PASTEUR

FRANKLAND

Edited by
Sir Henry E. Roscoe
D.C.L., LL.D., F.R.S.

THE CENTURY SCIENCE SERIES.

EDITED BY SIR HENRY E. ROSCOE, D.C.L., LL.D., F.R.S.

PASTEUR

LOUIS PASTEUR.

[*Frontispiece.*]

With kind regards from the writers. Feb 1898

THE CENTURY SCIENCE SERIES

PASTEUR

BY

PERCY FRANKLAND

Ph.D. (Würzburg), B.Sc. (London), F.R.S.

Associate Royal School of Mines, Fellow of the Institute of Chemistry, Formerly Professor of Chemistry in University College, Dundee; Professor of Chemistry in Mason University College, Birmingham

AND

MRS. PERCY FRANKLAND

Authors of "Micro-organisms in Water," etc. etc.

"The first point of wisdom is to discern that which is false; the second, to know that which is true."—*Lactantius*

CASSELL AND COMPANY, LIMITED

LONDON, PARIS & MELBOURNE

1898

PREFACE.

In the following pages we have endeavoured to present a sketch of the life and work of one of the most remarkable men of science this century has produced. His achievements are so interwoven with the circumstances by which our daily life is surrounded, that it is all but impossible to find anyone who is not directly or indirectly concerned with some part or other of his great life-work.

But although the lives of so many have been profoundly affected by his genius and labours, it is only the few who have any acquaintance with the man and the method, to whom and to which these great achievements are due.

It is our hope that these pages may raise the veil for many exposing to their view at once a picture of the Great Master, and of the scientific machinery which he knew so well how to set in motion and how to control.

In the execution of this attempt, we have to acknowledge the great assistance we have received from the admirable works of M. Vallery-Radot ("Histoire d'un Savant par un Ignorant"), and of M. Duclaux ("Histoire d'un Esprit"), as well as from the concise and artistic notice, entitled "L'Œuvre Médicale de Pasteur," given by M. Roux in the "Agenda du Chimiste" for 1896.

For the reproduction of the portraits we are indebted to the courtesy of the family of the late M. Pasteur.

P. F. F.
G. C. F.

BIRMINGHAM.

TABLE OF CONTENTS.

PASTEUR.

CHAPTER I.

EARLY YEARS.

In a poor quarter of Dôle stands a little house bearing the simple inscription in gold :—

"Ici est né Louis Pasteur
le 27 Décembre, 1822."

When an infant of but two years of age, Louis Pasteur's parents removed to the town of Arbois, where his childhood was passed, for here his father purchased a small tannery. That this hard-working tanner was a man of character and stern experience, is shown by the fact that he had fought in the legions of the First Empire, and that he had been decorated on the field of battle by Napoleon; but the rough soldier had his heart in the right place, and the home at Arbois appears to have been one of those establishments which revolve round the children, and the greatest sacrifices were made by the parents to secure the best educational advantages for the son. Nor was Pasteur unmindful of this unselfish devotion in after years, for the most celebrated of his works bears the dedication :—

"*A la Mémoire de mon Père, ancien militaire sous le Premier Empire, Chevalier de la Légion d'Honneur.*
Plus j'ai avancé en âge, mieux j'ai compris ton amitié et la supériorité de ta raison.
Les efforts que j'ai consacrés à ces Etudes et à celles qui les ont précédées sont le fruit de tes exemples et de tes conseils.
Voulant honorer ces pieux souvenirs, je dédie cet ouvrage à ta mémoire," *

a tribute surely more imperishable and more covetable even than the ribbon pinned to his tunic by the victor of Marengo and Austerlitz!

When old enough, Pasteur was sent as a day scholar to the Collège Communal; but books and study had little attraction for him, and he preferred to follow his favourite pastime of fishing, and to delight his companions and neighbours by sketching their portraits, some dozen of which are still shown with pride by the inhabitants of Arbois.

"What a pity he has buried himself amongst a heap of chemistry!" remarked an old woman of Arbois many years later. "He has missed his vocation, for he would some day have really succeeded in making a name as a painter;" and, indeed, the portrait of his mother which used to hang in his house in Paris is in itself evidence of the marked artistic talent possessed by Pasteur when a mere lad.

But as time went on, young Pasteur began to realise the sacrifices his parents had made for his education; and rousing himself from his lethargy, he put from him his hobby and his pastime, locked away his brushes and his fishing-tackle, so as to be delivered from temptation, and put his shoulder to

* "Etudes sur la Bière." Published in 1876.

the wheel. From that day onwards Pasteur may be said to have hardly ever paused in the pursuit of those Herculean labours, which his genius throughout his life supplied in such rapid succession for his indomitable energy to perform.

The college of Arbois having at this time no professor of philosophy, Pasteur left for Besançon, where at the end of the academic year he took his degree of bachelier ès lettres, and was at once appointed "maître répétiteur," or tutor, in the college. The fond ambition and hope of his father at this time was often repeated, "Ah ! si tu pouvais devenir un jour professeur, et professeur au collège d'Arbois, je serais l'homme le plus heureux de la terre." But fathers are not generally the best judges of the capacity of their offspring, and this was certainly far too modest an estimate of young Pasteur's powers ; for even in those early days his old schoolmaster, watching his work and progress, exclaimed, "Ce n'est pas vers la chaire d'un petit collège comme le nôtre qu'il faut le diriger, il faut qu'il soit professeur dans un collège royal. . . . Mon petit ami, pensez à la grande Ecole Normale ! "

Perhaps this encouraged Pasteur to attend special courses of instruction in mathematics in the time which he could spare from his other studies, so as to prepare himself for the examination in science of the Ecole Normale of Paris. It was at this time also that his special interest in chemistry began to show itself, and the eager questions with which he plied and embarrassed the venerable professor Darlay before his class, were such that the latter was at length reduced to telling his pupil that it was for him to interrogate Pasteur and not for Pasteur to submit him to a cross-examination before all his scholars. Pasteur was compelled to restrain his enthusiasm in the class-room, but he hunted out a pharmaceutical chemist in the town, who had acquired some local celebrity through being the author of a paper which had been deemed worthy of publication in the *Annales de Chimie et de Physique*, and him he persuaded to secretly assist him in his studies.

Pasteur subsequently presented himself for the entrance examination of the Ecole Normale. An incident attended his entry as a student which is worth recording as indicative of his extraordinary perseverance, and of the exacting standard of performance which he imposed upon himself. Although he passed and was admitted, he only obtained the fourteenth place. This position did not satisfy him, and he determined to withdraw and work for another year, and then go in for the examination a second time. For this purpose he went to Paris to study, and the following year, in October, 1843, on again submitting to the examination, he gained the fourth place.

Pasteur's love for chemistry had now developed into a passion, and with Dumas at the Sorbonne, and Balard at the Ecole Normale, he had every opportunity for gratifying his taste, for the students attended both courses of lectures. In each of these great masters of chemical science the young Pasteur was impressed by what was most admirable, by the great grasp of well-digested facts and details possessed by the discoverer of bromine, by the lofty generalisations indulged in by the author of the theory of types. It was at this time, too, that the foundations were laid of that strict habit of mind which led him to avoid all hypotheses, however seductive, which were not supported on a sound basis of experimental facts defying refutation: an attitude of mind which many years later found expression in the address to his colleagues at the public inauguration of the Institut Pasteur *:—

"For the investigator it is the hardest ordeal which he can be asked to face—to believe that he has discovered a great scientific truth, to be possessed with a feverish desire to make it known, and yet to impose silence on himself for days, for weeks, sometimes for years, whilst striving to destroy these very conclusions, and only permitting himself to proclaim his discovery when all the adverse hypotheses have been exhausted."

As a student, Pasteur's energy and enthusiasm were boundless. Not even on Sundays did he rest from his chemical studies; and some idea may be formed of his industry by the fact that on one of these days of rest he actually succeeded in the difficult task of preparing no less than sixty grammes of phosphorus from bones which he had bought at a butcher's, an operation which lasted from four in the morning to nine o'clock at night.

It is doubtless the experience of many who have attended great seats of learning that, much as may be the indebtedness to professors, the real fire of research is not unfrequently kindled by the fertile suggestions of junior men with whom students can associate on more equal terms; and whatever Pasteur may have owed to Dumas and Balard, there can be no doubt that he was helped on to the first rung of the ladder

