine was astringent and acid, and in a fair way to be soon entirely spoiled. Other trials turned out in much the same way, and soon the practice of heating became very prevalent and proved to be the means of enormous savings to the wine industries of France. In 1867 a jury of the Universal Exposition offered Pasteur a grand prize for his services to the wine industry. These successful efforts to check the diseases of wines evoked the gratitude of the Emperor who expressed surprise that Pasteur had not taken advantage of

his discoveries to enhance his own wealth. Pasteur replied that, "In France scientists would feel that they lowered themselves by such a procedure."

Napoleon III, as well as the Empress, conceived a personal liking for Pasteur and occasionally had him at the palace. They enjoyed having him expound the mysteries of the world of minute life, and sometimes the scientist would show them and their guests some of his organisms under the microscope. On one of these visits he required for one of his demonstrations some live frogs which he carried in a bag. Absent-mindedly he forgot the bag when he went away, and during the night some of the frogs made their escape and wandered about freely through the palace, some of them invading the bed chamber of the Empress. The Empress, happening to get up in the night, set her foot upon the cold and clammy back of one of these innocent wanderers and experienced a fright which only a person of feminine sensibilities can imagine. Notwithstanding this experience, so unusual in the royal circles, Pasteur continued to be in favor at court.

CHAPTER VII

THE DISEASES OF SILK WORMS

WHILE still at work on the diseases of wine Pasteur received from his old friend and teacher, Dumas, an urgent appeal to investigate a peculiar malady which was creating great havoc in the silk industry of France. Dumas represented as Senator a region in the south of France, which was particularly infested by this disease. Knowing intimately Pasteur's career and how successfully he had grappled with the diseases of wines and various other scientific problems, Dumas picked out Pasteur as the one man who would be most likely to bring relief to an important industry which was threatened with ruin. Dumas wrote, "I attach the greatest importance to seeing your attention fixed on the question which interests my poor country; the distress is beyond anything you may imagine." Pasteur had his misgivings about interrupting the work on which he was engaged and entering a field with which he was unfamiliar. "Consider, I pray you," he wrote to Dumas, "that I have never even

touched a silk worm. If I had a part of your knowledge on the subject I should not hesitate; it may perhaps lie within the sphere of my present studies. The recollection of your many favors to me would always leave me bitter regrets if I were to refuse your pressing invitation. Do with me as you like." To Pasteur's complaint that he was entirely ignorant of the subject Dumas only replied, "So much the better! For ideas you will have only those which will come to you as a result of your own observations."

Pasteur with mingled feelings of self distrust and hope soon left for Alais, a town in the thick of the silk worm epidemic. He little suspected that he had embarked upon one of the most arduous and perplexing investigations of his career. The great French naturalist Fabre, well-known for his fascinating writings upon the habits of insects, gives an amusing account of a visit which he received from Pasteur upon his arrival in the silk worm district in which Fabre happened to reside. Pasteur sought some instruction from the celebrated entomologist regarding the habits and life history of the silk worm, and requested to see some of the cocoons. "Nothing could be simpler," said Fabre who stepped out and soon returned with a pocket full

of cocoons. Pasteur took one and turned it around and around in his fingers as he attentively examined the unfamiliar object. Shaking it before his ear he exclaimed in surprise:

"It rattles; there is something inside of it!"

"Yes, certainly," said Fabre.

"But what is it?"

"The chrysalis."

"The chrysalis! What is that?"

"I might say it is a sort of mummy into which the caterpillar transforms before becoming a moth."

"Is there one of these things in every cocoon?"

"Certainly. It is to protect the chrysalis that the caterpillar spins."

"Ah!"

It is somewhat curious to find this celebrated man of science ignorant of simple facts of natural history which children usually learn in the grammar school. If there are any advantages in attacking a problem in entire ignorance of what has been previously done upon it Pasteur certainly possessed them. But he possessed what was infinitely more valuable than information and that is a fertile and resourceful mind trained in the methods of experimental investigation and endowed

with rare patience, determination, and energy. His work on fermentation and spontaneous generation with the many deceptive sources of error involved, and his conquest of the diseases of wine had given him a training in critical methods, in comparison with which his ignorance of entomology was but a trifling and easily remedied drawback. And yet in this work Pasteur was destined to be deceived and to labor on the basis of false hypotheses, but as he put them to the test of crucial experiments, he came finally out of darkness and confusion into clearness and order.

The disease in question had been introduced about twenty years previously and had been gradually becoming more widespread. It attacked the worms in all stages of their development, some dying before the first molt, or shedding of the skin; others succumbed in later stages. Commonly growth was checked, and the worms, ordinarily voracious, would eat little or nothing. One common, but not universal symptom was the appearance of black spots upon the skin which resembled grains of black pepper; this caused the disease to be called *pébrine*. Often the afflicted worms would begin a cocoon but would weaken and die before it was completed. Others would spin normally,

but the disease would attack the chrysalis, which might die in the cocoon or pass through its usual metamorphosis and emerge as a diseased moth. Silk worm moths mate soon after they emerge, and then the female lays her eggs. It was found that eggs from diseased moths produced diseased worms, so that the malady was spoken of as hereditary. It is, in fact, one of the very few diseases which may be transmitted through the germ cells from parent to offspring.

The disease had made such tremendous inroads upon the silk industry that France was producing but a small fraction of her previous yield of silk. In 1853, France produced 52,000,000 pounds of cocoons; but there were only 8,000,000 pounds, or less than one-sixth as much, produced in 1865. The distress in the silk-producing district was acute. "The traveler," wrote Pasteur, "who fifteen years ago had gone through the mountains of Cévennes, and who retraced his course to-day, would be surprised and shocked to see the changes of all kinds which have occurred in so short a time in that country. Formerly he would see, on the slopes of the hills, active and robust men breaking up rock in order to construct solid walls for the support of the fertile but laboriously prepared soil and raising ter-

races planted with mulberry trees even to the summit of the mountain. These men in spite of the fatigue due to their rough work were then contented and happy because plenty reigned in their domestic firesides.

“To-day the mulberry plantations are entirely abandoned; the tree of gold no longer enriches the country, and the faces formerly happy are now downcast and sad. Where abundance once reigned there is now poverty and distress.”

There were all sorts of theories as to the cause of the disease. All sorts of treatment were tried in vain. The unfortunate worms were dusted with ashes and charcoal, treated with chlorine gas and with fumes of nitric and sulphuric acid, sprinkled with rum, sugar, and quinine, and doped with creosote and copperas. Remedies of reputed efficacy were sold to the luckless growers, only to be used without the slightest success. There was nothing but groping in darkness and the empirical trial of remedies much after the style of old-fashioned medical practice upon afflicted humanity.

Pasteur, in his characteristic fashion, went straight after the cause of the disease. This must first be discovered beyond all else. When the cause is known, he thought, we shall at least know

what we are dealing with, and we shall be in a better position to grapple with it. In the search for the cause for the disease previous investigators had made some observations which gave Pasteur a point of attack. Guerin-Meneville in 1849 had seen in blood of silk worms some small, oval corpuscles which subsequent observers discovered in various parts of the body and even in the eggs. It was found that these bodies increase in number as the disease progresses, but there was much doubt as to what relation they bear to the disease.

When Pasteur began his investigations he was unaware of most of these previous findings, and he rediscovered a number of things already known. On the evening of his arrival at the scene of action he had observed the oval bodies in the tissues of diseased worms. He soon made himself familiar with the occurrence of these minute bodies in all stages of the life history of their host from the egg to the mature moth. The question which naturally occurred to Pasteur in the light of his previous investigations was, What relation do these small oval bodies bear to the disease? The supposed parasites do not occur, at least in abundance, in healthy worms; they increase in numbers as the disease progresses, and worms dying of *pébrine* are often

swarming with them. Pasteur found that the disease was contagious, that healthy worms could be infected by feeding upon leaves on which diseased worms had been crawling. They could be given the disease by a mere scratch from an infected worm or by the prick of a needle smeared with infectious material. Eggs containing the supposed parasite were found to give rise to diseased larvæ, and on this fact, a method of egg selection was practised in order to obtain healthy progeny. Examination of eggs, however, was soon replaced by an examination of the couples that produced the eggs. The procedure recommended by Pasteur in 1865 was as follows:

After the mating, the female, set apart will lay her eggs; then one will open her, as well as the male, in order to search therein for the corpuscles. If they are absent from both male and female, he will number their laying which shall be preserved as eggs absolutely pure, and bred the following year with particular care. There will be eggs diseased in various degrees according to the greater or less abundance of corpuscles in the male and female individuals which have furnished them.

Pasteur himself became a raiser of silk worms in order to be able to furnish pure "seed," as the

eggs were called, to the growers. The method he recommended, however, sometimes failed, and Pasteur was led to conclude that diseased progeny might arise from moths possessing no corpuscles. Often worms sickened and died from what he considered *pébrine*, without having any corpuscles at all. He was therefore led to regard the corpuscles as a sort of product of the disease instead of its cause,—a product, like certain other symptoms of diseases, which might or might not appear according to various circumstances which are little understood. He believed that the disease preceded the existence of the corpuscles, and that feeding worms with corpuscular matter would sometimes give them the disease without the appearance of corpuscles in the infected worms. He was also unable to find evidence that the corpuscles reproduced themselves like the bacteria and the yeasts by either fission or budding.

Thus far, in spite of some success, the disease proved to be baffling. Duclaux, one of his co-workers in the silk worm investigation, remarks, "In 1867 Pasteur had distributed by small lots the healthy eggs prepared in 1866, and the success, we knew, had been general. Meanwhile, as the letters came announcing the results of the cultures, we

found our master more and more disturbed. He kept us so far from his thoughts that we did not understand his inquietude until one day he appeared, almost in tears, and settling himself discouraged into a chair exclaimed, 'Nothing has been accomplished. There are two diseases.'

This fact, which Pasteur had suspected for some time, made it apparent that the investigations had been proceeding on the basis of a wrong assumption. It was necessary for Pasteur to retrace his steps and to repeat many experiments in the light of a new viewpoint. But notwithstanding the disconcerting effects of this discovery, the recognition of the existence of a distinct malady hitherto confused with *pébrine* had its reward in resolving many contradictions and inconsistencies in Pasteur's previous results.

This disease now recognized as distinct for the first time is commonly designated by the name of "*morts-flats*," or "*flacherie*." Like *pébrine* it is a peculiarly fatal disease, readily contagious, and having its peculiar complex of symptoms. It is primarily an intestinal infection accompanied by the development of enormous numbers of its characteristic bacteria in the alimentary canal.

Going back over previous work it became evident

that cases of *pébrine* without the corpuscles were not *pébrine* at all, but *flacherie*. The eggs without corpuscles which were supposed to produce *pébrine* were found to produce the other disease instead. In all cases of true *pébrine* there were the characteristic corpuscles, and in all cases of *flacherie* the characteristic bacteria. The discovery of two diseases where there was supposed to be only one removed most of the objections that prevented Pasteur from concluding that the corpuscles were the cause of the disease instead of its product. It was clearly established that without the corpuscles no *pébrine* could occur. The difficulty in regard to the mode of multiplication of the corpuscles is now resolved. As this parasite is now known to belong to the Sporozoa, a group with which Pasteur had little familiarity, it is not surprising that no evidence of fission was discovered, as the members of this group multiply by the formation of spores within the body of the parent organism.

The discovery by which Pasteur was at first so upset resulted in bringing order out of chaos, and it also resulted in perfecting methods for checking not only *pébrine* but *flacherie* as well. Diagnosis of both diseases now became certain. It could now be ascertained by examination of moths which ones

would be almost certain to produce eggs free from both maladies. Pasteur produced and distributed eggs which he could guarantee to be free from infectious diseases, and which would give rise to healthy worms provided they were protected from new infection from the outside.

“Would you like to find,” Pasteur asks, “whether a lot of cocoons will give you healthy eggs? Take a part of them and heat them so as to hasten by four or five days the hatching of the moths, and see if they are corpuscular. . . . If the moths are infected send the cocoons to the spinning mills. . . . But would you have the brood sound up to the very end and give healthy eggs? In this case take absolutely sound eggs derived from entirely healthy parents and hatch them in clean and isolated places to which infection cannot spread. But if, unfortunately, the disease should arise, I still give you the means of making a selection, and of separating infallibly the sound eggs from the diseased ones.”

By following Pasteur's directions the growers found that they could check the destructive disease of *pébrine* and also *flacherie*. The silk industry soon felt the benefit of the improved methods. The Lyons Silks Commission had asked Pasteur

for a sample lot of healthy eggs. Pasteur sent them several lots concerning which he made the following predictions:

1. One lot will produce healthy worms.
2. One lot will perish exclusively from *pébrine*.
3. One lot will perish exclusively from *flacherie*.
4. One lot will perish partly from *pébrine* and partly from *flacherie*.

Pasteur desired that these predictions be recorded in the minutes of the Commission and that the results be reported on. They turned out exactly as he had predicted.

After six years of labor the silk worm diseases were conquered and the silk industry of France was brought back to prosperity. Pasteur's methods were applied in other countries into which the diseases had extended (for they had become almost world-wide in their distribution) and they met with similar success. The work had been peculiarly taxing and full of difficulties and discouragements, but a dogged perseverance had brought it to a triumphal ending. Pasteur succeeded where so many others had failed, not only because of the fertility and ingenuity of his mind, but because he sought first, as he always did in attacking a

problem, the cause of the phenomenon with which he was dealing. The results of his investigations are collected in a work of two volumes entitled "The Diseases of Silk Worms" (*Les Maladies des Vers de Soie*), which he liked to have his students read because of the examples of scientific method which they contain. These volumes are of permanent value not only for the information they afford, but perhaps more as a record of an elaborate experimental research which, despite many false assumptions and errors of detail, led finally to a clear understanding of an intricate subject.

During the years spent upon the diseases of silk worms Pasteur was occupied intermittently with several other matters. He wrote an account of the scientific work of his friend Claude Bernard, and, at the request of Dumas, an article on the great chemist, Lavoisier. He also continued some of his investigations on wines, to which I have previously alluded, and he devoted considerable attention to the administration of the *École Normale*.