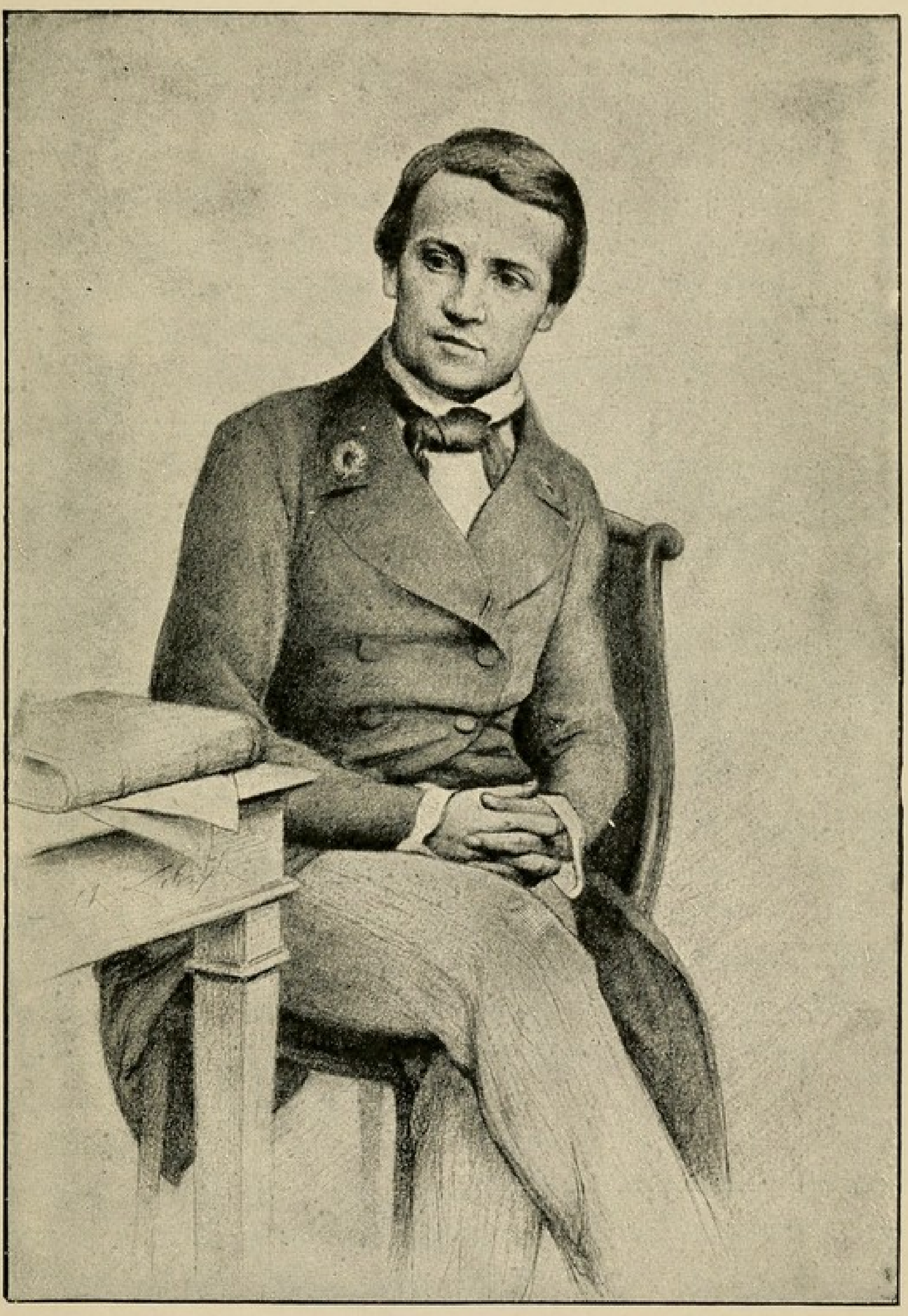
* *See* p. 186.

which he scaled with such dexterity and success, by a man of this kind. It was Delafosse, a former pupil and assistant of the renowned Haüy, who turned Pasteur's attention to the study of crystals and to problems of molecular physics, in which domain his first laurels were won.

In order to appreciate the importance of the part played by Pasteur in the particular field of research to which he first devoted his attention, a few words of introduction are necessary to indicate the stage at which the inquiry had arrived, when Pasteur and Delafosse were so eagerly discussing together intricate problems on the arrangement of molecules.

The phenomena of double refraction were already known to Huygens and Newton, but the subtle difference between the nature of the light composing the ordinary and extraordinary rays respectively was not understood until Malus made the far-reaching discovery in 1808 of the polarisation of light by reflection, and subsequently showed that the rays which are transmitted through Iceland spar differ from those of ordinary light in being polarised.

The wonderful and intricate phenomena of polarisation, which form such an attractive chapter in experimental optics, were investigated after the untimely death of Malus in 1812 by Arago, and more especially by Biot, who practically devoted his whole life to this study. It is almost impossible to over-estimate the debt which chemical science owes to the patient researches of this physicist; for in the course of his labours, he made in 1815 the discovery that there are a number of natural organic substances—such as sugar, camphor, tartaric acid, oil of turpentine, etc.—



PASTEUR WHEN A STUDENT AT THE ECOLE NORMALE.

[*To face page* 15.]

which possess the remarkable property of rotating the plane of polarisation when a beam of polarised light is passed through them either in the liquid or dissolved state. Nor was Biot slow in perceiving the enormous theoretical importance of this discovery; for he at once pointed out that whereas in the previously-known phenomena of the rotation of the plane of polarisation by crystals—*e.g.* quartz—the rotation is conditioned by the crystalline form, disappearing altogether as it does so soon as that form is destroyed, in the case of these organic substances this rotatory power must be inherent in the molecules themselves; for being exhibited by liquids, it must be dependent upon the one structure which still remains—the molecule itself.

This discovery of Biot's had thus placed the physical phenomena of polarisation on the doorstep of the chemist, and we shall soon see how the latter availed himself of this legacy.

It was in 1844, when Pasteur was still a student at the Ecole Normale, that Biot communicated to the Academy of Sciences a note by the German chemist, Mitscherlich, and it was this memoir which finally, as it were, set the ball rolling, and started Pasteur on that voyage of discovery which was coextensive with his life.

Mitscherlich had discovered that the two tartaric acids so familiar to chemists, while apparently identical in chemical composition, in chemical properties, in crystalline form, and, in fact, in every known detail, behaved differently in solution towards polarised light, the solution of the one turning the plane of polarisation to the right, whilst the solution of the other (generally called paratartaric or racemic acid) produced no effect whatever on the polarised beam. At the close of his memoir Mitscherlich adds, "The nature and number of atoms in these two bodies, as well as their arrangement and the distances between them, are identical."

"How," reflected Pasteur, "can we accept the identity in the nature and number of atoms, admit that the relative distance and arrangement and the crystalline form are the same in these two bodies, without admitting also their absolute and entire identity throughout? A profound incompatibility surely exists between Mitscherlich's discovery of the different relationship of these two tartrates towards polarised light, and his statements that they are identical in every particular." This problem haunted Pasteur continually, and his attention was now wholly devoted to the study of crystals, the determination of their angles and their form, when he heard with dismay that he had been nominated Professor of Physics at the Lycée of Tournon. Fortunately, however, through the intervention of Balard, to whom he was now acting as assistant, this threatened interruption to his work was avoided; the appointment was cancelled, and Pasteur was permitted to remain at the laboratory of the Ecole Normale.

In order to train himself yet more perfectly in the examination of crystals, Pasteur determined to repeat an elaborate piece of work which the celebrated crystallographer, De la Provostaye, had published on tartaric and paratartaric acids and their salts.

Many years later Pasteur refers with enthusiasm to the keen pleasure he experienced at this time in producing the crystals of tartaric acid and its derivatives "Dont les cristaux," he said, "rivalisent en dimension et en beauté avec les plus belles formes cristallines connues."

It was soon evident, however, that mere repetition and confirmation was not Pasteur's strong point; for although a comparative novice at the kind of work in question, he was able to see what had escaped the observation of his skilled predecessor in this field, and to detect a minute point of difference which had eluded the vigilance of the most accomplished crystallographers of the day—Mitscherlich and Biot, as well as Provostaye. On the crystals of the tartrate which was active to polarised light Pasteur found some minute faces which were absent from the crystals of the tartrate inactive to the polarised beam. Such importance did he at once attribute to these little faces, that he recognised that their presence relegated the substance possessing them to an entirely different class of objects from that to which belonged the substance in which they were absent.

The presence of such faces on crystals of quartz had not escaped the attention of Haüy, who, indeed, had further divided such quartz crystals into left and right-handed quartz, according to the side on which these faces were developed. Pasteur, intimately acquainted with the work and speculations of Haüy and others, had been profoundly impressed with the remarkable relations which subsequent experiments had proved existed between the power to turn the plane of polarisation, and the presence of these faces on quartz crystals. It was in consequence of his being so deeply imbued with the idea that polarimetric effect must be associated with crystalline form, that the appearance of these little faces on some of the tartrate crystals and their absence on others seemed to him of the very highest importance, and deserving of the most careful study.

Pursuing, therefore, his minute examinations of these crystals, he found that whilst the crystals of the inactive tartaric acid which were destitute of these little surfaces were symmetrical, the crystals of the optically active tartaric acid were unsymmetrical, or *dissymmetric,* as he called it. Now, to the symmetric character of the crystals of the one tartaric acid, generally known as paratartaric or racemic acid, he attributed the inactivity of this tartaric acid to polarised light, whilst with the dissymmetric character of the crystals of the other tartaric acid he connected its action on the polarised beam.

The intrinsic and fundamental difference between these two classes of bodies—the *symmetric* and the *dissymmetric*—is perhaps most easily realised by placing them before a mirror, when in the case of the symmetric body the image will be identical with the object, whilst in the case of the dissymmetric body the image and object are not identical, but bear the same relationship to each other as the left and right hands do, which are perhaps the most familiar instances of dissymmetric objects. Thus placing the crystal of active tartaric acid in front of a mirror, the reflection obtained is not identically the same crystal as the original, but related to it as the left hand to the right hand ; but on placing the crystal of the inactive tartaric acid before a mirror, the image is in every respect identical with the original crystal.

In studying these apparently insignificant details, Pasteur found that by crystallising the inactive tartaric acid (paratartaric or racemic acid) in a particular way,* he obtained two different kinds of crystals—the one set being identical with those of the active tartaric acid already known, whilst the other set were the mirror images of these, and had never been seen by the eye of man before. The young philosopher at once drew the conclusion that if the dissymmetry of the known tartaric acid caused it to turn the plane of polarisation to the right, the dissymmetry of this new tartaric acid would turn it to the left.

With infinite pains Pasteur picks out from the mixture the individual crystals belonging to each of the two types, and arranges them in two heaps. Each of these heaps of crystals was then separately dissolved in water, and the two solutions submitted to polarised light. In accordance with his anticipation, whilst the solution of the crystals of the known form was found to turn the plane of polarisation to the right, the solution of the new crystals, the mirror-images of the old, was found to turn the plane through precisely the same angle to the left.

This might have appeared to many a trivial discovery only; but such was not Pasteur's opinion of it, for rushing from the laboratory in a fever of excitement, and meeting Bertrand in the corridor, he embraced him, exclaiming, overcome with emotion, "Je viens de faire une grande découverte! J'ai séparé le paratartrate double de soude et d'ammoniaque en deux sels de dissymétrie inverse et d'action inverse sur le plan de polarisation de la lumière. Le sel droit

* By preparing the sodium ammonium salt and crystallising this.

est de tout point identique au tartrate droit. J'en suis si heureux que j'éprouve un tremblement nerveux qui m'empêche de remettre de nouveau l'œil à l'appareil de polarisation. Allons au Luxembourg; je vous expliquerai tout cela!"

As might have been anticipated, this discovery made by a young man but twenty-five years of age, his first venture in the scientific arena, and challenging the opinions and statements of such world-famed veterans as Biot, Mitscherlich, and Provostaye, whilst producing a great sensation in scientific circles, was received with no little scepticism by the Academy of Sciences.

We are, moreover, quite familiar with remarkable results obtained by mature and well-seasoned investigators being received with incredulity or reserve, as it is euphemistically called, and it is not surprising, therefore, that such a striking discovery made by a young and almost unknown man should have been accepted with considerable hesitation. The duty of reporting on this paper was entrusted to the highest living authority on such a subject, to Biot himself, and we are tempted to give Pasteur's own account of the extraordinarily stringent investigation to which the half-sceptical veteran submitted the young man's almost suspiciously plausible results:—

"He [M. Biot] sent for me to repeat before his eyes the several experiments. He gave me racemic acid which he had himself previously examined and found to be quite inactive to polarised light. I prepared from it in his presence the sodium ammonium double salt, for which he also desired himself to provide the soda and ammonia. The liquid was set aside for slow evaporation in one of the rooms of his own laboratory, and when 30–40 grms. of crystals had separated he again summoned me to the Collège de France, so that I might collect the dextro- and lævo-rotatory crystals before his eyes, and separate them according to their crystallographic character, asking me to repeat the statement that the crystals which I should place on his right hand would cause deviation to the right, and the others to the left. This done, he said that he himself would do the rest. He prepared the carefully weighed solutions, and, at the moment when he was about to examine them in the polarimeter, he again called me into his laboratory. He first put the more interesting solution, which was to cause rotation to the left, into the apparatus. Without making a reading, but already at the first sight of the colour-tints presented by the two halves of the field in the Soleil saccharimeter, he recognised that there was a strong lævo-rotation. Then the illustrious old man, who was visibly moved, seized me by the hand, and said, 'Mon cher enfant, j'ai tant aimé les sciences dans ma vie que cela me fait battre le cœur!'"

For more than thirty years Biot, who was the first to discover the behaviour of organic chemical substances towards polarised light, had urged that the polarimetric study of these substances might possibly prove an important avenue to the understanding of their constitution; but although he had led scientific thought, and directed experimental activity with marvellous instinct in the direction of that new realm of chemistry, so fraught with fascinating and absorbing interest to the investigator, it was not given to Biot himself to cross the frontier, but this advance was reserved for Pasteur.

Thus Pasteur pointed out that the differences in optical properties and in crystalline form exhibited by these two oppositely active tartaric acids were doubtless dependent on the two molecules having a different arrangement of their constituent atoms, the arrangement in each case being dissymmetric, and clearly indicated that whatever the dissymmetry of the one tartaric acid might consist in, it must be related to the dissymmetry of the other tartaric acid in the same sort of way as the dissymmetry of the left hand is related to the dissymmetry of the right hand; still, at the time, organic chemistry was not sufficiently advanced to make any immediate use of these speculations. The remarkable progress and development of organic chemistry which characterise the latter half of the present century before long led to the further interpretation of these phenomena exhibited by the tartaric acids. For some years later (1869) Wislicenus was confronted with similar phenomena in the case of lactic acid; and with the more perfect knowledge which had then been gained as to the grouping of the atoms in the molecule, he was led to hazard the suggestion that the difference between the two lactic acids was due to a difference in the arrangement of the atoms in the molecule which could not be represented by the ordinary plane formulæ of chemists, but required a consideration of the arrangement of the atoms in the three dimensions of space.

This suggestion, giving as it did further substance to Pasteur's previously expressed views of dissymmetry, was the foundation of that most fascinating and fertile field of chemical science which is now known as stereo-chemistry, the guiding principles of which were elaborated in 1874 with such rare skill and prescience by Van't Hoff and Le Bel, and which, like nearly all new and original departures in science, met at the outset with the most scathing criticism and even scornful ridicule from some of the conservative professors of the time.

These views concerning the spacial arrangement of the atoms within the molecule have, however, long since passed their probationary stage, and their provisional acceptance at any rate has become absolutely indispensable to a proper understanding of recent advances in our knowledge of the carbon compounds. The fertility of these views in stimulating successful researches has been almost limitless. Thus, some of the most brilliant achievements of modern chemists, such as the artificial synthesis by Ladenburg of the alkaloidal poison *Coniine,* which forms the deadly instrument of execution concealed in the cup of hemlock, and the wonderful series ot investigations which, in the able hands of Emil Fischer, has culminated in the preparation of some of the principal natural sugars: these investigations owe their success entirely to the guidance of those theories of stereo-chemistry which are the direct outcome of Pasteur's fundamental researches on the tartaric acids.

The theory of the arrangement of the atoms in space has, however, also been applied with great success to substances which have no action on polarised light at all. Amongst the enormous number of carbon compounds prepared and accurately studied during the past fifty years, it has repeatedly been found necessary to assume that in some the atoms are arranged in a closed chain or ring, as opposed to the open chain arrangement which must be assumed to exist in many others. Now one of the most striking things about these closed chains is the fact that they almost invariably consist of either five or six atoms; a vast number of these ring compounds are, in fact, derivatives of the well-known hydrocarbon benzene, in which chemists have long recognised the presence of a ring consisting of six atoms of carbon. This remarkable predisposition to form five- or six- atom rings finds a ready explanation when Van't Hoff's views with regard to the relative positions of the atoms in space are taken into consideration.

The fertility of these speculations has led to chemists constructing similar hypotheses with regard to the arrangement in space of the groups attached to nitrogen atoms, the investigation of which is being eagerly prosecuted by numerous workers at the present time, whilst others still more imaginative are extending stereo-chemical views even to some of the compounds of platinum, cobalt, and other metals.

By these first researches we see, then, that Pasteur became the father of one of the most wonderful departments of modern chemistry—namely, the one which has for its ambition the discovery of the spacial distribution of the individual atoms in the molecule. Thus, Pasteur's first researches possessed in themselves purely theoretical interest; they were, however, masterpieces of thoroughness, and exhibited so much experimental skill, intuition, and power of careful observation, combined with clear judgment, that, even had his career been cut short at this stage, we should have had no hesitation in recognising in him one of the most remarkable and exceptionally gifted of investigators.

From these early researches, however, we should have had no positive indication of the man's power of harnessing science to the problems of practical life. But his genius was not long to be retained in the exclusive service of abstract science, and it is interesting to follow the circumstances which led him to find scope for the practical side of his abilities. It was not, as many might suppose, that he had suddenly set himself some definite problem of great practical moment to work out, for in scientific investigation it almost invariably happens that one step leads to another; the experience gained in one piece of work qualifies the worker to follow on in some definite direction and not to plunge into the unknown at random. Thus in Pasteur's case the great practical work of his life followed almost as a necessary consequence, on his achievements in the purely scientific domain to which we have already referred.

CHAPTER II.

CHEMICAL RESEARCHES.

PASTEUR'S academic career was now assured, and already, at the end of the year 1848, he was appointed Professor of Physics at the Lycée of Dijon, and three months later he was nominated deputy professor of chemistry at the University of Strassburg, becoming full professor in 1852.

This translation to Strassburg, quite apart from its importance in giving Pasteur greater scope for the pursuit of his scientific work, was to acquire for him a profound personal significance, for here he met his future wife, the daughter of M. Laurent, Rector of the Strassburg Academy. Their marriage, which took place in 1850, proved a singularly happy one, and it is impossible to rightly appreciate Pasteur's life without some understanding of the immense assistance which he received in his own home. Whether in discussing forms of crystals, watching over experiments, shielding her husband from all the daily fret of life, or busy at the customary evening task of writing to his dictation, Madame Pasteur was at once his most devoted assistant and incomparable companion. His surroundings at home were entirely subordinated to his scientific life, and his family shared with him both his trials and his triumphs. At the time when Pasteur was engrossed with the study of anthrax, and after many difficulties and disappointments had at length succeeded in preparing a vaccine against anthrax, he at once hurried from the laboratory to communicate his great discovery first to his wife and daughter; and this is but an instance of the bond of sympathy which was maintained throughout his life between the great savant and those around him.

Pasteur had an extraordinary power of concentrating his attention upon a single subject, and perhaps the most important part of his work was done in those hours when he would sit silent and immovable, deep in thought, occupied with some difficult problem, allowing nothing to disturb or distract him until he had found some solution. But when he had discovered a key to the difficulty the whole expression of his face would alter; he would become radiant with delight, and eagerly communicate to those around the experiments he had planned and the hopes of success which he cherished. The sympathy which throughout his life he sought so constantly, whether in his troubles or triumphs, was never failing, and the loving support he received at all times helped him in after years to sustain those great physical trials which fell so heavily upon him, and which he endured with such patience.

During the five years he resided in Alsace, Pasteur devoted himself almost exclusively to the systematic investigation of asymmetric compounds; and with this period of his life are associated those important and now classical researches on the conversion of right-handed tartaric acid into inactive tartaric acid (racemic acid) on the one hand, and into a new form of inactive tartaric acid (mesotartaric acid) on the other; his discovery of the method of splitting up racemic acid into its component dextro- and lævo-tartaric acids by means of optically active bases; and his famous refutation of Dessaignes' reputed conversion of fumaric and maleïc acids into aspartic acid, identical with that hitherto only obtained from asparagine.

Pasteur had himself studied these various bodies before the publication of Dessaignes' memoir, and had found that whilst fumaric and maleïc acids were not dissymmetrical—that is to say, were destitute of all optical activity, had no effect on polarised light—aspartic acid, like asparagine, from which it is derived, was endowed with molecular dissymmetry and was active towards polarised light.