In 1865 he lost his father, and soon afterward his youngest daughter, then two years old. The following year an older daughter, Cecile, who was twelve years of age was taken with typhoid fever and died suddenly after a period of convalescence

which promised recovery. Deeply afflicted by these sorrows Pasteur sought consolation in work. The intense and arduous life which he had been leading brought on in 1868 a stroke of paralysis that seriously threatened his life. Beginning with a strange tingling on the left side followed by a chill, the attack did not prevent Pasteur from reading a paper before the Academy which he was especially desirous of presenting. In the evening a more severe attack followed which for a time deprived him of speech. The best medical aid was summoned, and for several days his family and friends watched him with the greatest anxiety. Intermittent states of paralysis alternated with intervals in which his mind was clear. Despondently he said to Deville, who was watching by his bedside, "I am sorry to die; I wanted to render many more services to my country." "Be assured," replied Deville, "you are going to recover; you will make still more marvelous discoveries; you will live happy days. You will live longer than I, for I am your senior. Promise me that you will pronounce my funeral oration. . . . I wish you would, because you would speak well of me." Pasteur did not then know that he was to perform this sad service.

It was a period of great solicitude for many friends who were anxious to be of service to the sufferer and his family. "All scientific Paris," wrote Pasteur's cousin, "comes with anxiety to inform itself concerning the condition of the patient; intimate friends take turns in waiting by him. Dumas, the great chemist, insisted yesterday in the most affectionate manner on fulfilling the same duty. Every morning the Emperor and Empress send a footman to obtain news."

Recovery was slow. A laboratory whose construction had been authorized by the Emperor for Pasteur's researches had been started, but work on it was discontinued, apparently on account of the probability that Pasteur might never be able to use it. During his illness the patient would enquire anxiously how the building was getting on, but he was put off with various evasive answers. Pasteur soon became aware of this and expressed himself with some bitterness. The Emperor hearing of Pasteur's disappointment wrote the following note to the Minister of Public Instruction:

MY DEAR MONSIEUR DURUY:

I have learned that, doubtless without your knowledge, work was suspended on M. Pasteur's laboratory on the

day when he became ill. This circumstance has strongly affected him, because it seemed to point to his non-recovery. I beg you to give orders that the work undertaken shall be continued. Rest assured of my sincere friendship.

NAPOLEON.

The work on the building was immediately resumed, and later as Pasteur improved he could see from his window the rising walls of his new laboratory.

It was several months before Pasteur was able to return, even partially, to his work. But as soon as his strength permitted he was back to Alais superintending work on silk worms. He was soon given an opportunity of testing out his methods of silk worm culture on a large scale. The Prince Imperial owned an estate, the Villa Vicentina, near Trieste, upon which there were many mulberry trees; but for several years, owing to the diseases of silk worms, its yield of silk had greatly fallen off. Pasteur was offered a lodgment at the Villa with facilities for experimentation. He soon installed himself there with his family and began to superintend the culture of silk worms raised from healthy eggs which he had supplied. The result

was that the Villa yielded a net profit of 22,000 francs, the first time it had paid anything in ten years. Pasteur remained at the Villa eight months completing there the *Studies on the Diseases of Silk Worms* which he dedicated to the Princess Mathilde.

CHAPTER VIII

THE DARK DAYS OF THE WAR: STUDIES ON BEER

WHEN Pasteur returned to Paris the air was full of rumors of an approaching war with Prussia. Feelings of hostility on both sides had reached an acute state, and many perceived that the countries were being carried inevitably toward conflict. Many were confident of victory, but others, who had followed the elaborate, well-planned preparations of Prussia for this event and who realized the inadequate defenses of France and the demoralized condition of her army foresaw only unavoidable disaster. With the outbreak of hostilities most of the students of the *École Normale*, although exempt from military service, volunteered as soldiers. Pasteur desired to join the National Guard, but his half paralyzed condition caused him to be rejected. The rapid successes of the Prussian army greatly oppressed him. He desired to devote himself to work that might be of value to his country, but as the deserted *École Normale* had been

converted into a hospital he was deprived of his usual facilities, and yielding to the entreaty of his friends who reminded him that he would be only an extra mouth to feed during the siege, he departed with his family for his old home at Arbois.

There he tried to interest himself in his favorite books and to make plans for future investigations. "His reading," says Radot, "afforded Pasteur a means of consoling himself in his sadness and anxiety, and he was wont to repeat one of his favorite sayings 'Laboremus.' But at times in the midst of hours passed with his wife and daughter there would sound one of those peals of the trumpet with which the public crier of Arbois would announce the receipt of news. The universal order of things now no longer existed. Full of anguish Pasteur concentrated himself upon that imperceptible point in the Universe which is called France. He descended the stairway and mingled with the crowds which gathered on the little bridge of the Cuisance. He listened anxiously to the official communications and then sadly returned to his room where certain souvenirs left by his father emphasized by contrast the present situation of his country."

In the old home his eye fell at almost every turn upon busts, pictures, or other souvenirs of the first Napoleon, which his father had collected with devoted zeal. Not improbably, in common with many of his countrymen, he wished that the little corporal might be recalled to life and lead again the now disorganized armies of France. "I wish," Pasteur wrote, "that France may fight to her last man, to her last fortress." The brother-in-law with whom Pasteur shared the old home continued the trade of a tanner and Pasteur began some studies on the fermentation of tan. As Radot states, "He enquired continually seeking to learn the scientific reason for each custom and routine procedure. He excelled in devising projects for research from the most common and apparently insignificant facts. Everything about him became a subject for study. When his sister made bread, he studied the rising of the dough, the influence of the air in the kneading of the dough, and his imagination proceeding always from a small point to problems of great import sought to obtain a more nutritive bread and consequently a bread of lower price."

The bombardment of Paris stirred him deeply. Prussian shells had crashed into the *École Normale* and the *Museum of Natural History*. In 1868 the

University of Bonn conferred upon him the diploma of Doctor of Medicine, in acknowledgement of his work on the rôle of micro-organisms, but unwilling to retain a parchment in which his own name appeared along with that of the German Emperor he returned the diploma with a caustic letter explaining the reasons for his action. His bitterness was probably all the more intense because of his inability to take an active part in the defense of his country.

Having had no news of his son, now a young man of 18 serving in the Army of the East, Pasteur went to seek him and was overjoyed at finding him safe among the disorganized retreating soldiers. He accompanied his son to Geneva and then went to Lyons and soon afterward to Royat where he stopped with his old collaborator Duclaux who was now Professor of Chemistry in the Faculty of Cleremont-Ferrand. Shortly before this Pasteur had written to Duclaux in the following terms: "My head is full of the most beautiful projects for research. The war has compelled my brain to lie fallow. Now I am ready for new productive labors; but alas, I may be laboring under an illusion! In any case I shall try. Oh, why am I not rich, a millionaire! I would say to you, to Raulin,

to Gernez, to Van Tieghem, etc., Come! we shall transform the world by our discoveries. How fortunate you are to be young and full of vigor. Oh, that I might begin a new life of study and work. Poor France, dear country, what would I not do to relieve your distress!"

Near by at Chamalières there was a brewery which Pasteur began to visit, interesting himself in all the details of brewing beer and the reasons for the various procedures followed in this industry. Here he was brought into contact with the many difficulties encountered in beer making. Germany had hitherto excelled in the manufacture of beer, and Pasteur conceived the idea of perfecting the brewing industries of his own country so that France would no longer pay tribute to her enemy by importing German beers. Why should not France produce as good beers as Germany! If Pasteur could not perform military duty he could at least aid his country in the field of industrial rivalry. Beers, like wines, suffered from several diseases. Some beers became sour, others ropy, and others putrid. As in the case of wines, Pasteur showed that these diseases were accompanied by characteristic foreign micro-organisms. Through the selection of pure yeasts, which could be tested

by microscopic examinations, the contamination of beers by foreign micro-organisms could be largely avoided. In this and in many other ways Pasteur was able to control the process of beer making so as to improve the flavor and keeping qualities of the product, and his methods came to be widely adopted in French breweries.

Wishing to extend his knowledge of beer making he paid a visit in 1871 to the great breweries of London. In one of the largest of these in which he was being shown about he requested a sample of the porter then being made and examined it with a microscope. Finding in it a considerable amount of foreign ferments which he pointed out to the managers, he remarked that the product must be considerably inferior to what was desired and would probably bring complaint from some of its purchasers. The managers, surprised at this criticism, admitted that they had just decided to replace their yeast by a new supply. A visit to the same brewery a week later showed that they had installed a microscope and were beginning to test with this instrument the purity of their supplies of yeast. On his return to France he inspected many breweries and initiated their managers into methods by which they might improve their products and

keep them from the intruding organisms that caused them to deteriorate. He could usually predict by a microscopic examination the particular defect from which a beer was suffering. Pasteur investigated not only the diseases of beer, but many phases of the process of brewing. He did not like beer, but he had friends enough who were not unwilling to pronounce upon his various samples. "Give me a good bock," said his friend Bertin, "and you can discourse learnedly afterward."

The results of his elaborate researches are brought together in a volume entitled, *Studies on Beer*, which was dedicated to his father. The practice of heating bottled beer to kill its many ferments dates from these investigations. The French speak of "pasteurizing" beer and wine as we speak of pasteurizing milk. French beers became practically as good as the beers produced in Germany and the Congress of French Brewers meeting in 1889 gave to Pasteur the credit for the great improvements which had been made in the brewing industry. Nowadays brewers are as careful of their strains of yeasts as an agriculturist is of his breeds of cattle and sheep.

CHAPTER IX

ANTISEPTIC SURGERY, FOWL CHOLERA AND ANTHRAX

WE have now come to a turning point in Pasteur's career. For several years Pasteur had pondered over the possible relation of his researches to the spread of human infections. He had often recalled to mind the prophetic remark made over two hundred years ago by the English chemist Robert Boyle, that "He that thoroughly understands the nature of ferments and fermentations shall probably be much better able than he that ignores them to give a fair account of the diverse phenomena of several diseases." Pasteur's work on spontaneous generation, the diseases of wine and beer, and the diseases of silk worms, naturally disposed him to look with favor upon the idea, which had gradually been growing more clearly defined in his mind, that contagion might be caused by micro-organisms, and in 1863 he remarked to Napoleon III, in the course of an interview at the Tuileries, that it was his great ambition to arrive at the cause of putrid

and infectious diseases. Would it be possible, he thought, to check the diseases of human beings as it was possible to check the maladies of wine, beer, and silk worms?

Pasteur's imagination inspired him with conceptions of the wonderful possibilities of discovery in the field of disease through the application of the same methods which had proven so successful in his previous work. With the loss of his own children through disease fresh in his mind, and deeply impressed with the fearful suffering of French troops, not only from epidemics, but from gangrene, blood poisoning, erysipelas, and the other scourges that were the common accompaniment of wounds and operations, Pasteur was stirred by the ambition to do something which would obviate some of the sufferings which disease and infections inflict on humanity. Provided now with a new laboratory exceptionally well equipped for carrying on bacteriological research he was eager to enter upon this new field.

In Pasteur's time the cause of infectious diseases was as little known as it was in the Dark Ages. Pestilences and epidemics have always excited in the human race a kind of superstitious awe. Primitive peoples quite generally look upon disease

as the result of possession by an evil spirit, and the practice of the medicine man, who is frequently also the priest, commonly consists in inducing the evil spirits by supplications, bribes, or threats to leave the body of the afflicted person. There has come down to us from primitive times as a part of the intellectual heritage of the race, a semi-superstitious attitude in regard to the healing art that even now betrays itself in a variety of ways. Epidemics a half century ago were entirely mysterious. Medical men in general vaguely conceived of disease as due to some subtle "morbid matter," which could be spread by contact or through the air and which had the power of multiplying itself in the body. Many had from time to time speculated on the possibility that diseases might be caused by living germs, but in the absence of any thorough-going experimental tests the doctrine remained as a mere plausible conjecture. Pasteur's work on fermentation and spontaneous generation brought the "germ theory," as it was called, more prominently before the public. The germ theory had been demonstrated for the maladies of wines and beers and later for those of silk worms and the analogy of these phenomena to infectious diseases of man and the higher animals could scarcely be overlooked.

There were other analogies. The disease popularly known as the itch had been shown to be caused by a minute mite which had the disagreeable habit of burrowing into the skin and setting up a peculiarly annoying type of irritation. This malady, which is highly contagious, was formerly much more prevalent than is happily the case now. A medical treatise written as late as 1833 stated that the cause of the itch is entirely unknown and, Hahnemann, the celebrated founder of homeopathy, affirmed that three-fourths of human ills were nothing more than the itch struck in ("*gale repercutée*"). Here was a perfectly definite and clearly demonstrated case of a contagious disease caused by minute organisms which could be dug out of the skin by a needle and observed to scramble about in the field of the microscope. Another "disease" caused by an animal parasite had been made known through the discovery of the minute worm, *Trichina spiralis*, which has the habit of burrowing into muscular and other tissues and lying coiled up in its so-called cysts. A disagreeable disease of the scalp called favus, was shown to be caused by a fungus growing in the skin. The rapidly growing knowledge of the numerous parasites, large and small, that infest animals and

plants created a certain presumption in favor of the germ theory of disease, which is simply an extension of the notion of parasitism to more minute forms of life. From the grosser parasites such as lice and bed bugs, which are spread from person to person, the smaller itch mites and worms responsible for itch, trichinosis, and hook-worm disease, down to the minute one-celled animals and plants we have a graded series of attacking forms bent upon the common aim of getting their living at the expense of another organism.

Disease from the standpoint of the germ theory is simply a result of the very common and widespread biological phenomenon of predatory activity. From this standpoint the mystery of contagion vanishes. The period of incubation common to all contagious diseases receives an almost obvious explanation as due to the time required for the entering pathogenic organisms to multiply until they are numerous enough to provoke disturbing symptoms. And the course of a disease is a consequence of the varying outcome of the struggle between the body and its invading enemies.

In 1873 Pasteur became a candidate for membership in the Academy of Medicine and was elected by a majority of one vote. He valued his

connection with this body chiefly as a means of creating interest in the germ theory of disease and he attended the meetings, dry as he doubtless found many of them, with considerable regularity. Opportunities not infrequently presented themselves for discussing the germ theory, as this doctrine was scouted at by several of the foremost representatives of the medical profession, many of whom believed in the doctrine of spontaneous generation and thought that the bacteria sometimes observed in diseased conditions of the body were created by the body itself. As Pasteur was not a medical man, being as was said, a "mere chemist," his incursions into the field of medicine were regarded as not entitled to much consideration. Little did his medical colleagues then realize that they were dealing with the man whose discoveries with regard to disease were to be of greater value than those of all the academies of medicine in the history of the world.

The first successful applications of Pasteur's discoveries were made in surgery. The transformation which surgical methods have undergone as a result of these discoveries is, as Osler has remarked, "one of the greatest boons ever conferred upon humanity." The mortality from surgical opera-

tions was appalling. It was the rule that wounds became charged with pus, and it was fortunate if they were not followed by gangrene and general blood poisoning. Hospitals as places for operating were simply hotbeds of infection, and many hospitals had reputations that led them to be regarded as mere portals to death. The leader in the effort to eliminate infections from surgical operations was Joseph Lister, Professor of Surgery in the University of Edinburgh. Lister, whose name is now so frequently coupled with that of Pasteur, was a medical man of unusually broad training and an investigator of note in the science of physiology. Primarily he was a man of science. He had followed with great interest Pasteur's work on fermentation, putrefaction and the problem of spontaneous generation, and he became convinced that the mischievous agents of infection which give the surgeon so much trouble are bacteria, which gain access to wounds from the outside. If this were true it should be a part of surgical technic to get rid of these offending organisms. Accordingly Lister thoroughly disinfected everything used in an operation; the hands of the surgeon, instruments, bandages and other apparatus were washed in a solution of carbolic acid, and at first, a fine spray

was sent out around the seat of operation, in order to kill possible germs that might be floating in the air. The wound was frequently washed with the same solution and the dressings employed were changed with great care.

Although Lister was criticized by his colleagues for the employment of these curious procedures, the success of his operations as compared with those carried on by the old methods spoke so eloquently and forcibly that they compelled conviction. In 1874 Pasteur received the following letter from this celebrated surgeon:

MY DEAR SIR. Permit me to present to you a paper sent herewith which gives an account of some investigations of a subject upon which you have shed so much light. . . . Let me take this occasion to extend to you my most cordial thanks for having shown to me, by your brilliant researches, the truth of the germ theory of putrefaction and for having thus furnished me with the sole principle by which the antiseptic system could be perfected.

If you should ever come to Edinburgh you would be rewarded, I think, by seeing at our hospital how greatly humanity has profited by your labors. I need hardly add what a great satisfaction I should experience in showing you here how much surgery owes to you.

Excuse the freedom which is inspired by our common love of science.

Believe me, I am, with profound respect,

Very sincerely yours,

JOSEPH LISTER.

Lister's letter afforded Pasteur much gratification. I do not know whether it was read before the Academy of Medicine, but at any rate it should have been. Other surgeons who were led to employ antiseptic methods were rewarded by an unusually high percentage of successful operations. Pasteur pleaded for the employment of antiseptics in surgery before the Academy of Medicine, and the more open-minded members of this body came to realize that there was much to be learned from this non-medical member of their organization, for he had much to tell them of micro-organisms, their tenacity of life and means of spread. Antiseptic surgery, the spontaneous generation of germs, and the germ theory of disease provoked continued and warm discussion. In the field in which he had carried on investigations Pasteur had the advantage of extensive and accurate knowledge based on most carefully controlled experiments, and he took a peculiar pleasure in defying his adversaries to

prove their case. He had much prejudice to overcome, but he drew about him a following, especially among the younger men, who perceived the great value of his discoveries and were anxious to apply the newer knowledge to the healing art.

In 1874 the National Assembly rewarded Pasteur's services by an annual grant of 12,000 francs. Paul Bert, a prominent scientist who was a member of the National Assembly (for the French, unlike ourselves, sometimes honor scientific men with political office), said, in presenting the recommendation of the Commission, "Pasteur's discoveries, gentlemen, after having thrown new light on the obscure question of fermentation and the mode of appearance of microscopic organisms, have revolutionized certain branches of industry, of agriculture, and of pathology. One is struck with admiration on witnessing so many important results proceeding, by a chain of facts, followed step by step, in which nothing is left to hypothesis, from theoretical studies on the manner in which tartaric acid turns the polarized ray. Never has the famous saying, 'Genius consists in taking pains,' received a more striking confirmation.

"It is this admirable collection of theoretical and practical achievements which the Government pro-

poses to honor by a national recompense. Your Commission unanimously approves the proposal." The bill was passed by a vote of 523 to 24.

This annuity was particularly acceptable to Pasteur, as he had been compelled on account of ill-health to give up his academic positions. Although his physician had strongly advised him not to undertake serious work and notwithstanding the counsel of his friends that he rest from his labors, Pasteur, who thought that if he did not work he might as well not live at all, was actively engaged in his laboratory.

The disease anthrax or splenic fever was then engaging the attention of the medical world. This disease had been for many years a scourge of cattle and sheep causing an annual loss of several million francs. Occasionally it attacks human beings who have come into contact with infected animals or their products. As far back as 1850 Davaine and Royer had seen small rod-shaped bodies in the blood of animals dying of anthrax, but they were quite unaware of the significance of their observation. Stimulated by Pasteur's studies Davaine recurred to the subject in 1863 and proclaimed these "bacteria" as he had named them, to be the sole cause of the disease. This conclusion was disputed

by a number of investigators who claimed that in many cases of anthrax the bacteria could not be found. Davaine replied by showing evidence that the bacteria had been overlooked or that the disease had been wrongly diagnosed as anthrax. Davaine found that rabbits inoculated with the blood of animals suffering from anthrax would take the disease and die. But if the blood had been passed through a filter so as to remove its corpuscles and bacteria it could be inoculated into rabbits with no ill-effects.

But the disease presented many puzzling problems. Davaine adduced evidence that the bacteria of anthrax disappeared from the blood of dead animals after it began to putrefy, but he also observed that dried blood retained its virulence for a long time. It had long been known that fields over which diseased animals had grazed might infect healthy animals after a lapse of several years. Much confusion and difference of opinion prevailed, therefore, as to the mode of transmission of this disease.

Much light was thrown upon the problem by the labors of Robert Koch, a German investigator who was then at the beginning of his famous career. Koch had studied the germ of anthrax in its various

phases of development and observed that in the presence of oxygen, and at not too low a temperature, there appeared in the rod-like bacilli several small round bodies or spores. These frequently became liberated from their bacilli, and Koch proved that they were very much more resistant than the bacteria and were capable of producing anthrax when inoculated into healthy mice. Koch also succeeded in cultivating the bacilli of anthrax in blood serum and aqueous humor by inoculating one drop with a minute amount of material taken from another drop. After making eight successive transfers in this way, the bacteria multiplying in the meantime, he found that the cultures would convey the disease to new animals.

These experiments of Koch resolved some of the difficulties that had troubled Davaine. The persistence of anthrax germs, despite the fact that the bacilli disappear soon after death, was shown to be explicable through the vitality of the spores; and the fact that the blood of animals dying of anthrax is sometimes infectious and sometimes not, was very readily accounted for as due to the circumstance that the spores appear or fail to appear owing to varied conditions of temperature and the supply of oxygen.

All of this work lent strength to the hypothesis that it is the germ that is the cause of the disease. But it was possible for objectors still to urge that it is not germs that cause disease, but something that goes along with germs, a sort of virus that may not appear in the fluid part of the blood, but which may nevertheless be a product of the body. The culture experiments of Koch could be interpreted as simply diluting this something without getting rid of it. It was this problem to which Pasteur in his studies on anthrax first directed his attack, and he attacked the problem in a thorough-going way that left no reasonable doubt as to the issue between the two rival theories. He began by making culture experiments using sterile urine in which the bacillus of anthrax grows very well, and also various other culture media. He inoculated a relatively large amount of culture fluid with a drop of blood from an animal with anthrax. The characteristic bacteria of the disease were soon swarming throughout the culture medium. Then a drop of this culture was introduced into a fresh lot of fluid, and when this was teeming with bacteria, a drop from the latter was introduced into a third lot. If the first dilution is 1 to 1,000, the second would be 1 to 1,000,000 and the third 1 to

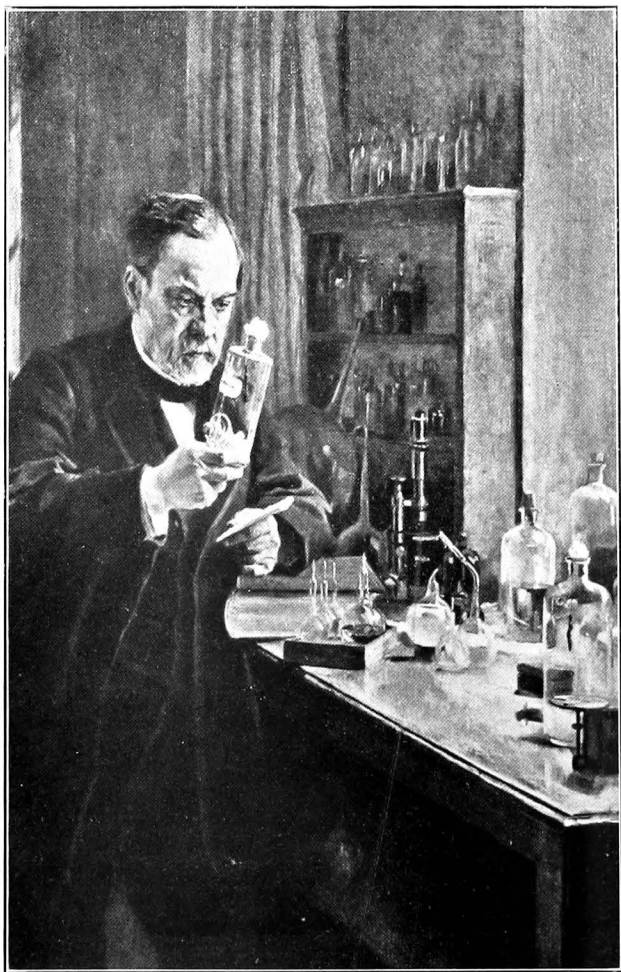


FIG. 12. PASTEUR IN HIS LABORATORY

1,000,000,000. After ten such transfers the amount of material originally present would be diluted so that it would be like a drop in the ocean, but Pasteur kept on diluting and diluting until he had made forty successive transfers. Any material associated with the original germs would have been diluted until not an atom of it could on the average be left in the final flask of the culture medium. Yet Pasteur showed that a drop of this culture injected into a rabbit or guinea pig would cause the animal to die with symptoms of anthrax. "Anthrax, therefore," said Pasteur, "is the disease of the bacteridium, as trichinosis is the disease of the trichina, as itch is the disease of the itch mite, with this difference, moreover, that in anthrax the parasite, in order to be seen, must be observed with a microscope of high power of magnification." The evidence that anthrax is caused by the bacillus is of the same kind and is just as conclusive as the evidence that trichinosis is caused by the trichina or itch by the itch mite.

Pasteur delighted in perfectly rigid, clean cut, and demonstrative experiments, and in face of the attacks on the germ theory, he took a peculiar satisfaction in bringing forward arguments which left his opponents no loop-hole by which they

might squirm through. Paul Bert, had claimed that animals might be given anthrax if inoculated with blood subjected to compressed oxygen which could be seen to destroy the bacteria of this disease as well as the septic vibrios which are sometimes associated with it. It must be something beside the bacilli, he argued, that caused the disease. The explanation, as Pasteur showed, is that although oxygen may destroy the bacteria it is not deleterious to the spores. Bert visited Pasteur's laboratory and became convinced of the correctness of this interpretation and acknowledged his mistake, acting, as Pasteur observed, "like a loyal Frenchman."

Anthrax is a disease which attacks different species of animals with different degrees of virulence. Rabbits and guinea pigs are very susceptible; rats and dogs are relatively immune to it. Fowls ordinarily do not take the disease. What is the reason for the immunity of the fowl? It occurred to Pasteur that since the temperature of fowls is several degrees higher than that of mammals, it might be that the temperature of the fowl's blood is unfavorable to the development of the anthrax bacillus. To test this supposition Pasteur immersed a hen in a bath of cold water in order to

lower its temperature. Then he inoculated it with a culture of anthrax bacilli. The next day the hen died. "All its blood," said Pasteur, "the spleen, lungs, and liver, are filled with the bacilli of anthrax susceptible of further cultures either in inert liquids or in the bodies of animals. Up to the present time we have not met with a single exception."

There had been considerable controversy in the Academy of Medicine over the cause of anthrax, and the question of the immunity of the fowl had been under dispute. The Academicians were probably somewhat surprised to see Pasteur come into one of the meetings with a cage containing four hens which he placed on the desk. In his account of his curious exhibit he stated that the dead hen had been inoculated, after being chilled, with five drops of a culture of anthrax three days before. To obviate the objection that the cold bath and not the germ had been the cause of death, another hen, which was perfectly healthy, was exhibited, which had been chilled but not inoculated. The third hen, also in good spirits, had been inoculated without having had its temperature reduced and was enjoying the effect of its natural immunity. The fourth hen was reserved for a further experiment.

It was inoculated, placed in a cold bath, and kept there until symptoms of the disease became clearly apparent. Would it recover if restored to its normal temperature? The hen was wrapped in cotton wool and put into a warm container at 35° C. and soon made a complete recovery. Here is a most instructive experiment in proving that the natural resistance of the body to infection may be broken down by unfavorable conditions and allow an invasion of bacteria which would normally be overcome.