If Dessaignes' facts were correct they would mean that he had accomplished what Pasteur firmly believed to be unrealisable—the preparation by artificial chemical means of an optically active molecule from an inactive one. Of such pressing importance did the settlement of this doubt appear to Pasteur that he at once, with his usual restless energy, set off for Vendôme and obtained from Dessaignes a specimen of his artificial aspartic acid. On returning to his laboratory, Pasteur examined it with the minutest care, and found that in spite of its great resemblance to the acid derived from asparagine, it differed from it in a very important particular, inasmuch as it was entirely devoid of the action on polarised light which characterised the latter, and he had no difficulty in showing that

Dessaignes' acid was not identical with the natural aspartic acid, but only a so-called inactive isomeride.

The dogma set up and so obstinately clung to by Pasteur, that asymmetric bodies cannot be artificially prepared, led him into some abstruse speculations concerning their production in nature, which have hitherto only received negative illumination from direct experiment. He points out that it is necessary and quite sufficient to suppose that at the genesis of a vegetable organism some asymmetric force must be in operation, and suggests that light, electricity, magnetism, and heat may be subject to asymmetric influences of a cosmic nature. Are these, he asks, perhaps connected with the motion of the earth, or with those electric currents by means of which physicists explain the magnetic poles of the earth? At any rate, these asymmetric forces are wanting in our synthetical reactions, or are without influence on them, possibly in consequence of their rapid course.

Nor did Pasteur simply propound these questions, but on the contrary the great master of the experimental method undertook a bold campaign into this highly speculative domain, from which, however, he soon deemed it more prudent to retreat; doubtless realising that his intellectual forces might be more advantageously employed in other directions than in a territory where only negative victories were to be won. Thus at Strassburg he actually had powerful magnets constructed with a view to introducing dissymmetric influences during the formation of crystals. At Lille, again, in 1854, he had a clockwork arrangement made with which he intended by means of a heliostat and reflector to reverse the natural movement of the solar rays striking a plant from its cradle to the grave, so as to see whether in such an artificial world, in which the sun rose in the west and set in the east, the optically active bodies would not appear in the opposite forms to those which the existing order of nature provides.

Pasteur, however, soon realised, doubtless instructed by his experience gained in other voyages of discovery on which he shortly embarked, that the task of turning the Creator's universe upside down was even beyond his experimental skill; recognising that, however he might reverse these external influences, he would still have to deal with the asymmetric agencies already present with all their irresistible albeit latent power in the germ of life itself, and that without the possibility of spontaneous generation there was also no possibility of realising this dream of a new world with its plants and animals producing the optical antipodes of the natural celluloses, albumens, starches, sugars, terpenes, etc., for the edification of the young stereo-chemical philosopher.

So far Pasteur had kept strictly to the domain of pure chemistry and molecular physics, and his attention was entirely absorbed by problems which, while of profound theoretical interest, gave no indication of the direction which his future labours would take, and to the pursuit of which his whole life was subsequently to be devoted.

Hardly realising it, however, Pasteur drifted away from his original anchorage, as it were, and while still eagerly pursuing the fascinating occupation of searching out physico-chemical problems, he found himself confronted and hemmed in by questions and problems of an entirely different order, and awoke to find that he had passed out of the comparatively quiet reaches of abstract science into the troubled waters of science in its relation to practical life.

It was an incident trifling in itself which first suggested to Pasteur the application of fermentation processes to the study of chemical substances, and which subsequently led him to devote the whole of his energies to the study of biological phenomena. A German firm of manufacturing chemists had observed that if solutions of impure commercial tartrate of lime were left in warm weather in contact with organic matters, they fermented and gave rise to various products.

Pasteur, to whom no phenomenon was trifling or insignificant, at once conceived the idea of utilising this fact by inducing, in the first instance, fermentation in a solution of ordinary right-handed tartaric acid. For this purpose he dissolved a salt of this acid, and added to its solution a small quantity of albumen. Fermentation followed, and the liquid, originally clear, became gradually turbid, a phenomenon which Pasteur found was due to the presence of small living cells, upon which he subsequently showed the process of fermentation to be dependent. This method he also applied to solutions of the paratartrate (racemate), with the same results. On examining these solutions after fermentation with the polarimeter, the most profound difference was, however, found to exist between them.

In the case of the paratartrate (racemate) the liquid, originally inactive, exhibited as the fermentation proceeded a gradually stronger and stronger deviation of the plane of polarisation to the left, until the maximum was reached and the fermentation ceased. It was then found that during the process of fermentation the right-handed acid had been consumed, leaving the left-handed acid alone master of the field; and the latter, thus freed from the constraining influence of its right-handed brother, was able to assert itself and exhibit for the first time its left-handed rotatory power.

In plain language this means that, whilst right-handed and left-handed tartaric acids are chemically identical, and are distinguishable only by their crystalline form and opposite action on polarised light, they are, nevertheless, utterly different from a physiological point of view; for the right-handed tartaric acid is alone taken up and transformed by the fermentative bacteria, which refuse to have anything to do with the left-handed tartaric acid. Thus the apparently trivial difference in the arrangement of the atoms in space in the case of these two tartaric acids, makes an overwhelming difference in their physiological character. This phenomenon, which is undoubtedly one of the most striking in the whole domain of chemical science, appears to be a very general one in the case of bodies admitting of two or more different arrangements of their atoms in space. Although not further pursued by its discoverer, this physiological difference has been largely utilised by subsequent investigators for the preparation of optically active compounds.

A couple of years later, in 1856, our Royal Society conferred the Rumford Medal upon Pasteur in recognition of his researches on the polarisation of light with hemihedrism of crystals.

This, in briefest outline, is the work of Pasteur in the domain of pure chemistry and molecular physics; as an example of the combination of rare experimental skill and precision with consummate deductive power, it stands out as one of the most remarkable and artistic monuments in the annals of chemical science. This work, begun, continued, and ended within the short period of ten years, is an achievement on which an investigator might look back with pride at the close of a life-time, and yet on its completion Pasteur stood but on the threshold of his great career.

CHAPTER III.

FERMENTATION STUDIES.

A NEW chapter in Pasteur's life opens with the year 1854, when, at the age of thirty-two, he was nominated the first Dean of the Faculty of Sciences, which had just been created in the industrial centre of Lille.

As dean or principal of this new institution at Lille, Pasteur at once realised that its work should, to some extent, be brought in touch with one of the leading industries of the district—the manufacture of alcohol from beetroot and grain—and he therefore determined to offer courses of lectures on fermentation, and threw himself with his characteristic energy into the serious study of this subject.

Thus it was that, at a time when Pasteur's mind was absorbed with the possibilities which had just been opened out to him of approaching chemical problems from an entirely novel point of view, and whilst hesitating whether he should allow himself to be carried away by a more intimate study of these fermentation processes, the choice was practically taken out of his hands, and the accident of his removal to Lille virtually decided what course his investigations should take.

At this time fermentation processes were not generally regarded as vital phenomena at all, for the dominant opinion concerning them was that of Liebig, who viewed the classical transformation of sugar into alcohol as a purely chemical process, depending not upon the living yeast cells which the microscope revealed, but upon the dead yeast undergoing *post-mortem* decomposition. In Liebig's own words:—

"Beer yeast, and, in general, all animal and vegetable matters in putrefaction impart to other bodies the state of decomposition in which they are themselves. The movement which, by the disturbed equilibrium, is impressed on their own elements, is communicated also to the elements of bodies in contact with them."

A few words of retrospect are necessary to show how these views of Liebig had gained ascendancy. Already in 1776, Spallanzani had shown that putrescible liquids and organic materials in general could be permanently protected from undergoing fermentation and decomposition by being thoroughly boiled and subsequently shielded from all access of air. Indeed, the well-known method of preserving the most varied food-stuffs, first turned to practical account by the ingenuity of the cook and confectioner Appert, and which has assumed such colossal dimensions at the present time, was the outcome of Spallanzani's experiments. The results obtained by Spallanzani were explained by Gay-Lussac as due to the exclusion of atmospheric oxygen from the substances employed. Gay-Lussac was led to this conclusion by an examination of Appert's contrivance for the preservation of animal and vegetable substances, which consisted in hermetically sealing them in vessels and subsequently submitting them to a high temperature in a water bath. He observed that a sample of grape-must which had been preserved by this means unaltered for a whole year entered into fermentation after it had been transferred from one vessel to another, and had thus, Gay-Lussac pointed out, come in contact, although only momentarily, with atmospheric oxygen. Gay-Lussac therefore argued that it was the presence of oxygen which was responsible for and essential to fermentation processes, and this view was the generally accepted one during the next twenty years, until the vital theory of fermentation was again revived by Cagniard-Latour in 1837.

This investigator showed that the yeast cells, already observed and described in the deposit formed during fermentation by the famous Dutch investigator Leeuwenhoeck, as far back as 1675, were independent organisms multiplying by budding. Latour also suggested that the life of these cells was intimately associated with the process of fermentation. Following close upon the publication of Cagniard-Latour's work came the extensive and masterly researches of Schwann. Looking back upon these investigations to-day, it is difficult, so convincing do they appear to us now, to realise how it was that twenty years later Pasteur had to begin as it were *de novo* to rescue the vital theory of fermentation from extinction at the hands of the greatest scientific men of the day, Helmholtz and Liebig.

Schwann showed that Gay-Lussac's theory of the dependence of fermentation processes upon the access of oxygen was untenable, for he proved that putrescible substances could be preserved unchanged even if they were brought in contact with air, as long as the latter had been thoroughly heated first. He also showed that the alcoholic fermentation of sugar and the production of yeast cells did not take place as long as boiled grape-juice was only brought in contact with heated air. These results suggested to Schwann that the presence of organisms might play an important part in these processes; and he therefore proceeded to try and impede the alcoholic fermentation by the addition of various presumably noxious substances, and he found that whilst nux vomica, so poisonous to animals, produced no deleterious effect, the addition of arsenic did interfere with the fermentation process, and he therefore concluded that these organisms were of a vegetable rather than animal character. He moreover confirmed Cagniard-Latour's observation that the deposit produced during fermentation consisted of budding yeast cells. Schwann went still further, and showed that the fermentation commenced with the appearance of these cells in the "must," and that with their multiplication the fermentation progressed, whilst with its cessation the growth of the former stopped also.