At this time anthrax was causing serious losses among cattle and sheep in several districts of France, and Pasteur was commissioned by the Minister of Agriculture to make a study of so-called spontaneous anthrax which broke out without apparent cause. This feature of the disease made it particularly difficult to cope with. When herds were infected they were commonly taken to some other locality, as it was held that it might be the water, dampness, or dryness of the soil, or some peculiarity of the pasturage that was responsible for the outbreak. Pasteur visited one of the infected regions in the vicinity of Chartres accompanied by M. Roux, one of his devoted collaborators, who was destined to attain a prominent

position in bacteriological research. Going over one of the fields Pasteur noticed a part in which the soil had a color somewhat different from the rest. This part the owner explained was where the sheep, which had died of anthrax, had been buried the year before. Observing the little pellets of earth which had been brought to the surface by earthworms Pasteur thought that some of this earth might contain spores of anthrax carried from near the bodies of the buried animals. The pellets therefore must be tested. Inoculated into guinea pigs this earth produced anthrax. "One should insist," says Pasteur, "that animals are never buried in fields intended for growing hay or pasturing sheep. Whenever it is possible, one should choose burying grounds on sandy or chalky soils, infertile, readily dried, and unsuitable to the life of earthworms."

Pasteur's crowning achievement in the battle with anthrax had to wait upon a very remarkable discovery which he made in connection with chicken cholera. Poultry raisers, the world over, have long had experience with this fatal malady. Fowls previously healthy may be stricken and die in only a few days. The ruffed up feathers, drooping head, and drowsy aspect of the fowls, as they sit quietly

or move about in a sluggish manner are the characteristic symptoms of this malady which often carries off ninety percent of the infected brood. The few which recover seem to be immune to future attacks. The disease is highly contagious and may be conveyed by food contaminated with the excreta of infected birds.

Very minute bodies described as "granulations" had been observed by Moritz in the blood of chickens suffering from cholera. Are they the cause of the disease? Toussaint, who had brought forth evidence of the causal rôle of these organisms had made rather unsuccessful attempts to cultivate them. Pasteur, after having tried a number of culture media which proved unsuitable, discovered that in a sterilized broth made of chicken gristle the organisms would multiply with almost incredible rapidity. Successive cultures were made, the one from the other. Fowl inoculated with these speedily contracted the disease. Pasteur found that chicken cholera, like anthrax, affects different animals in different ways. Rabbits are quite susceptible, but guinea pigs are much less so, the inoculations producing only a local abscess, in which, however, the germs multiply and from which they may be recovered and inoculated again into fowl

with fatal results. These animals, although betraying no obvious signs of the disease, may nevertheless transfer it to fowl, thus playing the part of what we now would call "carriers" of the disease.

Pasteur's experiments had to be interrupted for several weeks and when he recurred to his old cultures which had been set aside and attempted to carry them on by inoculating new media and fresh fowl he found that growth in the new media was very slow or absent, and that the inoculated fowl were apparently unaffected. Being about to throw the old cultures away and begin anew it occurred to Pasteur to inoculate these fowl with a fresh, virulent culture of the bacilli. To his surprise nearly all of these fowl withstood the disease, whereas new fowl recently purchased, which were inoculated with the same fresh culture, succumbed in the usual way. The idea immediately suggested itself that the first lot of fowl had been rendered immune by their previous inoculation with the old cultures of the germ. We may well believe that there was excitement in the Pasteur laboratory over this striking and unexpected result! Further experiments which were made served to confirm the conclusion that by proper culture the chicken cholera germ could be weakened so that when it was

inoculated into healthy fowl it would not only do them little harm, but would protect them against the disease in a virulent form. Pasteur had made his great discovery—the attenuated virus.

The results naturally recalled the celebrated vaccination for smallpox discovered by Jenner, and Pasteur believed that he had hit upon the explanation of the success of that procedure which had hitherto been a complete mystery. Visions of great possibilities in the control of epidemic diseases flashed before his mind, and he was filled with enthusiasm over the prospects of further discoveries in the fields which were now opened up.

That germs could be modified, that modified germs were less deadly when injected into animals and that animals so treated became protected against attacks of virulent strains of the same kind of germs was a discovery whose generality he was eager to put to the test. Being occupied more or less with anthrax while he was working with chicken cholera, and being familiar with the method of cultivating the germs of that disease, the next object of attack was, as it were, marked out for him. He set out to attenuate or weaken the germs of anthrax.

The culture of the anthrax bacillus under con-

ditions unfavorable for its life presented difficulties owing to the formation of spores, but Pasteur found, after considerable experimenting, that if it were grown in neutral chicken bouillon at 42-43° C. the spores would not develop. A month of this régime usually suffices to kill the bacilli; they become weaker and weaker apparently, and after ten or twelve days they may be injected into rabbits, guinea pigs, and sheep without producing fatal results. If the weakened bacteria were grown at 35° C., thus allowing them to form spores, the bacteria subsequently emerging from these spores were found to produce the same mild effects as the bacteria from which they were derived. This is a fortunate circumstance, as it enables one to preserve the attenuated virus in a relatively permanent form. Pasteur found, as in chicken cholera, that the inoculation of animals with attenuated virus would produce mild effects which would render the animals immune to inoculation with the unmodified bacilli of this disease. After making sure of the success of his vaccine he announced his discovery to the Academy of Sciences. "I could not be consoled," he remarked to his family, "if this discovery which my collaborators and I have made had not been a French discovery."

This discovery which was of so much promise to the owners of cattle and sheep naturally excited much comment. Some received it with enthusiasm and others regarded it with distrust. The Society of French Agriculturists offered Pasteur a medal of honor, but as extensive experiments on the larger animals had not been carried out, the general attitude on the subject was one of suspended judgment.

An opportunity of performing an experiment on an extensive scale soon presented itself through the instrumentality of M. Rossignol, one of the editors of the Veterinary Press. Rossignol represented a typical attitude on the germ theory of disease. A short time previously he had written, "Microbiolatriy is now the fashion, it reigns as a sovereign; it is a doctrine which one must not discuss; one must accept it without objections, especially when its chief priest, the learned Pasteur, has pronounced the sacramental words, 'I have spoken.' The microbe alone is and shall be the characteristic of a disease; this is understood and agreed to; henceforth the theory of germs should take precedence over pure clinics; the microbe only is eternally true and Pasteur is its prophet."

Shortly after making this characteristically edi-

torial pronouncement Rossignol began an active campaign for funds for the purpose of purchasing animals for his proposed experiment. Pasteur's alleged discovery of a vaccine for anthrax should not remain as a mere laboratory procedure. Would Pasteur dare to subject his vaccine to a public test? "The excitement which these experiments will necessarily arouse," said he, "will strike all minds and end by convincing those who are still skeptical; the evidence of facts will have the result of dispelling all uncertainty." The Agricultural Society of Melun endorsed the proposal, and its chairman was delegated to wait upon Pasteur with the proposal, or perhaps we should say the challenge, that he carry on a public demonstration under the conditions laid down. The conditions had been printed and widely distributed by Rossignol.

Pasteur was game. He prepared his attenuated virus and made the preliminary inoculations at the farm Pouilly le Fort, near Melun, where the trial was to be staged. A large crowd had assembled, for the test had been widely advertised. Doctors, farmers, and veterinarians turned out in numbers and were speculating on the probable success or failure of the experiment. Many were secretly rejoicing over the prospect of a humiliating failure,

and Pasteur's friends and followers were filled with anxiety over the outcome of the bold step which their leader had taken. It was specified that twenty-five sheep were to be inoculated with anthrax vaccine and afterwards inoculated with anthrax. Twenty-five unvaccinated sheep were to be inoculated with anthrax alone. Six cattle were to be inoculated and four others kept as controls. Two weeks after vaccination the sheep and cattle vaccinated and unvaccinated alike were to be given an injection of virulent germs of anthrax and three days later the meeting was to be called to witness the results. The preliminary inoculations were carried out on May 5, 1881. "These experiments," wrote Rossignol, "are solemn ones and should become memorable, if, as M. Pasteur affirms with so much conviction, they confirm all that he has already claimed. We express the ardent hope that M. Pasteur will succeed and depart as victor from a contest which has now lasted sufficiently long. If he succeeds, he will have conferred upon his country a great benefit, and his adversaries should, like the ancient captives, wreath their brows with laurel, and prepare to follow, chained and bowed down, the chariot of the immortal victor; but he must succeed; that is the price of triumph. How-

ever, M. Pasteur should not forget that the Tarpean rock is close to the Capitol."

On June 2nd the crowd again assembled to witness the results. As Radot remarks, "When Pasteur arrived at 2 o'clock in the afternoon at the farmyard of Pouilly le Fort, accompanied by his young collaborators, a murmur arose which soon became a burst of applause ending in loud exclamations from all lips. Delegates from the Agricultural Society of Melun, from medical societies and veterinary societies, representatives from the Central Council of Seine et Marne, journalists, small farmers who had been influenced in diverse ways by laudatory or injurious newspaper articles and who were in doubt whether to accept or deny a great discovery—all were there. The carcasses of 22 unvaccinated sheep were lying side by side; two others were dying; the last of the sacrificed lot still living presented all the characteristic signs of anthrax. All of the vaccinated sheep were in perfect health. The cows which were unprotected by vaccination were all showing severe symptoms of splenic fever. In the vaccinated cows there was not even an elevation of temperature and their appetite seemed unimpaired."

The conclusiveness of the experiment could not

be gainsaid. The skeptical Rossignol pronounced it a "stunning success," and made a handsome acknowledgment of his previous errors in regard to microbiology. He assisted at the examination of the blood of two of the dead sheep. This showed an abundance of the bacilli of anthrax. The last unvaccinated sheep died in the evening of the day of the demonstration.

Further trials of Pasteur's protective vaccine yielded additional evidence of its efficacy. There was a wide demand for vaccine, and about 34,000 animals had been vaccinated by the end of 1881, and about 500,000 by the end of 1883. The method became widely used in stock raising countries throughout the world, and has resulted in saving millions of dollars and the lives of many thousands of animals.

CHAPTER X

THE DAWN OF A NEW ERA IN MEDICINE

THE idea of conquering contagious diseases by preventive inoculation filled Pasteur with an intense ardor to apply to other maladies the methods which he had found so successful in chicken cholera and anthrax. What may not be hoped for in the battle with contagious diseases in general? It may even be possible some day, he thought, to banish contagious diseases from the earth. The secret of transmissible disease had now been revealed. A method had been discovered by which two of these diseases, the first two in which it had been tried, could be checked. What wonderful possibilities lay ahead!

News that yellow fever had been brought by a vessel into Bordeaux caused Pasteur to hasten to that city in the hope of finding the microbe of this disease. To the warnings he received of the danger of infection he only replied, "What does it matter? Life in the midst of danger is the life, the grand life, the life of sacrifice, of example, of fruitfulness." The vessel had lost 18 persons,

but the patients who did not die had recovered when Pasteur and his associates arrived. It is not likely that Pasteur would have discovered the germ of yellow fever, and he certainly ran no risk in coming in contact with those afflicted by it. It was many years later that the remarkable mode of transmission of this malady was revealed, and the mosquito convicted of being the agent of its transmission,—a discovery which has led to the almost complete extermination of this widespread and deadly scourge, and the saving of thousands of human lives.

In the intervals of his work on anthrax Pasteur interested himself in various human diseases. A minor discovery was made in 1880 as to the cause of boils. Duclaux, then one of Pasteur's collaborators, was suffering from a series of these afflictions. When Pasteur's attention was called to them, he had one of the boils pricked open, for he was averse to performing any kind of operation himself, and he succeeded in making a culture from its contents. In this and in other cultures, a small, rounded organism, now known as a staphylococcus, was discovered, which is at present recognized as the common cause of these infections.

"Seek the microbe," became Pasteur's motto. Pasteur made many visits to hospitals with his medical colleagues in order to familiarize himself with the problems of the physician. Witnessing an operation on a little girl for osteomyelitis he gathered some pus from the inside of the bone and found it to contain numerous rounded microbes susceptible of culture like those of boils from which they could not be distinguished. Somewhat boldly he affirmed that the two infections were essentially the same; it is only the place in which the germs find lodgment and multiply that causes the difference between these very dissimilar afflictions.

Visiting patients and observing operations and autopsies was very repulsive to Pasteur. Roux, who was his frequent attendant in those days, remarks that, "His sensibility was extreme, and he suffered morally and physically from the pains of others; the cut of the bistoury which opened an abscess made him wince as if he received it himself. The sight of cadavers and the sad necessity of autopsies filled him with disgust. We have often seen him come away ill from those operating rooms of the hospital. But his love of science, his desire for truth, were the stronger; he returned the next day."

Puerperal fever, the great affliction of child-bearing women, enlisted his particular interest. For a long time it was not recognized that this trouble was contagious, and it is one of the services of Dr. O. W. Holmes, who is so well known as a man of letters, and so little known as a physician and professor of anatomy, that he brought forward convincing evidence that puerperal fever is a transmissible disease and is frequently conveyed through the hands and instruments of the physician. Certain lying-in hospitals had an unenviable record for fatalities among child-bearing women. In 1856 The Paris Maternity Hospitals had in less than six weeks 64 deaths out of 347 confinements. Epidemics of puerperal fever frequently swept through maternity hospitals which were commonly the worst possible places for bearing children.

Pasteur had discovered, in cases of puerperal fever, characteristic rounded microbes appearing commonly in chains like a string of beads, and he affirmed them to be the cause of this disease. "One day," says Roux, "in a discussion on puerperal fever at the Academy of Medicine one of his most distinguished colleagues was eloquently discoursing upon the causes of epidemics in lying-in hospitals; Pasteur interrupted him from his

seat: 'What causes the epidemic is nothing of the sort; it is the doctor and his staff that carry the microbe from an infected woman to a healthy one.' And as the speaker replied that he feared that one would never find the microbe, Pasteur went to the blackboard and drew a picture of the chain-like organism, saying, 'There, that is what it is like!' His conviction was so strong that he could not keep himself from expressing it forcibly. It would be difficult now to describe the state of surprise and even stupefaction into which he would throw the doctors and students when, at the hospital, with a simplicity and assurance which appeared disconcerting in a man who was entering a lying-in ward for the first time, he criticized the methods of dressing wounds and declared that all the linen should be put into a sterilizing stove." Through the adoption of strict antiseptic procedures in assisting child-birth, puerperal fever has now become a rarity, and a case of it would be regarded as a disgrace in any well-regulated hospital.

There were many controversies in the Academy of Medicine. Several physicians and surgeons were adopting Pasteur's ideas, but a considerable number of conservatives regarded them with dis-

dain. At an open meeting attended by medical students and the public Pasteur, apparently despairing of many of his medical colleagues, thus addressed the students: "Young men, you who sit on those benches, and who are perhaps the hope of the medical future of the country, do not come here to seek the excitement of polemics, but come and learn method." Never was wiser advice given. Never in the history of medicine had there appeared one so thoroughly qualified to give medical students instruction in method; and never had the value of scientific method been more clearly exemplified than in the work of this lay member of the Academy.

Pasteur had a passionate love of science. He had an equally strong love of humanity. But with him it can hardly be said that science and humanity were two separate objects of affection, for he saw in science the means of performing the greatest service to his fellow man. Serious, tremendously in earnest, a man of deep feelings, and intensely patriotic, he lived a life of severe labor with a devotion to his work which was essentially religious. "Happy is he," he says, "who carries with him his own ideal and lives in obedience to it." To a rare degree he possessed that faculty which

his friend and admirer Tyndall has so well extolled,—the scientific imagination; but it was an imagination held down to facts with a strong tether. As Poincaré remarks, “he had sudden inspirations which bore him on toward unexpected discoveries; he had instincts of divination which pushed him forward along unexplored paths; he had swift, headlong rushes of thought that overleaped and anticipated the establishment of truth, prepared the way for it, made its attainment more rapid, and more sure. But when a scientific problem had taken shape before him, in one of those general flashes of illumination, he never considered it solved until he had questioned all nature, until he had classified or eliminated all the facts; until he had forced them each and every one to give him an answer.”

Pasteur's remarkable series of discoveries brought him many honors. In 1881 the Republic offered him the Grand Cordon of the Legion of Honor. Feeling that much of the credit for his recent achievements was due to his able collaborators, Roux and Chamberland, he imposed one condition upon which he would receive this mark of distinction; it was that the Red Ribbon of the Legion of Honor should go to his two collaborators; and he

wrote to his friend Paul Bert to "intervene most warmly in their favor." The request was granted and the news was conveyed to the laboratory. "Hearty congratulations," wrote Madame Pasteur, "were exchanged in the midst of rabbits and guinea pigs."

In the same year Pasteur was asked to represent France at the International Medical Congress in London. Upon his arrival at the well-filled hall in which the Congress was held he was invited to the platform, and as he passed along the aisle there was a great outburst of applause. "It is doubtless the Prince of Wales who is arriving," Pasteur remarked to his companions, "I should have come sooner." "But it is you that they are all cheering," exclaimed the President as Pasteur reached the platform. The Prince of Wales and the German Crown Prince entered later. In the opening address of the President, Sir James Paget, the mention of the name Pasteur brought such applause that Pasteur had to rise and bow to the enthusiastic audience. "I was very proud," he wrote to Madame Pasteur, "not for myself,—you know how I regard success,—but for my country, in reflecting that I was exceptionally distinguished in the midst of that immense concourse of for-

eigners, especially Germans, who were there in considerable numbers, much greater than those of the French, of which the total did not reach 250. Jean-Baptist and René were in the hall. You can judge of their emotion.

“After the meeting, lunch with Sir James Paget, with the Prince of Prussia on his right, the Prince of Wales on his left. Afterwards, an assemblage of twenty-five or thirty guests in the salon. Sir James presented me to the Prince of Wales, to whom I bowed saying that I was happy to greet a friend of France. ‘Yes,’ he replied, ‘a great friend.’ Sir James Paget had the good taste not to ask me to be presented to the Prince of Prussia; although there was no place under such circumstances for anything but courtesy, I could not bring myself to appear to have requested such an introduction. But who should approach but the Prince himself, saying, ‘M. Pasteur, permit me to present myself to you and to say that I have just been applauding you’; the rest of his conversation was very cordial.”

Invited to give a lecture before the general meeting of the Congress, Pasteur described his experiments with attenuated virus and paid a tribute to the English physician, Doctor Jenner, the great

precursor of his own discoveries. Doctor Darenberg, the correspondent of the *Journal des Debats*, wrote that, "Pasteur was the greatest success of the Congress," proud that it was the representative of France that received such hearty applause.

On his return to Paris several of the friends of Pasteur belonging to the *Academie Française* endeavored to induce him to become a candidate for the vacancy in that body created by the death of the great scholar, Littré. It was the custom for candidates to call on members and solicit their support. Alexandre Dumas, the dramatist, refused to allow Pasteur to call on him, declaring, "It is I, who will go and thank him for consenting to become one of us"; and M. Grandeau wrote that, "When Claud Bernard and Pasteur consent to enter the ranks of a Society, all the honor is for the latter." Pasteur, who had declared, "I have never in my life contemplated the great honor of entering the *Academie Française*," was duly elected and began his preparation for the formal ceremony that marked the initiation of new members. Radot in his life of Pasteur has given us a most interesting description of the ceremonies of this occasion and I may refer to his book for fuller details. Ernst Renan, to whose lot it fell, as President of

the Academy, to welcome the new member, spoke with his usual charm of style. After modestly disclaiming any competence of the Academicians to pass judgment on Pasteur's scientific labors, he continued in the following words: "But apart from the basis of the doctrine, which is not within our province, there is a mastery, Sir, in which our experience of the human spirit gives us a right to express an opinion. There is something which we can recognize in the most diverse applications, something which belongs in the same degree to Galileo, to Pascal, to Michael Angelo, to Molière, something which gives sublimity to the poet, profundity to the philosopher, fascination to the orator, divination to the scientist. This common basis of all beautiful and true work, this divine flame, this indefinable spirit, which inspires science, literature, and art, we have found it in you, Sir,—it is genius. No one has traversed with so sure a step the regions of elemental nature; your scientific life is like a luminous track across the great night of the infinitely small, in the last abysses of being in which life is born."

Shortly after his reception at the Academy, the town of Aubenais, in the midst of the silk producing region, honored Pasteur by the formal presen-

tation of a medal. "His arrival," according to Radot, "was a triumphal affair; there were decorations at the station, music, triumphal arches of flowers and shrubs in the streets, speeches from the Mayor, presentation of the Municipal Council, of the Chamber and Tribunal of Commerce. All the village was *en fête*. The music of the band was almost drowned by the acclamations of the people." "For us all," the President of the Aubenas Silk Syndicate said, "you have been the kindly genius whose magical intervention conjured away the curse which was ruining us; in you we salute our benefactor."

Before he could return to Paris the Agricultural Society of the Gard gave a banquet in his honor at Nîmes and presented him with a medal for his services to agriculture. A demonstration of the efficacy of the anthrax inoculation was planned (for there were still many doubting Thomases) and the next day the experiments were carried out. The plan of the experiments was practically the same as those conducted at Melun and the results were equally decisive and convincing. The Agricultural Society of Herault, before whom Pasteur gave a lecture, desired him to turn his attention to a disease prevalent in the region termed "the rot."

The remark of the Vice-President, "He will surely find the remedy for it," illustrates the confidence which the people had come to place in his ability to grapple with problems of disease. After returning to Nîmes to witness the final results of his experiments on anthrax inoculation, he took the train for Paris with the remark, "Now let us go back to work."

Further recognition of his services had been planned by the Academy of Sciences which had enlisted the coöperation of the Scientific Societies of France, in presenting him with a medal engraved by the artist Alphée Dubois. On Sunday, June 25, 1882, a delegation called upon Pasteur who was living with his family at his home in the École Normale. Heading the delegation was Pasteur's old teacher, Dumas, who in presenting the medal spoke in the following words: "My dear Pasteur, it is forty years ago when you entered as a student into this building. From your first appearance your masters have foreseen that you would be an honor to them, but none of them dared to predict the brilliant services that you were destined to render to science, your country, and the world." And after speaking briefly of Pasteur's discoveries, Dumas continued: "My dear Pasteur, your life has

known only success. The scientific method of which you make so sure a use, owes to you its most beautiful triumphs. The École Normale is proud to count you among the number of its pupils; the Academy of Sciences is proud of your work; France ranks you among its glories. At this time when marks of public recognition are coming to you from all parts, the homage which we come to offer, in the name of your admirers and of your friends, may seem to you worthy of a particular attention. It emanates from a spontaneous and universal sentiment and it preserves for posterity the faithful image of your features.

“May you, my dear Pasteur, long enjoy your glory and contemplate the ever more abundant and rich fruits of your labors. Science, agriculture, industry, humanity will retain for you an eternal gratitude, and your name will live in their annals among the most illustrious and the most beloved.”

Pasteur, listening with bowed head to these words of his revered master and struggling to control his deep emotion, replied, “My dear Master, it is indeed forty years since I had the good fortune to know you and since you have taught me to love science. I came from the country. After each of your lessons I came away from the Sorbonne trans-

ported and often moved to tears. From that time your talent as professor, your immortal works, your noble character, have inspired me with an admiration which has only grown with the maturity of my mind. You have been able to divine my sentiments, my dear master. There is not a single important circumstance of my life or of that of my family, happy or painful, which you have not in some way blessed with your presence. To-day again you take the first place in the expression of the testimony, which I consider very excessive, of the esteem of my masters, who have become my friends.

“And what you have done for me, you have done for all your pupils. It is one of the distinctive traits of your nature. Beyond the individuals you have always considered France and her greatness.

“What shall I do henceforth? Until the present great praise inflamed my ardor and inspired me with the idea of making myself worthy by new efforts; but that which you have come to address to me in the name of the Academy and the Scientific Societies is in truth beyond my courage.” Pasteur had received the honor which he had valued most,—praise from his scientific colleagues and especially from his esteemed teacher.

In 1883 recognition of a substantial character came in the form of an additional stipend from the Government, an annual grant of 25,000 francs. Both Senate and Assembly passed the bill by an unanimous vote. Paul Bert, who was again instrumental in Pasteur's behalf, quoted in his report the remark of Professor Huxley before the Royal Society of London, "Pasteur's discoveries alone would suffice to cover the five milliards paid by France to Germany in 1870." We now recognize that this was a very modest estimate.

Of the honors which were being showered on him at this time, the one which perhaps touched Pasteur most was the celebration at Dôle, in which a memorial plate was placed upon the house in which he was born. In behalf of the Municipal Council, the Mayor read the following words: "M. Pasteur is a benefactor of humanity, one of the great men of France; he will remain for all the inhabitants of Dôle, and especially those who, like him, have come from the ranks of the people, an object of respect as well as an example to follow. We believe that it is our duty to perpetuate his name in our village." There was a representative of the Government present, Mr. Kaempfen, Director of Fine Arts, who said: "In the name of

the Government of the Republic I salute this inscription which recalls the fact that in this little house on this little street there was born on December 27, 1822, one who was to become one of the foremost scientists of this century, which is so great in science, and who has by his admirable labors added to the glory of his country and deserves well of all humanity." Proud little town of Dôle!

Amid all the praises which Pasteur received from his grateful countrymen, there were several attacks which lent at least variety to his eventful life. Koch had attacked Pasteur's culture experiments, claiming that pure cultures were not in most cases made. He also minimized the value of Pasteur's work on anthrax and claimed that the inoculation experiments with dirt brought up by earthworms were of no scientific value. In regard to the purity of Pasteur's cultures Koch was probably right. The method of cultivating bacteria on solid media which was first introduced by Koch has been of great service to bacteriology, because it makes it possible to isolate particular strains of bacteria from an originally mixed culture. At the medical congress held at Geneva, in which Pasteur defended his position, Koch failed to reply to the challenge

of Pasteur, stating that he would submit his reply later in writing. When the reply appeared Koch did not deny the principle of attenuation but spoke of it as a most important discovery. Nevertheless he expressed doubt of the practical benefits of vaccination for anthrax. In response, Pasteur submitted, among other evidences, data supplied by the veterinary surgeon, Bontet, in regard to 79,392 vaccinated sheep, with a mortality of less than one percent, whereas in the same district in the last ten years the mortality had been more than nine percent. Equally favorable results were reported also for cattle. Time and fuller experience, however, have now settled all controversy over the efficacy of inoculation for anthrax.

Being pressed by some veterinarians to study the disease known as swine plague or rouget, Pasteur began by seeking to cultivate the microbe of this disease. Thuillier, in 1882, had discovered numerous very small bacteria in swine afflicted with rouget, and Pasteur, who succeeded in cultivating the germs in a suitable medium, found that these cultures inoculated into healthy swine would set up the disease. The next step was to develop an attenuated virus. In experimenting on the behavior of the disease in several small animals it was found

that when inoculated into pigeons it becomes increased in virulence as it becomes transferred from pigeon to pigeon, killing the birds more and more quickly the longer the inoculations are continued. Introduced from pigeons to the pig the germs became more frequently fatal to these animals, thus proving that they had become more virulent while in the bodies of the birds.

On the other hand, it was found that in successive inoculations into rabbits the severity of the disease becomes reduced. When the germs that have been passed through a series of rabbits are introduced into the pig they produce only a mild attack of the disease, and after recovery the animals are immune to future attacks. The treatment founded on these experiments has proven successful in checking swine plague, which is a very destructive malady. Unfortunately swine plague was at first confused with hog cholera, a deadly disease, now known to be caused by a filterable virus and which has been greatly reduced by the administration of a protective serum. The fact demonstrated by these and other experiments that virulence is not a fixed property of micro-organisms, but something which may be increased or decreased, and to a certain extent manipulated at

will in the laboratory, has proven of capital importance in later work on disease. Like so many of Pasteur's discoveries its value is attested by the great benefits that were to flow from it in the future.

In the Academy of Medicine the reactionaries still kept up the battle over the germ theory of disease. A Dr. Peter was particularly active and persistent in his attacks. "The excuse of M. Pasteur," he exclaimed, "is that he is a chemist, who, inspired by the desire of being useful, has tried to reform medicine, to which he is a complete stranger," and he prophesied a victory to the "old medicine" over the new-fangled notions which were misleading so many of his colleagues. This "old medicine" had made little progress since it incurred the delightful and well deserved ridicule of Molière. Pasteur, who, wearied by its sterile squabbles, had not been present for some months at the Academy of Medicine, returned and defended his position, but he might have made a better use of his time.