In the face of all these facts which he had established, Schwann felt justified in restating emphatically the conviction already expressed by Latour, that there existed an undeniable connection between alcoholic fermentation and the growth of the yeast cells, and he suggested that the latter utilised the sugar as their food material, and the part which they could not assimilate they separated out in the form of alcohol.

Schwann was, however, prevented from fulfilling his promise of furnishing more extensive experimental evidence in support of these preliminary investigations, but shortly afterwards Turpin repeated these researches, and was really the first who definitely formulated the vitalistic theories of fermentative and putrefactive processes.

These conclusions were, however, far from being generally accepted by the scientific authorities of the day, and a few years later (in 1843) Helmholtz, at that time a young medical student, made his first début before the scientific world in a paper which he published on fermentation and decay. Helmholtz repeated Schwann's experiments and confirmed his observations that fermentation and putrefactive processes were suspended, when the substances employed were boiled and allowed only to come in contact with heated air, thus again disproving the oxygen theory of fermentation brought forward by Gay-Lussac. But, said Helmholtz, if the admission of ordinary air to these boiled substances induces fermentation and decay, then either germs must be held responsible or else these changes are due to the action of gaseous materials present in the atmosphere, and which are destroyed by heat. With the object of deciding this point he placed boiled liquids in vessels covered with a bladder, arguing that whereas no impediment was thus offered to the passage of these diffusible gases, an insurmountable barrier was provided against the admission of solid particles like germs.

A vessel containing boiled grape-juice was covered with a bladder and immersed in another vessel containing fermented " must," so that the two liquids were only separated by the bladder. No fermentation was subsequently set up in the boiled must, and this gave support to the opinion that the process of fermentation was dependent upon the presence of germs.

When, however, experiments carried out on the same lines, in which boiled and putrid infusions of meat replaced the boiled and fermented musts respectively, the above results were not confirmed, for the boiled infusion of meat became subsequently putrid. Helmholtz, not able to find any evidence of germ life in these putrid liquids, and not suspecting, as we now know to be the case, that this result could be due to imperfect methods of operation, drew the inference that, although alcoholic fermentation apparently was to a certain extent dependent upon vital processes, the putrefaction of nitrogenous substances, on the contrary, was independent of germ life. Helmholtz therefore came to the conclusion that the presence of germs was only a matter of secondary importance—putrid materials possibly providing them with an attractive food substance—and that such germs when present might perhaps be capable of modifying to some extent the exact course of the putrefaction process. Finally, Helmholtz stated that the position of germs even in alcoholic fermentations was doubtless very similar to that which relegated them in his opinion to a secondary and subordinate place in putrefaction processes.

Thus a cloud was cast over the brilliant and stimulating work of Cagniard-Latour, Schwann, and Turpin, and the obscurity was materially increased by the determined opposition which Liebig maintained towards their vitalistic theory of fermentation. Liebig, blinded by his preconceived opinion, already referred to, refused to recognise that the setting up of fermentative and putrefactive processes, accompanied by the growth and multiplication of the fermenting and putrefying agents respectively, were phenomena having no sort of analogy whatever to anything taking place in reactions of a purely chemical nature. Pasteur, although wholly a chemist, even as Liebig, had from the very first been differently impressed by the essential features of the problem, having at once recognised that there was nothing in the whole range of chemical phenomena which could be compared with the transmissibility or further communication and continuation of the processes of fermentation and decay from one material to another. Much in the same way as he had approached the refutation of Mitscherlich's memorable conclusions as to the constitution of chemical compounds, Pasteur now set to work to solve the problems of fermentation, not permitting himself to be blinded or disheartened by contradictory observations and experimental difficulties, but, with infinite patience and scientific courage, starting afresh, altering the conditions, regarding failure not necessarily as supporting the assumptions of the non-vitalist party, but rather attributing it to faulty manipulation and his own inaptitude in conducting experiments surrounded with such unusual and hidden difficulties.

Pasteur had been indirectly brought in contact with fermentation phenomena in the course of his researches on asymmetry, for amongst the optically active compounds known at the time was the amyl alcohol, which is obtained as a by-product in a number of fermentations, and is a constituent of the well-known "fusel oil," obtained in whisky distilleries. The manner in which the study of this amyl alcohol launched Pasteur into the investigation of fermentation phenomena with a preconceived idea opposed to Liebig's doctrine is clearly set forth in his own writings. Liebig's theory would obviously interpret the optical activity exhibited by amyl alcohol as conditioned by the asymmetry of the sugar from which it is derived in the fermentation process; but Pasteur distinctly states that he considers the molecule of amyl alcohol to be too remotely related to that of sugar to have preserved the dissymmetry of the latter. The dissymmetry of the amyl alcohol must, therefore, be a new creation, so to speak, and such creation of an asymmetric molecule was, in Pasteur's opinion, as we have seen, only possible by the intervention of life. It would follow, then, almost as a necessary corollary, that the fermentation in which the amyl alcohol had been formed must be a vital process, and not the purely chemical transformation which Liebig would have us believe it to be. We have seen what a tremendous power a preconceived idea proved in the hands of Pasteur in the case of his investigations on molecular dissymmetry, and we must now follow the consequences which resulted from such a preconceived idea in the domain of fermentations.

This brings us to the year 1857, a year momentous in the annals of bacteriology, in which Pasteur by dint of new methods brought forward new and convincing proofs in support of the vitalistic theory of fermentation, and communicated to the scientific world his researches on the lactic fermentation, the first of that series of masterly investigations on fermentation which he was to pursue during the next twenty years.

In the lactic fermentation, which is familiar to everybody in the apparently spontaneous souring of milk, Pasteur noticed that a greyish solid material was deposited, and that the quantity of this increased during the process. On examining some of this substance under the microscope he found that it consisted of very minute corpuscles, rod-like in shape and quite distinct from the yeast cells observed in the alcoholic fermentation. Imbued with the idea of the transmissibility of the process of fermentation, Pasteur took a trace of this grey material and introduced it into a solution of sugar, to which he had added a decoction of yeast and some chalk, and soon had the intense satisfaction of witnessing the lactic fermentation in full activity in this artificially prepared liquid. From this fermenting liquid he transferred again a minute trace into another similar solution of sugar, and so on, invariably obtaining the same fermentation, invariably finding also the same corpuscles in the deposit.

Pasteur, however, did not rest until he had furnished even more conclusive proofs that the process of fermentation was directly dependent upon the life of these minute microscopic forms, for he at once realised that Liebig and his supporters might attribute the fermentative change in the sugar to the decomposition of the albuminoids derived from the decoction of yeast employed in his experiments, and he therefore determined to cut off this retreat, which through its inaccessibility had so long sheltered Liebig's theory, and which, devoid as it was of any sound foundation, could not have survived even for a day had it been exposed to the direct fire of experimental criticism.

To this end Pasteur abolished the albuminoids in his fermentations altogether, replacing them by ammonium salts, as a source of nitrogen for the nutrition of the fermenting organism; and in these solutions of pure sugar, with nothing but mineral additions, he demonstrated that ordinary brewer's yeast grew and multiplied, and that its growth was accompanied by the conversion of the sugar into alcohol and carbonic anhydride; whilst similarly those totally distinct living corpuscles, to which he gave the name of *levure lactique*, proliferated in solutions of the same composition, their multiplication being accompanied by the transformation of the sugar into lactic acid.

The conclusions drawn by Pasteur from these laborious researches are summarised in the following words, as sober as they are incisive and uncompromising :—

"As for the interpretation of the group of new facts which I have met with in the course of these researches, I am confident that whoever shall judge them with impartiality, will recognise that the alcoholic fermentation is an act correlated to the life and to the organisation of these corpuscles, and not to their death or their putrefaction, any more than it will appear as a case of contact action in which the transformation of the sugar is accomplished in the presence of the ferment without the latter giving or taking anything from it."

Both the memoir on the lactic and that on the alcoholic fermentation published in 1860 end with the above words, as though Pasteur enjoyed hearing the sound of the hammer on the last nail knocked into the coffin of the dogma which had by so many years delayed the scientific prosecution of the study of fermentations on the lines inaugurated by Cagniard-Latour and Schwann. It was Pasteur's firm conviction that the fermentative process depended on the life of the organism, and his repugnance to the shallow form of words dignified by the name of theory which simply served to cloak the chemical ignorance of the day concerning these mysterious phenomena of fermentation, that stimulated and spurred him on to undertake this extraordinarily comprehensive and laborious series of researches.

The amount of new experimental material collected by Pasteur in connection with this work fills the reader with admiration; whilst his pre-eminent power of seeing what others had failed to observe before him, is again exemplified in his discovery of succinic acid and glycerine as the invariable products of the alcoholic fermentation of sugar.

But these researches, besides being of fundamental importance in throwing light upon one of the oldest but hitherto obscurest departments of scientific investigation, opened up an entirely new field of work; for with the inauguration by Pasteur of artificial culture solutions, that path was first indicated which has gradually expanded into the fascinating science of Bacteriology.

CHAPTER IV.

DISCOVERY OF ANAËROBIC LIFE.

During the progress of these fermentation researches an important event had occurred in Pasteur's life, for October, 1857, witnessed his removal from the provincial Lille to the metropolis of France, in the palmiest days of the Second Empire. His advancement to the post of director of scientific studies at the Ecole Normale in Paris was not, however, an unmixed advantage to Pasteur, for it deprived him of that which he most valued—a scientific laboratory. Nor did there appear to be any prospect of obtaining one, as the French Government of forty years ago appears to have been on much the same level of enlightenment in regard to scientific work as our own rulers of both parties to-day. Berthelot, already distinguished for most important investigations, was yet only a demonstrator at the Collège de France; Claude Bernard, the great physiologist, was compelled to work in a cramped and unhealthy laboratory; and Pasteur was publicly informed by a Government minister that the budget had no means at its disposal to provide him with the sum of 1,500 francs (£60) a year for experimental researches. Pasteur, however, was not to be baffled by such obstacles, and what the nameless and long-since forgotten minister would not concede was procured at Pasteur's private expense, and a laboratory was constructed out of one of the garrets of the Ecole Normale.