From some professors of the Veterinary School at Turin there had come the report of a complete failure of an inoculation against anthrax. All the sheep vaccinated and unvaccinated alike died after being inoculated with the blood of a sheep which

had died of this disease. Pasteur wrote immediately to the Director asking how long the sheep had been dead before its blood was used for inoculation. Upon learning that the animal died the day before, Pasteur affirmed that the inoculated animals probably died of septicemia instead of anthrax. This led to a controversy more or less drawn out and finally to a challenge from Pasteur who offered to go to Turin and demonstrate publicly that blood in sheep dying from anthrax would after twenty-four hours give rise to septicemia in healthy and in vaccinated sheep. Pasteur's challenge was not accepted. The professors at Turin contented themselves with continuing their arguments and in publishing a pamphlet entitled *On the Scientific Dogmatism of the Illustrious Professor Pasteur*.

In a field requiring a refined and perfected technique and in which there lurk unexpected sources of error it is easy for experimenters who are not particularly well trained for their work to get discordant results. Pasteur, if he failed to convince his opponents, pointed out many errors of procedure which vitiated their conclusions. His strongest ally, however, was the growing evidence that his methods were yielding tangible results. He had the satisfaction of observing a remarkable de-

cline in the mortality from surgical operations to about one-tenth the rate which obtained before the application of antiseptic methods. Lying-in hospitals that witnessed the death of more than ten percent of their child-bearing women showed a death rate of less than one percent. Erysipelas and gangrene had been almost abolished from hospitals in which they formerly ran riot. France became relatively free from certain diseases of animals, against which a battle had long been waged in vain. All these facts spoke more eloquently than any words of controversy concerning the great value of Pasteur's labors and the work which he inspired.

CHAPTER XI

THE CONQUEST OF HYDROPHOBIA

THE annals of hydrophobia form a curious chapter in medical history. This disease was recognized in animals by the ancient Greeks and its transmission from one animal to another through bites was commented on by Aristotle, although he was apparently unacquainted with hydrophobia in man. Its uniformly fatal termination after its symptoms became manifest and the frequently horrible sufferings that attend its last stages made the disease an object of unusual dread. Remedies for it, like most remedies for most diseases, were entirely useless. Pliny, in an unconscious approach to the guiding principle of homeopathy, recommended as a cure the liver of a mad dog; and Galen prescribed a preparation made from the eyes of crayfishes. For a time, sea bathing enjoyed a reputation for its curative influence, and various other remedies were employed in the vain hope of alleviating the sufferings of the patient. As a boy in Illinois I not infrequently heard stories of people

cured of hydrophobia by the application of a so-called mad stone which was believed to have the curious property of clinging to the wound to which it was applied, drawing the poison from the system and dropping off after it had done its work. I have never seen any one who had actually seen a mad stone, but many people had heard of some one else who knew of some one who had known it to effect a cure. People commonly thought that hydrophobia was caused by hot weather, and, despite the fact that this supposition has been definitely disproved, it still prevails more or less in the popular mind. For a long time it was thought that the disease could be communicated by touch or through the breath, and in the fear that its unfortunate victims might be sources of contagion to others they were sometimes smothered between mattresses or otherwise disposed of. A person suffering from hydrophobia was smothered as late as 1819.

The term hydrophobia owes its origin to the dread of water which is a not uncommon symptom of this disease in man. This dread of water apparently is not shown by rabid dogs or other animals, and consequently the term rabies has now come to be employed as not carrying the misleading implica-

tion of the older designation. It is, however, of little importance which term is used so long as it is well known what is meant, and despite possible protests I shall use whichever word seems the more suitable and euphonious.

Pasteur had long pondered over this mysterious disease. M. Bourrel, a veterinarian, who had sought for a means of preventing the spread of hydrophobia in dogs and who had found nothing more effective than filing down their teeth, sent two rabid animals to Pasteur in the hope that this investigator might succeed where his own efforts had failed. One of the dogs was half paralyzed, his jaw hanging down and his tongue covered with foam. The other was in the furious state more typical of the disease, biting ferociously at everything within reach, and giving utterance to the most doleful howls. From these and other rabid animals subsequently obtained, Pasteur took some of the saliva and inoculated it into rabbits. He did the same with saliva drawn from a human subject, a little girl of 5 years of age who had just been admitted to a hospital. She was suffering from spasms, thirst with inability to swallow, and fits of furious mania; after twenty-four hours of agony she died. Saliva from the little girl and also that

from rabid dogs was found to cause the death of rabbits in about two days. A micro-organism was observed in the blood of these rabbits, and it was found that it could be cultured in veal broth and that the cultures, when injected into other rabbits, would cause their death. Pasteur was too cautious to jump to the conclusion that he had found the germ of hydrophobia. The incubation period, or period between the first inoculation and the development of symptoms of hydrophobia, is a relatively long one, varying from about two weeks to, in some cases, several months. It was more probable, therefore, that the rabbits died from the effects of some organism associated with the saliva of rabid animals instead of the germ of hydrophobia, a supposition which was confirmed by inoculating rabbits with saliva from human beings with other diseases and also with saliva from healthy persons. This commonly proved fatal to rabbits. Saliva, even in a healthy person, contains a multitude of different kinds of bacteria as may readily be seen by examining a drop of it under a microscope. Some of these while harmless in our own mouths are deadly when they gain access to the blood of rabbits or guinea pigs. Consequently efforts to induce rabies by the inoculation of saliva from

rabid animals was a very uncertain procedure. Experiments with the blood and tissues of rabid dogs were equally unsatisfactory, as were Pasteur's efforts to obtain a culture of the supposed microbe of hydrophobia in the usual artificial media.

Not daunted by these failures, Pasteur simply said, "We must try other experiments." On account of its characteristic symptoms it occurred to Pasteur that hydrophobia might have its principal seat in the nervous system. Accordingly some of the matter of the brain of dogs that had died of rabies was removed and injected, with precautions to exclude all outside contamination, under the skin of rabbits. In most cases the inoculated animal died of hydrophobia. "The seat of the rabid virus," Pasteur concluded, "is therefore not in the saliva only; the brain contains it, and it is found there in a degree of virulence at least equal to what it has in the saliva of rabid animals."

The next step was to inoculate the nervous matter from rabid animals directly into the brain. A dog was placed under chloroform, a circular disc was sawed out of his skull, and a small amount of nervous substance from a rabid animal was introduced directly into the dog's brain. The wound was dressed and soon healed. After coming from

under the anesthetic, the dog behaved in a perfectly normal manner, but in about two weeks it developed unmistakable symptoms of hydrophobia and died. By similar experiments on dogs and rabbits Pasteur showed that hydrophobia could be produced, in practically every case, by the direct inoculation of the virus into the nervous system. Not only is the transfer of the disease by this method practically certain, but its period of incubation is shorter than when it is introduced by means of saliva. Moreover, Pasteur found that in rabbits the incubation period became shorter and shorter with successive inoculations from brain to brain. The virus had apparently been increased in virulence as it is sometimes known to do in other diseases. After a time, however, when the incubation period was shortened to a little less than seven days, it could be reduced no more. The virus had reached its maximum potency; it had become, as it is now called, a fixed virus. Here, at last, the disease, instead of being of uncertain transfer and indefinite incubation period, was made a thing which could be definitely controlled, and whose time of appearance in an inoculated rabbit could be accurately predicted.

Efforts to cultivate the virus obtained from nerv-

ous tissue proved fruitless. How then could one apply the principle of attenuation in this disease and obtain a vaccine as in chicken cholera and anthrax? Pasteur attacked the problem by attempting to weaken the virus in its favorite seat, the nervous system. The spinal cord of a rabbit with hydrophobia was removed and suspended in a sterile tube. Into this the air was admitted through a plug of cotton wool, and was kept dry by a piece of caustic potash in the bottom of the tube which absorbed the moisture. After fourteen days an emulsion of the cord injected into a dog's brain showed that the material had lost its power of producing rabies. Then an injection from a cord dried for thirteen days was tried, followed by an injection from a cord dried only twelve days, and so on until finally material was used from a rabbit that had died on the same day. Several dogs that had been put through this treatment were allowed to be bitten by rabid animals. The brains of other protected dogs were inoculated directly. All of the protected animals failed to develop hydrophobia.

The success of these experiments was very encouraging. Realizing that his conclusions would probably be attacked, Pasteur desired that his dis-

covery be verified by a Commission. Accordingly one was appointed consisting of several of the foremost medical authorities in France and the Director of Agriculture. The Commission performed many experiments according to the method of Pasteur, subjecting dozens of treated and untreated dogs to the bites of rabid animals and to intracranial inoculation, and finding that the treated ones failed to develop hydrophobia, while those that had not been previously protected generally developed characteristic symptoms of the disease. A report was drawn up substantiating Pasteur's claims and recommending that further provisions be made for more extensive experiments.

Soon after the Commission reported favorably upon his new discovery, a meeting of the International Medical Congress was held at Copenhagen and Pasteur was chosen as a representative of France and he was invited to read the first paper. The presentation of the results of his experiments on hydrophobia was followed with the greatest interest. At that time he attacked the doctrine of the spontaneous origin of hydrophobia. As this doctrine was then widely held, Pasteur thought it desirable to correct this erroneous opinion. "No matter what the physiological or

pathological conditions may be under which dogs are kept they never contract hydrophobia," according to Pasteur, "except when bitten or licked by a rabid animal. This is why several countries are free from hydrophobia, and it is only necessary to follow the procedure of Australia, which compels every imported dog to be held for several months in quarantine so that it would have time to develop hydrophobia if it had been infected by it, in order to keep the country entirely free from the disease."

Pasteur's account of his success in the preventive inoculation against hydrophobia aroused the keenest interest and it was followed by enthusiastic applause. Among the entertainments planned for the members of the Congress by the hospitable Danes was a visit to the large Carlsberg Brewery. Several years before (1879), the philanthropic owner of this brewery, J. C. Jacobson, had engaged the artist, Paul Dubois, to make a marble bust of Pasteur, and had it placed in the Carlsberg Laboratory in honor of Pasteur's services to science. The visit to the brewery showed the application of many of the processes which Pasteur had recommended as a result of his studies on beer, and Pasteur was gratified to see a bronze bust of himself placed in a niche near the entrance. In the Carlsberg labora-

tory Hansen was studying the influence of different strains of yeast upon the flavor of beers and perfecting methods of obtaining these strains in pure cultures.

Returning to France Pasteur plunged again into his studies upon hydrophobia. He had perfected a means of preventive treatment against this disease. Could the treatment be made to cure the disease after it had already been introduced by the bite of a rabid animal? The great value of Pasteur's discovery thus far lay more in its promise than its actual utility. With most diseases preventive inoculation after infection with virulent microbes would probably be of little avail, as there would hardly be time for the former to establish immunity before the virulent, unmodified organisms would gain the ascendancy. In any case it is a race between immunization and the development of infection. In hydrophobia, however, one circumstance favors the immunizing process in this race, and that is the slow incubation period of the disease. It is believed now that the virus of rabies enters the central nervous system along the course of the nerves. This accounts in part for the length as well as the variability of its period of incubation. There is a further advantage in hydrophobia be-

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cause, in most cases, the time of infection is definitely known, whereas with such diseases as diphtheria, scarlet fever, or tuberculosis people are quite unconscious of when they may have picked up the infection.

Pasteur's next step was naturally that of applying his treatment to animals after they had been infected with hydrophobia. His procedure was to take two dogs and allow them both to be bitten by a mad dog; one he would vaccinate; the other would be left without treatment. The vaccinated dogs proved to have been protected against hydrophobia, while the others commonly succumbed to this disease. The immunizing process thus won in its race against the slower but more deadly onset of the unmodified disease. Here was a discovery which could be directly applied to saving the lives of animals which had been bitten by rabid dogs.

The interest and hope kindled by this discovery of a cure for hydrophobia became widespread. The Emperor of Brazil wrote to Pasteur enquiring anxiously about the progress of the investigations and especially when the treatment for hydrophobia could be applied to man. Similar enquiries came in from various other quarters, but Pasteur felt great hesitancy about risking the treatment upon human

beings. To the Emperor of Brazil he wrote, "Even when I have multiplied examples of prophylaxis of rabies in dogs, I believe that my hand will tremble when it comes to deal with man." He had thought of proposing that experiments be tried first on condemned criminals, giving the criminal the option between suffering his sentence and inoculation with hydrophobia, subsequent treatment, and his freedom if the treatment were successful. There was, however, no way in which this could be done in accordance with existing laws. What dangers might attend the introduction of the attenuated virus into the new soil of the human body could not be foreseen. The preparation used doubtless contained the living though weakened germs of this horrible disease. Persons bitten by a rabid animal do not always contract rabies; in fact statistics placed the proportion developing the disease from sixteen to twenty-five percent. There was the possibility that the person treated might be given hydrophobia by the preventive inoculations, and that he would not contract it if he were let alone. The responsibility of applying the treatment to a human being was therefore a grave one. A failure would be a calamity which could not fail to arouse public condemnation. And yet people were not

infrequently dying in the hospitals of Paris from this horrible and painful disease. "I have not yet dared to treat human beings after bites from rabid dogs," Pasteur wrote to Jules Vercelet, "but the moment is perhaps not distant, and I have almost decided to begin by myself,—that is, inoculating myself with rabies, and then arresting the consequences, for I am beginning to feel better and am growing very sure of my results."

While Pasteur was making more sure of his methods a circumstance occurred which overcame his indecision. A little nine-year-old boy, Joseph Meister, was brought by his mother to Pasteur's laboratory. Two days previously the boy, while on his way to school, had been furiously attacked by a mad dog, thrown to the ground and severely bitten about the face and hands. He was rescued by a laborer who happened to be near, and the dog was subsequently shot. An examination showed that its stomach was filled with hay and bits of wood which the infuriated creature had devoured in its mania for biting. The boy's wounds (he had been bitten in fourteen places) were covered by saliva. Doctor Weber, who was consulted in the evening, washed and cauterized the boy's wounds, and advised the parents to take him to Paris for a

consultation with Pasteur. The position and number of the bites, their severity, and the obvious contact of the dog's saliva, together with the circumstance that so long a time had elapsed between the bites and the application of cauterization, made the case a particularly dangerous one.

Pasteur secured quarters for the mother and child, and consulted Doctor Vulpian, in whose careful judgment he had much confidence, as to what should be done. Both Doctor Vulpian and Doctor Grancher, when they had examined the bites, decided that the first inoculation should be performed as soon as possible. They administered the fourteen-day preparation of spinal cord, and followed this by the inoculation with cultures of decreasing age according to the usual method. The boy, who had looked with alarm upon the approaching ordeal, finding that it amounted to little more than a pin prick, soon lost his fear and was quite happy during the subsequent days of his treatment.

As the inoculations increased in strength Pasteur's anxiety became greater as he counted the days until the period of danger should be passed. "Your father has had another bad night," Madame Pasteur wrote to her children; "he can hardly

bring himself to make the last inoculations of the child. And yet it is necessary to go on with it now! The boy continues to be very well." "Pasteur," says Radot, "passed through a series of diverse and contrary emotions, all equally intense,—hopes, fears, anguish, and an ardent yearning to snatch little Meister from death. He could no longer work. Every night he was troubled with a fever, dreaming of little Meister whom he had seen playing in the garden suffocating with hydrophobia, like the dying child he had seen at the Trousseau Hospital in 1880. In vain did his experimental genius assure him that the virus of this most terrible disease was about to be conquered, that humanity was about to be delivered from this horror, but his human tenderness was stronger than all else. If he made the sufferings and anxieties of others his own, what were his feelings in the presence of 'the dear lad!'"

The last inoculation having been given, the lad, after claiming a kiss from "dear Monsieur Pasteur," as he had come to call him, went to sleep in the evening, quite unconscious of the anxiety which his benefactor was suffering in his behalf. For many days after the completion of the treatment, Pasteur had little rest until time gradually abated

his fears and finally assured him that his little patient was entirely safe.

It was not long before Pasteur was confronted with another case as urgent as that of Joseph Meister. A mad dog in the Jura district had attacked a group of six shepherd boys, the oldest of whom, J. B. Jupille, a boy of fourteen, in order to save his comrades, courageously attempted to beat off the animal with a whip. The dog seized the boy's left hand, but the lad, after some severe bites, succeeded in throwing the dog down, and with the aid of his comrades, tied the animal's jaws with the lash of his whip. Subsequent examination of the dog convinced veterinary surgeons that it was certainly rabid. Pasteur was communicated with, and the lad, with the consent of his parents, was sent to Paris for treatment. In this case treatment was begun six days after the boy had been bitten. But nevertheless it proved to be completely successful.

The history of these two cases was communicated to the Academy of Sciences. Many people who had been bitten by rabid dogs now flocked to Pasteur's laboratory. A regular service for giving treatments had to be organized. Success continued to follow the preventive inoculations, but it was

too much to hope that every case which presented itself could be saved. As we have said, the success of preventive inoculation depends upon the outcome of the race between the processes of immunization and infection. If a patient comes too late after the deadly virus has gained headway it is hopeless to attempt to stay its course. On one occasion a little girl of ten was brought thirty-seven days after she had been severely bitten about the head. Pasteur thought the case hopeless and daily expected the appearance of hydrophobia; nevertheless, in response to the urgent appeal of the father and mother, the treatment was applied. The inoculations were hardly completed before the dreaded symptoms of hydrophobia began to appear; the little girl was seized with spasms and inability to swallow, and soon died. Pasteur, moved to tears as he watched by her bedside, said to the grief-stricken parents, "I do so wish I could have saved your little one!" The cruel disease had too long a start, and its claim to its victim could not be successfully disputed.

By means of a subscription started by the *New York Herald*, four children of workingmen were sent across the Atlantic to Pasteur's laboratory. Although they arrived at the end of their long

journey many days after they had been bitten by rabid dogs, the treatment was in every case successful. Pasteur, a great lover of children, took a keen interest in the young people who had been under his care. The following letter to Jupille, the lad previously mentioned who so bravely fought with the rabid dog, is characteristic of Pasteur's sympathetic attitude:

MY DEAR JUPILLE:

I was glad to receive all your letters. The news you have given me of your good health has afforded me much pleasure. Madame Pasteur thanks you for remembering her. She and I and all the staff of the laboratory hope that you will continue to be well, and that you will make the most rapid progress in reading, writing, and arithmetic. Your writing is already much better than it was, but make more efforts to improve your spelling. How are you getting on in your classes? Who gives you lessons? Work by yourself as much as you can. You know that Joseph Meister, the first to be vaccinated, writes me often. I find, although he is no more than ten years old, he has made more rapid progress than you have. Apply yourself then as much as you can. Do not lose time with your playfellows, and follow in all things the advice of your teacher and of your father and mother. Remember me to M. Perrot, the Mayor of Villers-Farlay.

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Probably without his foresight you would have been ill, and to be ill of hydrophobia means certain death. You owe him, therefore, a great obligation. Good-bye and keep well.

Among the various people who came to Pasteur's laboratory were nineteen Russians who had been bitten by rabid wolves. Some of them were in a very bad condition on account of the severity of their wounds. The percentage developing hydrophobia after being bitten by rabid wolves was known to be very high, being on the average of about eighty-two per hundred. Two weeks had passed since the unfortunate Russians were bitten, and it was therefore very doubtful if they could be saved. Two inoculations a day, a morning and an evening one, were given in order to speed up the process of immunization. Greatly to Pasteur's grief, three of the Russians soon died, but the others, who were followed with the greatest anxiety, recovered, and were sent back to their native country. In behalf of these and other Russians who had been saved, the Tsar presented to Pasteur a diamond cross of the Order of St. Anne, and a hundred thousand francs for the Pasteur Institute for which funds were then being collected.

The reports of the success of the Pasteur treatment caused the British Government to appoint a Commission to make a first-hand investigation of the facts. On this Commission were several men of international fame, such as Lauder Brunton, Quain, Joseph Lister, Burdon Sanderson, Victor Horsley, and Sir James Paget. Delegates visited Paris, observed the methods followed, and took account of the results. Looking over Pasteur's records of ninety persons who were treated within the neighborhood of Paris, they visited all of them in their own homes. Further experimental work was carried on by the Commission in both France and in England. Fourteen months were spent in a most exhaustive and critical investigation, and for this reason it was all the more gratifying that the Commission fully verified all of Pasteur's results. "It may be considered as certain," says the report, "that M. Pasteur has discovered a preventive method against hydrophobia comparable to that of vaccination against smallpox. It would be difficult to overestimate the utility of this discovery."

The support of this Commission was much appreciated by Pasteur who in spite of his striking successes was, as in most periods of his career, not

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lacking in opposition and hostile criticism. Part of this came from certain reactionary members of the Academy of Medicine, but they were becoming less numerous, and Pasteur's cause was defended by an increasing number of the most influential members of this organization. Rabid newspaper attacks, and insulting anonymous letters, disturbed Pasteur more than he should have allowed them to, because he was always easily stirred by opposition. "I did not know that I had so many enemies," he said; but if he had enemies, he soon had on his side the almost unanimous support of competent scientific men.

Among Pasteur's antagonists there were several people who were opposed to any form of experimentation that involved the infliction of pain upon dumb animals. There are many persons who have the same attitude to-day. The claim is frequently made that it is morally wrong, for any purpose, to inflict suffering on a defenseless creature, and it is maintained, by some extremists, that no results of value to science or humanity have come from such procedures. There are organizations in several countries whose object it is to secure legislation that would greatly restrict or entirely prevent experiments involving vivisection, even when pain-

lessly performed, as well as all experiments on inoculation or the production of protective serums and vaccines.

In so far as these organizations aim to check the infliction of useless cruelty, reasonable people cannot fail to sympathize with their efforts. Unfortunately, the opponents of animal experimentation, however good their intentions, are much more impressed by the sacrifices of a few laboratory animals than by the saving of thousands of human and animal lives that has resulted from the knowledge so secured. Pasteur employed a few sheep and rabbits in his experiments on anthrax, but he discovered a preventive vaccine for this deadly disease that has saved thousands of sheep and cattle. It required the sacrifice of several rabbits and dogs to discover the cure for hydrophobia. Any one who had a pet dog given this disease for experimental purposes might be indignant at the investigator. If he had a child who had been saved from a horrible death because of the knowledge gained through the death of the dog, he would probably have a different feeling. Were our intellectual vision limited to the discomforts of a few animals which the investigator uses in his research, we might be inclined to stay his hand. But if our

vision reaches beyond to the multitude of other animals saved from cruel death by disease, the case appears in an entirely different light. What might appear to our limited vision as cruelty becomes, when seen in its wider bearing, an act of mercy.

Many naturally sympathetic persons who have little knowledge of how animal experimentation is conducted have been led to oppose it by the misrepresentations and greatly exaggerated tales of cruelties that are often circulated by those who have allowed their fanaticism to overcome their scruples. Most animal experimentation that is now carried on is conducted in a humane manner, the animals being given an anesthetic for all operative procedures. And the men engaged in this research, far from revelling in wanton cruelty as they are sometimes accused of doing, are laboring, as best they can, to check the suffering of animals and men alike. I have been closely associated with experimental laboratories for many years, but I have never witnessed anything but the considerate treatment of the rabbits, guinea pigs, or the occasional stray dogs which are used for experimental purposes. At times cruelties may occur, but they are infinitesimal in amount as compared with what is inflicted by hunters, trappers, and careless or

callous owners of live stock. On the other hand, no one with the least knowledge of modern biology and medicine can deny that the information gained by animal experimentation has resulted in an enormous saving of human and animal life, and the prevention of untold suffering through disease.

Even the giving of anesthetics, incredible as it may now seem, met with violent opposition from fanatical persons who thought it was wrong to check pain which the Creator had designed to inflict. The opponents of animal experimentation are analogous to those who, for humanitarian reasons, would spare a child the discomfort of a surgical operation only to condemn him to a life of suffering afterward for want of the relief which the operation would bring. They would allow animals and human beings to go on suffering and dying of lingering and painful diseases as they have done in the past, rather than employ a relatively few animals for the increase of our knowledge. A humanity that would sacrifice the many to save the few is no humanity at all, and those who are guilty of the real cruelty to animals and human beings alike are not the investigators, who are laboring to reduce the field of useless suffering,

but the misguided individuals who would stop the progress of experimental research.

The career of Louis Pasteur affords a striking illustration of the truth that the cause of science and the cause of humanity are one. Nothing would have been more repugnant to this kindly man than the infliction of useless pain. He shrank from operations, and he sometimes forced himself to carry on work in his investigations on hydrophobia which was painful for him to perform. But he had visions of the possibility of conquering disease and abolishing needless suffering and death that made his natural sympathies an aid rather than an obstacle to research. As the treatments for bites of rabid animals increased in number he was rewarded with the certain knowledge that he had saved many persons from a death that is frequently of the most painful kind. Such persons scattered about through many countries became object lessons to the people around them of the efficacy of the Pasteur treatment, and when the project was started for creating a great institute for the work of Pasteur and his colleagues it was supported by an unparalleled burst of generosity. Not only from France, but from Italy, England, Russia, the United States, and many other countries, contribu-

tions were sent in for the benefit of this institution. The long list of subscribers included workmen, students, and poor women, as well as millionaires and the members of royal families. To a great extent the Pasteur Institute, as it came to be called, was an expression of the interest and generosity of the common people. Among the subscribers from Alsace-Lorraine, Pasteur noted with peculiar emotion the name of little Joseph Meister, who eleven months before, received the first treatment for rabies administered to a human being.

The Pasteur Institute became a great research institution which was devoted not only to the treatment of increasing numbers of people bitten by rabid animals, but also to carrying on investigations in bacteriology and the control of epidemic diseases. The Institute since its foundation has published in its annals the results of the treatment for all of its cases of rabies. Up to 1912 it had treated over thirty thousand cases of rabies with a mortality of less than one percent. The relatively small percentage of failures include several cases in which treatment was administered several days or even some weeks after the bites were inflicted.

In order to avoid sending persons over long distances to Paris, as was formerly done, branch in-

stitutes have been created in many other countries. There were over forty of them in 1914. In the course of eighteen years they had treated over 100,000 persons with a mortality of 0.73 percent; if we exclude the probably hopeless cases who died within two weeks after treatment, the mortality was 0.54 percent. Even though hydrophobia is not a common disease these figures indicate a saving of many thousands of human lives. I happened to live near an institution, the State Hygienic Laboratory at the University of California, which makes and administers the materials used in the Pasteur treatment. California was practically free from hydrophobia before 1909, but at this time some rabid dogs gained entrance into the state and the disease rapidly spread. In parts of the state it became prevalent among the coyotes which did considerable damage by biting sheep and cattle. Efforts were made to check it by having dogs muzzled, but this aroused lively opposition among many people, who are always unreasonable in such matters, and muzzling was not thoroughly carried out. The people of the state paid dearly for their failure to take prompt measures to stamp out the disease. Many people were bitten by rabid animals, but, fortunately for them,

preparations for meeting the emergency were quickly made at the Hygienic Laboratory. Up to July, 1923, the Pasteur treatment was administered to 1,490 persons with a mortality of about one percent. If we were to exclude the obviously hopeless cases in which the disease set in very quickly or in which treatment was delayed the mortality would be considerably less.

CHAPTER XII

LAST DAYS

THE conquest of hydrophobia was the crowning achievement of Pasteur's career. In the Pasteur Institute, which afforded unrivalled facilities for research, an efficient corps of well-trained co-workers carried on investigations in the fields opened up by Pasteur's genius. After 1888, Pasteur devoted most of his time to the work of this institution and to superintending the treatments given to patients for hydrophobia. It was his habit to go the rounds of the patients in the morning, inquiring how they were progressing and cheering them with words of encouragement. The children enlisted his especial concern. "When I approach a child," he says, "he inspires me with two sentiments; that of tenderness for what he is now, and respect for what he may hereafter become."