Wholly absorbed by his work, and dividing his time between his official duties and his beloved laboratory, Pasteur saw scarcely anyone except Biot, Dumas, De Senarmont, and Balard, with whom he discussed divers scientific questions arising out of the daily progress of his researches.

And now one brilliant discovery succeeded another in rapid succession, but there was one which, in respect of its wide and fundamental significance in relation to the economy of nature, is perhaps without an equal amongst his numerous and great achievements. Moreover the manner in which this discovery was made affords another illustration of his penetrating scrutiny of the smallest detail in the phenomena which passed before him.

It was in studying the butyric fermentation that he took, as was his wont, a drop of the fermenting liquid and examined it in the thin film obtained by mounting on slip and cover-glass under the microscope, but on this occasion he was struck by the fact that along the periphery of the drop, wherever it was in contact with the air, the bacilli appeared motionless and inert, whilst the bacilli in the central portion of the drop were executing those remarkable movements which form one of the most fascinating spectacles which the microscope provides. The question at once arose in Pasteur's mind, were these vibrios in the centre fleeing from the oxygen at the periphery, and had the latter paralysed the activity of those which had been brought in contact with it? There was nothing more easy than to interrogate them on the subject, by passing a stream of air through a flask containing a liquid in butyric fermentation; nor had he long to wait for an answer: the fermentation soon slackened and was ultimately arrested.

Thus was science enriched by the revelation that there exist living forms which grow, multiply, and develop mechanical energy in the absence of that oxygen, which it had hitherto been regarded as one of the most far-reaching discoveries to have shown was indispensable for the whole living creation. Moreover, this remarkable life was actually shown to be either destroyed or paralysed by the very element upon the presence of which all life was supposed to depend.

We have seen already that Pasteur's first discovery of the resolution of racemic acid into the left and right-handed tartaric acids was received with incredulity; and it is not surprising that such a revolutionary discovery as this of *anaërobic life,* as he called it, should have raised a perfect storm of opposition.

But Pasteur's confidence in his own results was not to be shaken by that kind of criticism which is based on reverence for tradition, nomenclature, and classification; and his firm, uncompromising, if not defiant attitude towards his opponents is well illustrated by the following words—"Que le progrès de la science fasse de ce vibrion une plante ou un animal, peu importe: c'est un être vivant, doué de mouvement, que vit sans air et qui est ferment." This anaërobic life of the butyric ferment was not allowed to remain an isolated observation without bearing on other facts; but on the contrary, its relationship to other known facts was at once discerned by Pasteur, who already in the same year, 1861, makes another communication to the Academy of Sciences in which he develops in outline that celebrated theory of fermentation which has served to stimulate so many valuable researches.

The considerations which led to the evolution of this theory in Pasteur's mind are apparent from the following passage, with which he concludes this note:—

"Thus, beside all the beings known to-day, which without exception (as is believed) cannot breathe and nourish themselves except by the assimilation of free oxygen gas, there would be a class of beings possessing such vigorous respiratory power that they are able to live without the influence of the air by taking oxygen from certain compounds, thus occasioning in the latter a slow and progressive decomposition. This second class of organised beings would be constituted by the ferments, similar in every respect to the beings of the first class, living even as they are, assimilating after their fashion carbon, nitrogen, and phosphates, and also standing, like them, in need of oxygen, but differing from them, inasmuch as they can, in the absence of free oxgyen gas, take oxygen from compounds of little stability."

Pasteur, who before had had passages of arms with the great Liebig, was now gradually approaching that combat which is one of the most memorable in the whole annals of scientific history, and upon which the attention of the world, both scientific and unscientific, was to be riveted.

One of the most striking characteristics of Pasteur's genius was the comprehensive view which he took of scientific phenomena, and the clearness with which he mapped out before him the subtle relationship existing between facts of apparently the most varied and disconnected order. Nothing seemed to escape his eager and accurate scrutiny, and whilst apparently engrossed with one problem, his mind was busily engaged in surveying further ground at a distance which would of necessity have to be broken, made to yield up its fruitful secrets, and in its turn become annexed to that new territory of science which his genius had discovered and revealed.

Thus it was that Pasteur from a study of fermentation was led to a consideration of the processes of putrefaction and decay, which he was not slow in announcing as also dependent upon the presence of living organisms.

That putrefactive processes were possibly associated with living organisms was no new suggestion, but had been long ago brought forward by those who discovered so-called *microscopic animalculæ* in decomposing materials; but the time was then not ripe for the production of a positive proof, and although the hypothesis remained, it was left for Pasteur to rigidly demonstrate its complete justification. It is difficult for us at the present time to realise the necessity for such a proof, and it is particularly interesting now to read the contemptuous words with which Liebig discussed and thought to dismiss the vitalistic theory of putrefaction. "Those who attempt to explain the putrefaction of animal substances by the presence of animalcules," wrote Liebig, "argue much in the same way as a child who imagines he can explain the rapidity of the Rhine's flow by attributing it to the violent agitation caused by the numerous water-wheels of Mainz, in the neighbourhood of Bingen. Can we legitimately regard plants and animals as the means whereby other organisms are destroyed, when their own constituent elements are condemned to undergo the same series of putrefaction phenomena as the creatures which preceded them? If the fungus is the agent of the oak's destruction, if the microscopic animalcule is the agent in the putrefaction of the elephant's carcase, I ask in my turn, what is the agent which works the putrefaction of the fungus and the microscopic animalcule when life has been removed from these two organised bodies?"

Liebig's insistence upon an explanation of these processes on a physiologico-chemical basis was justified, for the part played by micro-organisms in fermentative and putrefactive phenomena Pasteur himself regarded as but the first phase in that cycle of changes which ultimately restores all substances to their original source, the atmosphere and soil.

Pasteur now proceeded to show that the final destruction of animal and vegetable matters took place in consequence of a process of slow combustion, by the fixation of atmospheric oxygen.

The complex materials produced in the preliminary processes of fermentation and decay Pasteur attributed to the agency in great part of anaërobic microscopic forms performing their work of decomposition in the absence of oxygen, these complex materials being again, in their turn, attacked by aërobic miscroscopic forms, dependent upon the presence of oxygen, and Pasteur, by most ingenious experiments, actually showed how these minute living forms did indeed possess the property of fixing atmospheric oxygen.

He took two sets of flasks; in one series he placed an aqueous decoction of yeast, together with solutions of sugar, milk, etc., which had been previously heated, and to these flasks only air was admitted, which he designated as *pure*—*i.e.* from which all dust particles had been removed. The second series of flasks also contained an aqueous emulsion of yeast, but no precautions were taken either to heat the solutions or to purify the air which was admitted. Both sets of flasks were then kept at a temperature of from 25 to 35 deg. Centigrade, and after the lapse of some time the air of all was carefully analysed.

In the flasks containing heated liquid, and to which only pure air had been admitted, the air present still contained large quantities of oxygen, but in the other flasks, where the access of microscopic organisms was not in any way impeded, there was absolutely no oxygen present, its place having been taken by carbonic acid gas. This absorption and fixation of atmospheric oxygen had taken place in the course of a few days, whilst in the flasks in which microscopic life was absent a quantity of free oxygen was found even after several years.

Thus Pasteur was able to again demonstrate the stupendous importance of micro-organisms in the economy of nature; for only with their assistance is the organic *débris* in the world broken up and presented to us again in a serviceable form, instead of encumbering the whole surface of the globe and so rendering it uninhabitable, as would inevitably be the case but for the agency of these minute forms of living matter.

Pasteur, in his investigations of fermentative phenomena, had thus, by the year 1861, shown, firstly, the worthlessness of the form of words by means of which Liebig and the chemists of the time sought to banish all biological considerations from the study of these questions; secondly, he had worked out a method of scientifically attacking these problems, in which for the first time both the chemical and biological aspects of the subject received their due share of attention.

It is here that we are again brought in contact with those peculiar endowments which are the key to Pasteur's success throughout his career. Just as his brilliant achievements in the domain of molecular asymmetry were due to the facility which he displayed in bridging the gulf between pure physics and chemistry, and co-ordinating the facts belonging to each, so here again we find him closing the breach between chemistry and biology, and moving with equal facility along the main lines of each of these sciences; and it is to this altogether exceptional versatility that we owe his successful exploration of borderlands which can only be traversed by those capable of adapting themselves to the special means of locomotion necessary in two countries differing widely in their character and configuration.

Thirdly and finally, by the systematic use of this new method of investigating fermentation phenomena he had discovered the possibility of life without air, and had collected sufficient experimental data to venture upon a new theory of fermentation. The additional researches which this new theory stimulated were deferred for some years in consequence of his attention being directed to certain phenomena closely related to fermentation, and demanding a full and final explanation before further progress could be made in, to use his own words, "ces travaux dont la difficulté ne me laisse ni trêve ni repos."

CHAPTER V.

SPONTANEOUS GENERATION CONTROVERSY.

ALTHOUGH Pasteur's victories in the field of fermentation had been won in the teeth of the opposition of the entire scientific world, he was on the eve of an even fiercer battle, in which he was to measure his strength almost single-handed against some of the subtlest intellects of the day.

The inquiry to which Pasteur in the next instance devoted his commanding energies might appear to us at the present time almost a work of supererogation, for during more than twenty years past we have heard nothing of that great question which has exercised the mind of man from the earliest ages: Does life originate spontaneously? The history of this subject is, however, of great interest in many ways—chiefly, perhaps, on account of the proof which it furnishes of the danger of accepting evidence on authority.

Some of the greatest thinkers and observers of past ages have had very definite views on this subject of the generation of life. Aristotle categorically affirms that "every dry body becoming moist, and every moist body becoming dry, engenders animals." Virgil is more specific still in asserting that bees originate within the putrefying carcase of a young bull:—

"Aspiciunt liquefacta boum per viscera toto
Stridere apes utero, et ruptis effervere costis."

Van Helmont actually supplies the prescription for producing by spontaneous generation the domestic mouse. His formula consists in squeezing some soiled linen into the mouth of a vessel containing some grains of wheat, which arrangement gives rise to the transmutation of the wheat into mice in the course of about twenty-one days. The mice so generated are said to make their appearance in the adult state, both sexes being duly represented.

In the present century the advocates of spontaneous generation had abandoned their ground as regards such tangible forms of life as bees, frogs, and mice, and had restricted their views to those minutest of organisms which the microscope had rendered visible.

The interrogation of nature by direct experiment in regard to this problem does not commence until the middle of the last century, when, in 1748, Father Needham, an Irish priest, declares in favour of spontaneous generation, convinced by the result of experiments which he had made on quite modern lines, viz., of placing putrescible substances in vessels which he subsequently hermetically sealed and submitted to heat. He assumed that the heat would destroy all life in these materials, and when he afterwards found that an abundance of microscopic living forms made their appearance in these vessels, he concluded that they had arisen by spontaneous generation.

That this investigation carried conviction at the time is shown by the fact that within two years of its publication he was elected a Fellow of the Royal

Society of London, and a little later he had the honour of becoming one of the eight Associates of the French Academy of Sciences.

It was not until 1765 that these results were challenged by the Abbé Spallanzani in a dissertation which led to a lively dispute between these two divines.

Spallanzani repeated Needham's experiments, but he heated the hermetically sealed vessels more thoroughly and for a longer period of time, with the result that no signs of life subsequently made their appearance. Father Needham, however, raised the objection that this additional "torture"—to use his own expression—had enfeebled or perhaps totally destroyed the "vegetative force" of the substances and "entirely corrupted" the air present in the vessels. This objection was subsequently strengthened by the discovery made by Gay Lussac that the air present in the hermetically sealed vessels containing various vegetable and animal substances preserved by Appert's process was entirely destitute of oxygen.

Schwann, however, dispelled this objection in 1837, by introducing an important modification into the method of experiment. He sterilised the putrescible substance in the vessel by heat, and then allowed air to enter; but this air, before being admitted, was passed through a tube heated nearly to the boiling-point of mercury in a bath of fusible metal. Under these conditions, in nearly all cases the putrescible or fermentable substances remained intact; but the exceptional experiments in which a contrary result was obtained, shook even the faith of their author in the trustworthiness of the investigation.

Similarly indecisive results were obtained by Ure, Helmholtz, Schultze, who passed the air through chemicals (caustic potash and sulphuric acid), and by Schroeder and Dusch, who in 1854–59 again altered the *modus operandi* by filtering the air through cotton-wool.

This unsatisfactory state of affairs was brought to a crisis in the year 1859, when Pouchet, Director of the Natural History Museum in Rouen, appeared with a paper before the Academy of Sciences, in which he threw down the gauntlet to the vitalists declaring, "Les adversaires de la génération spontanée prétendent que les germes des êtres microscopiques existent dans l'air, que l'air les charrie, les transporte à distance. Eh bien ! que diront ces adversaires si je parviens à déterminer la génération de quelques êtres organisés en substituant un air artificiel à celui de l'atmosphère ?"

Pouchet's method of experiment consisted in taking a flask of boiling water, which he hermetically sealed and then plunged upside-down into a basin of mercury. When the water had become quite cold, he opened the flask under mercury and introduced half a litre of pure oxygen, and also a small quantity of hay previously exposed for a long time to a very high temperature. Thus Pouchet conceived that he had satisfactorily removed every loophole for the admission of living organisms into his flask, and it was with triumph that he appeared a few days later before the Academy with his flask, the contents of which exhibited growths.

"Whence had they come, and how could their presence be accounted for except on the theory of spontaneous generation?" confidently demanded Pouchet.

In the hopes of putting an end to a controversy which appeared only to increase in difficulty and complexity as time went on, the Academy in 1860 gave as a subject for a prize-competition: "Essayer, par des expériences bien faites, de jeter un jour nouveau sur la question des générations spontanées."

It is at this moment that Pasteur enters the lists, and the circumstance that we have for more than twenty years heard nothing of the doctrine of spontaneous generation, is due to the effectual manner in which he successively hurled into the dust the several champions who appeared on its behalf in the intellectual tournament which followed.

The intimate contact in which Pasteur had lived with these microscopic forms during his researches on fermentation, naturally led him to take a deep interest in this controversy, although many of his scientific friends—amongst whom were Biot and Dumas—strongly dissuaded him from taking an active part in the discussion, fearing that nothing but loss of valuable time would come of joining in this controversy.

But Pasteur was renowned for the audacity, if we may use the word, with which he singled out subjects for research. "He makes me uneasy," remarked one of the comrades of his youth, who had early divined the extraordinary gifts of this eager and silent worker. "He does not recognise the limits of science, he only loves quite insoluble problems;" and true enough, he was not to be deterred from attacking this, to his colleagues, hopeless and inscrutable question, and he commenced by quickly dispelling the momentary triumph achieved by Pouchet. By means of most skilfully planned experiments he showed that the surrounding air is full of dust particles, and that to these dust particles living organisms are attached. He repeated the experiments of Schroeder and Dusch, but instead of using ordinary cotton-wool he employed gun-cotton as the filtering material for the air, and by subsequently dissolving this in a mixture of alcohol and ether he showed that it had arrested a multitude of living organisms. He pointed out that Pouchet had neglected an important precaution for insuring the absence of all life in his flask and hay infusion; that this source of error lay in the use of mercury, from the surface of which the living organisms had found their way into the flask.

Pouchet and his supporters, however, once more took shelter behind the favourite hypothesis, supported so eloquently by Gay Lussac, that decomposition was dependent upon the presence of oxygen, and the opinion soon became current in the scientific world that the smallest bubble of oxygen or air was sufficient to produce putrefaction. If, urged Pouchet, decomposition is due to the germs present in a minute bubble of air, then the latter must of necessity be so heavily laden with living forms that we should be surrounded by a thick fog, "dense comme du fer."

Pasteur, however, demonstrated as had Schwann before him, the erroneous nature of Gay Lussac's oxygen theory of decomposition, but in this new argument he perceived another important source of error which it behoved him to at once correct.

He recognised that the assumption as to a very minute quantity of air being in *every* case capable of provoking germ life was incorrect, and he proceeded, by means of a series of experiments as simple as they were conclusive, to show how the air may vary in its richness as regards germ life.

A small quantity of clear broth was introduced into a number of little flasks, the necks of which were then drawn out to a fine aperture. The contents were then heated to boiling for some time, and by so doing, not only was the air driven out of the flask, but the contents were rendered sterile ; after this the aperture was closed by heating it in a flame.

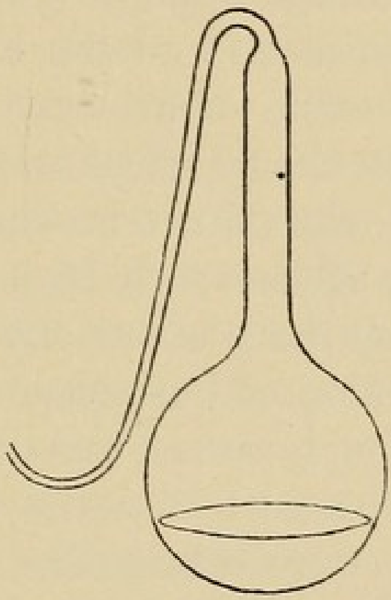
Armed with his little battery of such flasks, Pasteur started for Arbois. Here, in the open country, away from all houses, he opened twenty; on the lower heights of the Jura mountains twenty more were opened ; and again the same number at the Montanvert close to the Mer de Glace, at a height of upwards of 6,000 feet. On re-sealing all the flasks, he straightway returned to Paris and deposited them in the bureau of the Academy of Sciences in November, 1860.

The results, which were awaited with the utmost interest, were as follows : of the twenty flasks opened near Arbois eight developed living organisms ; of the twenty opened on the Jura five became affected ; of the twenty flasks, however, opened on the Montanvert only one exhibited germ life.

Thus Pasteur once more disposed of the oxygen theory of putrefaction by pointing to the flasks in which, despite the access of oxygen, no germs made their appearance ; but he did more, he demonstrated the fallacy of Pouchet's argument that if germs were present in the air they must be present in such numbers as to render it opaque, and at the same time he gave the first indication of the uneven manner in which micro-organisms are distributed in the atmosphere.

Pasteur, however, was not yet satisfied that he had exhausted every argument which might be raised against the correctness of his conclusions, and this time he anticipated attack, suggesting that during the boiling of the liquids he employed, the latter might have become so changed in chemical composition as to render them incapable of exhibiting the supposed phenomenon of spontaneous generation; an objection already, it will be remembered, raised by Father Needham to the acceptance of Spallanzani's experiments. To silence this objection, Pasteur devised an experiment as remarkable for its extreme simplicity as for its convincing force; he placed his organic infusions in flasks, the necks of which were each subsequently drawn out into a long tube curved downwards and then upwards as in the following figure. The extremity was left open, so that on sterilising the contents by boiling and then allowing it to cool, the air would obviously enter by this open tube. The putrescible infusion, however, remained unaltered, and Pasteur proved that the reason for this was not that the liquid was incapable of developing germs, but that the germs suspended in the incoming air had been all deposited in the bend of the tube. On inclining the flask, so as to allow a few drops of the liquid to run into the bend, the latter soon developed growths. Thus once more the oxygen theory of putrefaction was effectually set aside, and Needham's contention as to the devitalisation of the liquid during heating likewise dismissed once and for all.

But yet another difficulty confronted Pasteur, and one which had so often perplexed and blinded his predecessors, and this was the fact that milk developed microscopic growths, even after being subjected to boiling for some minutes. Instead, however, of recognising in this any support to the theory of



PASTEUR'S FLASK.

spontaneous generation, he inferred that the milk doubtless contained originally some peculiarly refractory organisms, and by raising the temperature of sterilisation to 110° C. he found, in point of fact, that no growths did subsequently make their appearance.

During the progress of these investigations, Pasteur was continuously harassed by the publications of his opponents, who claimed to have obtained results entirely at variance with his own. This opposition was long endured, but his patience ultimately gave way when some of his experiments were directly challenged by Pouchet, Joly, and Musset, who asserted that in repeating them they had obtained diametrically opposite results.