After perfecting his treatment, which was now administered by the efficient staff of the Institute, Pasteur could rest with the assurance that all had

been done for hydrophobia that one man could well do. He looked forward to new fields to conquer,—to diphtheria, cholera, tuberculosis, the plague, and many other diseases which afflict mankind, but his strength did not permit of further active investigations. The work on rabies had been peculiarly taxing. Added to the intense labor devoted to the struggle with this disease, there was the anxiety over the outcome of the treatments which gave him many sleepless nights and robbed him of much nervous energy. He was frequently called upon to address or preside at public meetings, and his correspondence, which was punctiliously attended to, took much of his time. In 1889, despite his failing strength, he went to Alais to take part in the ceremony of raising a statue to J. B. Dumas for whose memory he cherished the deepest reverence. The silk growers of that region, in memory of Pasteur's control of the silk-worm disease, presented him with a token of their gratitude in the form of a silver branch of heather adorned with the golden cocoons of the silk worm. In his acknowledgment of the gift, Pasteur said, "In the expression of your gratitude, by which I am deeply moved, do not forget that the rôle of initiator was played by M. Dumas."



FIG. 13. PASTEUR AND MADAME PASTEUR

Tokens of respect and gratitude came to Pasteur from many quarters. The Canadian government gave his name to a district adjoining the State of Maine. The Governor-General of Algiers informed Pasteur that his name was given to a village in Algiers, adding that, "I am happy to have been able to render this slight homage to your illustrious person." Streets bearing Pasteur's name were laid out in several cities and towns, and letters full of expressions of gratitude for some one near to the heart of the writer who was saved by Pasteur's discoveries, gave him a deep satisfaction that more than offset the effect of other letters roundly abusing him for the sacrifice of the animals which made these discoveries possible.

Pasteur is regarded by his countrymen with mingled feelings of gratitude and pride. He is one of the few men of science whose name has become a household word. His work, directly or indirectly, has touched every home. It has called forth the homage of the people, not so much because of its revelations of the secrets of nature, as because, in many thousands of homes, it has meant the saving of human lives. There is consequently little ground for surprise over the results of the popular vote which was conducted a few years ago by an enter-

prising Parisian newspaper as to who was the greatest man whom France had produced. The great Napoleon who probably would have been awarded this distinction a generation before stood well down the list. The first place was given to Louis Pasteur whose discoveries have probably saved more lives than Napoleon had destroyed.

As Pasteur approached his seventieth birthday, preparations were made for a fitting celebration. Norway, Sweden, and Denmark took the initiative in this movement, which was enthusiastically supported by the Academy of Sciences in France. The meeting was held in the large theater of the Sorbonne on December 27, 1892, and was presided over by the President of the Republic, Sadi Carnot. On the platform were the Ambassadors from England, Russia, Austria-Hungary, Denmark, Belgium, Holland, Sweden, Norway, and of Bavaria, and also the chief officials of the French government. There were representatives of the Academy of Sciences, the Academy of Medicine, the École Normale, the École Polytechnique, the School of Pharmacy and many other scientific societies in France and in foreign countries. There were delegations from many nations, consisting of their foremost men of science,—Lister, Burdon Sanderson,

Ray Lankester from England, Haskovek and Schottelius from Germany, Metchnikoff from Russia, and distinguished representatives from Belgium, Denmark, Holland, Italy, Poland, Greece, Switzerland, and Spain. Masses of students composed a large part of the great audience which was stirred by a deep enthusiasm for the man whose life-long labors were being so signally honored. As Pasteur entered, leaning upon the arm of the President of the Republic, the band of the Republican Guard played a triumphal march, and the entire audience rose and greeted him with prolonged applause. It was, as Keim and Lumet have remarked, "the supreme homage."

The opening ceremonies over, M. Dupuy, Minister of Public Instruction, addressed Pasteur, recounting his great achievements and concluding in the following words: "Who can say at this hour how much human life owes to you, and what it will owe to you in the years to come? A day will come when some new Lucretius will sing in a new poem of Nature the immortal master whose genius has engendered such great benefits. He will not picture him a solitary and unfeeling man as the Latin poet has portrayed his hero; he will show him mingled with the life of his time, the sadness and

joy of his country, dividing his life between the severe pleasures of scientific research and the sweet intercourse of family life, passing from his laboratory to his fireside, finding among his dear ones who knew him and who therefore loved him, the encouragement in daily work and comfort at all times, without which so many troubles would perhaps have diminished his ardor, checked his perseverance and enervated his genius. May France possess you for many years to come and show you to the world as a worthy recipient of her love, her gratitude, and her pride!"

A large engraved golden medal was then presented to Pasteur, and after a few words from M. Daubrée, a former colleague of Pasteur's at Strasbourg, an address was made by Lord Lister, who was chosen with peculiar appropriateness as the representative of the Royal Societies of London and Edinburgh. "M. Pasteur," he said, "the great honor has been accorded me of bringing you the homage of the sciences of medicine and surgery. As a matter of fact, there is no one living in the entire world to whom the medical sciences owe so much as they do to you. Your researches in regard to fermentation have shed a powerful light that has illumined the fatal darkness of surgery and changed

the treatment of wounds from a matter of empiricism, uncertain and too often disastrous, to a scientific art of assured beneficence. Thanks to you, surgery has undergone a complete revolution which has robbed it of its terrors and extended its efficacious powers almost without limit. Medicine is indebted no less than surgery to your profound and philosophic studies. You have lifted the veil which for centuries had overhung infectious diseases. You have discovered and demonstrated their microbic nature. Thanks to your initiative and in many cases to your special and personal labors, there are already a number of these pernicious disorders of the causes of which we have a complete knowledge. . . .

“Infectious diseases constitute, as you know, the great majority of the maladies which afflict the human race. You can therefore well understand that the sciences of medicine and surgery are eager upon this solemn occasion to offer you the profound homage of their admiration and gratitude.”

At the close of this address, the greeting of Pasteur and Lister, the two great figures in the creation of a great epoch in medicine and surgery, brought tumultuous applause. No one in that re-

markable audience could ever forget the sight of these two men. The Academy of Medicine, the scene of so many controversies, paid its homage through its Dean, who said, "More fortunate than Harvey and Jenner, you have lived to see the triumph of your doctrines, and what a triumph!"

Gifts, expressive of the admiration and esteem of several organizations, were presented to Pasteur on that occasion, but one which perhaps touched him most was an album containing the signatures of all the inhabitants of his native village of Dôle, a photograph of the house in which he was born, and a facsimile of his birth certificate at the end of which was the signature of his father. One wishes that the old soldier, who sacrificed so much in his ambition for his son's success, might have been brought back to life and given a seat of honor on the platform during the impressive celebration of that day.

Pasteur, whose voice was weakened by his broken health, had his address read by his son. After expressing his appreciation for the honors conferred upon him, he said, in addressing the foreign delegates, "You who have come from so far to give a proof of sympathy to France, you bring me the deepest joy that a man can experience, who believes

invincibly that science and peace will triumph over ignorance and war; that peoples will come to a common understanding, not to destroy but to build, and that the future will belong to those who will have done most for suffering humanity. . . .

“Young men!” he continued, addressing the students, “have confidence in that sure and powerful method of which we do not yet know the fundamental secrets. . . . Live in the serene peace of laboratories and libraries. Say to yourselves, first of all: What have I done for my instruction? and as you go on further, What have I done for my country? until the time comes when you may have the immense happiness of thinking that you have contributed in some way to the progress and to the welfare of humanity.”

Although Pasteur could no longer endure the strain of active labors, he followed with keen interest the experiments of his associates at the Institute. Metchnikoff, destined to be known throughout the world for his investigations on immunity and the rôle of the white corpuscles of the blood, came to join the staff of the Institute. The able, energetic, and ambitious men, whom Pasteur drew around him, regarded their master with unflinching devotion. Pasteur's dream of a great

research institution, devoting itself to the conquest of disease, was realized, and as he followed the work of its able staff, he had reason to feel a profound satisfaction in its achievements and promise. Roux and Yersin had made a discovery of the highest importance in regard to diphtheria. The bacillus of this disease had been discovered by Klebs in 1883, and isolated and cultured later by Loeffler. Roux found that the liquid filtered from cultures of the diphtheria bacillus was highly poisonous. A very small amount of this injected under the skin of small animals caused death with many of the symptoms of diphtheria, although, of course, without the presence of the bacilli of diphtheria in the body. Roux drew the conclusion that the germs of diphtheria and presumably other germs also produce their deadly effects through the production of poisons or toxins.

This discovery paved the way for another which was made by Behring and Kitasato, the discovery of antitoxins or substances produced by the body which have the property of combining with and neutralizing the toxins, and hence of relieving the body from the poisonous effects which the latter produce. The Pasteur Institute began to make the antitoxin for diphtheria. By injecting gradually

increasing doses of diphtheria toxin into a horse, the blood of the animal comes, after a time, to contain a quantity of antitoxins. After this occurs, some of the blood of the horse is withdrawn, the serum is extracted and preserved in vials with a small amount of antiseptic. It is then ready to use for cases of diphtheria.

The gratifying results of the use of diphtheria toxin are well known. If given early in the course of the disease, it effects a cure in a very high percentage of cases, and the mortality of all cases treated with antitoxin, as compared with the mortality of untreated cases, is relatively low. Diphtheria is a treacherous disease; it sometimes snatches away its victims before the nature of the malady is determined. Highly contagious and often carried by persons not themselves affected, it is remarkably persistent and still ranks among the principal causes of death in the period of childhood. The work of Roux on diphtheria antitoxin was suggested by some of the earlier experiments of Pasteur on chicken cholera. Pasteur found that the liquid obtained by filtering a culture of the bacteria of chicken cholera would produce some of the symptoms of this disease if injected into a healthy fowl. He did not follow up the line

of enquiries to which the experiments pointed, as he was then chiefly interested in establishing the important principle of attenuation. This was left for others, and the investigations thus started and continued in the Pasteur Institute and elsewhere have led, step by step, to the most striking results in serum therapy and allied procedures.

In 1894, Yersin, who had gone from the Pasteur Institute to China, discovered the germ of the plague, and found that it could be cultured in artificial media, and inoculated into rats, mice, and guinea pigs. The subsequent discovery of the rôle played by rats in harboring the germs of the plague, and its transmission from animal to man and from man to man by fleas, has made it possible to stamp out this disease in several places in which it had gained a foothold. The epidemics that formerly swept over nations carrying away thousands in their course may now be controlled. Where plague occurs war is made on the rats and fleas, the patients are strictly quarantined and the epidemic dies.

Pasteur was profoundly gratified by the discoveries of his co-workers. They were bringing nearer to realization his dream of the conquest of disease though the methods which he had discovered and

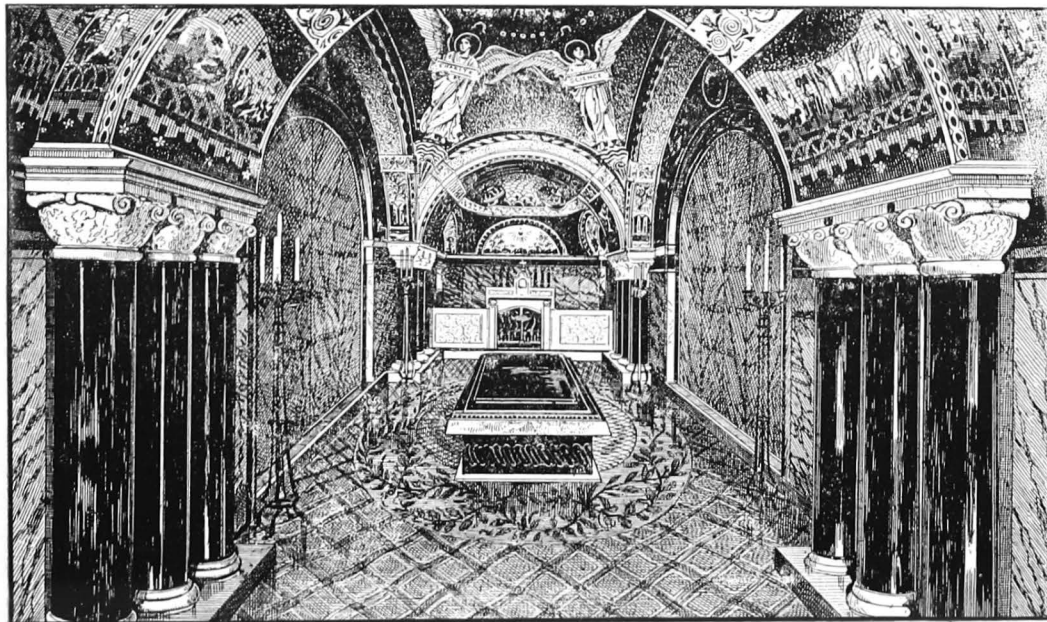


FIG. 14. TOMB OF PASTEUR

so successfully applied. In 1895 he had almost ceased to visit the laboratories of the Institute. His growing weakness apprised him of the approaching end. Alone one evening with his grandchildren, who were playing about his knees, he took them in his arms and affectionately kissed them while tears rolled down his careworn face. To the anxious questions of the children he replied, "I am weeping, my children, because I am so soon to leave you." The paralysis which had affected him years before began to recur, and made it more difficult for him to speak. The loving care of his family and the solicitude of many friends did everything possible to cheer his declining days. On September 27, 1895, holding in one hand a crucifix, for he had always lived in the Catholic faith, and with the other resting in the grasp of Madame Pasteur, he passed away.

At the request of the French Government the body of Pasteur was placed in a beautiful chapel at the base of the Pasteur Institute. Its marble walls bear the names of the chief fields of investigation in which he had won renown,—molecular asymmetry, fermentation, spontaneous generation, studies on wine, studies on silk worms, studies on beer, the cause of contagious diseases, curative vaccines, the

prophylaxis of hydrophobia. In the decorations of his tomb are wreaths and garlands of grape vines, mulberry leaves and figures of cattle, sheep, dogs, and poultry, whose diseases he did so much to conquer. And on the vault above his grave are four angels watching over him, Faith, Hope, Charity, and Science. In the laboratories above his tomb his great work is going on.

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