To put an end to this unbearable criticism, Pasteur conceived the idea of settling the dispute by a method which has recently played such an important part in the arrangement of a great political difference between this country and America. Pasteur determined to have recourse to arbitration. He appealed to the Academy of Sciences to appoint a special commission to judge between himself and his opponents. Whatever may be the value of arbitration as a means of settling disputes in the political and industrial worlds, there can be no doubt that it is wholly unsuited as a means of arriving at the truth in a scientific conflict, for in such matters there is but one court of appeal—Time and the opinion of Posterity.

The commission, however, was duly appointed, and the method of procedure and the result were as remarkable as they were instructive. It was arranged that both parties should appear at the bar of the Academy and there perform their rival experiments.* On the day appointed Pasteur, and his assistants, arrived laden with apparatus which they were ready at once to put into operation. Pouchet and his adherents were there also, but they had come empty-handed. They asked for time, and urged that the weather was unpropitious to the success of their

* Some of the flasks containing putrescible infusions prepared by Pasteur himself for this occasion are still preserved with reverential care at the Institut Pasteur. On the labels, now yellow with age, may still be read the signature of M. Balard, the secretary of the Commission. Even after the lapse of all these years the liquids in these flasks are as clear as they were on the day of preparation.

experiments, which had been made at a different season of the year!

The Commission, however, would not accede to the remand. Pasteur successfully performed his experiments, and a strong judgment was given in his favour, pronounced by M. Flourens, Secretary of the Academy of Sciences, with all the solemnity and finality of a judge delivering a sentence.

"As long as my opinion was not formed I had nothing to say; to-day it is formed and I speak it. The results are conclusive. To have animalcules, what, then, is essential if spontaneous generation is true? Air and putrescible liquids. Now, M. Pasteur puts air in contact with putrescible liquids and nothing happens. There is, therefore, no spontaneous generation. To still doubt is not to understand the question."

But before the superior court of Time even the most distinguished Academicians must bend, and we now know that Pasteur and his opponents were in reality both right as regards what they had actually observed in their respective experiments.

The facts are these: Pasteur had used infusion of yeast as the putrescible material in his experiments, Pouchet had used infusion of hay in his; the infusion of yeast is easy, the infusion of hay excessively difficult to sterilise by heat. The heat applied by Pasteur was sufficient to sterilise the yeast infusion, it was insufficient to sterilise the hay; and consequently the heat applied by Pouchet, which was the same as that used by Pasteur, failed to remove the life originally present in the hay infusion, and quite irrespectively of the access of any fresh germs from the air afterwards admitted, Pouchet's flasks would have subsequently exhibited life, the latent condition of the germs still present in the hay infusion being changed into activity as soon as they obtained a supply of oxygen from the air. Neither Pasteur nor his opponents were, however, aware at that time of this fact.

Through the want of confidence in themselves exhibited by Pouchet and his associates in this extraordinary trial, and by the academic tribunal giving judgment in default, the knowledge of the whole truth was delayed several years, for doubtless the authoritative pronouncement of the Academy succeeded in protecting Pasteur from his French antagonists, throttling renewed research in the country in which their judgment was accepted as final. Fortunately, however, for science, it could not blockade research throughout the world; it could not protect him from attack by scientific foes owning no allegiance to the august body whose aid had been so successfully invoked.

The prize before referred to, offered by the Academy, was unanimously awarded to Pasteur, and in 1862, at the early age of forty, he was elected a member of the Academy of Sciences.

In 1876 the contest was reopened, and this time by one of our own countrymen, Dr. Bastian, and it was in repeating the experiments and fighting the conclusions of this new antagonist that the truth with regard to spontaneous generation was finally established on an indestructible basis by Pasteur.

Pasteur and his assistants set to work with renewed zeal, and discovered that the difficulties presented by Bastian depended upon the fact that micro-organisms exist which are more difficult to destroy by heat than Pasteur himself had before suspected, and that they may remain dormant and to all appearance absent in infusions until they obtain the opportunity to assert themselves or multiply. "C'est le concours des germes et de l'oxygène," declared Pasteur when Bastian maintained that the development of life in these heated infusions was due to spontaneous generation.

The experiments which Pasteur conducted to prove his case had a convincing finality which admitted of no further dispute, and his conclusions have been accepted by a whole generation of scientific men who have unhesitatingly endorsed the statement made by him in the following words: "No; there is to-day no known circumstance which permits us to affirm that microscopic beings have come into the world without germs, without parents like unto themselves. Those who held that they do have been the plaything of illusions, of experiments badly made, tainted with errors, which they have not known how to perceive, or which they have not known how to avoid." "La génération spontanée est une chimère."

In looking back upon this period of Pasteur's career, one is disposed to regret that his great powers should have been so long absorbed in this work of exterminating a mere superstition; but as a matter of fact, much good came of this crusade in a number of ways. Incidentally, experiments, which have now become classical, were made on the distribution of micro-organisms in our surroundings, such as air and water, whilst healthy urine and the blood of normal animals were in 1862 and 1863 shown to be free from microbes and capable of being preserved without alteration for an indefinite period of time, provided that they were collected under suitable precautions. Van der Broeck had, indeed, already in 1857 and 1858 proved that grape-juice, white and yolk of egg, gall, urine, and arterial blood, if suitably collected, could be preserved without change in their natural condition; whilst, subsequently, sterile milk in its natural state was obtained direct from the udder by Roberts, Lister, Cheyne, Meissner, and others.

The spontaneous generation controversy was moreover, highly fertile in developing the general methods of bacteriological research, and many of the most familiar operations employed in the study of micro-organisms date from this period.

CHAPTER VI.

STUDIES ON THE VINEGAR ORGANISM.

PASTEUR had thus fully justified himself before Biot and Dumas, and those other scientific friends who had taken so unfavourable a view of this excursion from fermentation studies into a region of investigation, from which alone De Senarmont had ventured to prophesy he might not emerge empty-handed. "Laissez faire Pasteur," he said to Biot, "s'il ne trouve rien dans la voie où il s'engage, soyez tranquille, il n'y restera plus. Mais je serais surpris qu'il ne trouvât rien."

The fame of and interest in Pasteur's researches had now passed beyond the pale of the scientific world, and had attracted the attention of practical men, and the year 1862 finds him once more immersed in fermentation studies, to which he had returned, armed with all the weapons and experience of which he had become possessed in his recent exploits in the spontaneous generation controversy.

About this time we hear of him delivering an address to the vinegar manufacturers of Orléans, an address which has since become memorable by reason of the important revelations which it brought before the industrial world concerning the production of vinegar.

The city of Orléans has long been famous for its vinegar factories, and the method in vogue when Pasteur commenced his studies on this subject consisted in nearly filling vats with a mixture of vinegar and the wine to be acetified. In those vats in which the process is taking place satisfactorily the surface of the liquid becomes covered with a fragile pellicle, which the manufacturer watches over with the greatest care lest it should become submerged or disturbed in any way. Long and bitter experience has taught him the importance of this pellicle, and that, provided it remains intact on the surface of the liquid, all will go well; but that if by any chance this thin veil should get broken up, the process will be interrupted, and that nothing then remains but to endeavour to produce a new one—a matter often of great difficulty, and involving not only loss of time but of money also.

What, then, is the nature of this pellicle, at once so precious and so fragile? Pasteur had asked himself this question long ago, and had thought over it frequently, and it was natural, therefore, that on resuming his fermentation studies he should begin by endeavouring to elucidate this mystery in vinegar manufacture.

In accordance with his anticipations, he discovered that the importance of this pellicle consists in its being produced by, and, in fact, consisting of, certain micro-organisms whose function it is to convey the oxygen of the air to the liquor in the vats, yielding by this oxidation the highly-prized vinegar. The conversion of wine into vinegar he thus showed to be the work of a minute rod-like organism which he called *mycoderma aceti*, and which in its relationship to oxygen was the precise antipodes of the butyric ferment which he had previously discovered (*see* p. 46).

It is to the discovery of the butyric and acetic ferments respectively that we owe the introduction of the terms *anaërobic* and *aërobic*, devised by Pasteur and his colleague, the professor of Greek at the Ecole Normale, to designate the respective idiosyncrasies of these two microbes towards air—terms which have since become household words amongst bacteriologists. So carefully did Pasteur study the habits and mode of life of this the latest addition to his microbial museum, that he was able to indicate to these experienced employers of labour at Orléans the manner in which it ought to be housed, fed, and treated, in order to induce it to accomplish the maximum amount of work in the shortest period of time and for the lowest possible wage. He pointed out that, instead of waiting the customary two or three months for the completion of the process, the vinegar could be elaborated in from eight to ten days by simply exposing the vats containing the mixture of wine and vinegar to a temperature of from 20 to 25 degs. Centigrade, and sowing on the surface a small quantity of this organism.

In order to impress upon his scientific colleagues at the Academy of Sciences some idea of the fabulous rapidity with which this minute microbe could multiply, Pasteur declared when reading his memoir that he "would undertake to cover a surface of vinous liquid equal in extent to the area of the hall in which we are assembled with *mycoderma aceti* in the space of twenty-four hours. I have only to sow in various places the day before little spots hardly visible of the *mycoderma aceti.*"

This *mycoderma aceti* is, however, a peculiarly difficult employé to deal with, for if supplied with an insufficient allowance of alcohol he revenges himself by consuming the acetic acid which he has been engaged to produce, a mode of retaliation which possibly would commend itself to more exalted beings placed under similar circumstances!

As in the case of the alcoholic fermentation, so in that of the vinegar or acetic fermentation, Pasteur was neither the first to discover the process, nor the first to see the living ferment, nor yet even the first to connect the process with the life of the micro-organism. The chemical change involved and the part played by oxygen in the souring of wine were already indicated by Lavoisier; the process was ascribed to catalysis, or contact action, by Berzelius in 1829. The familiar skin which forms on the surface of the acetifying liquid was already named *mycoderma* by Persoon in 1822, and the bacterial cells of which this pellicle is composed were seen and actually described under the name of *ulvina aceti* by Kützing in 1837, who even suspected a connection between the life of the organisms and the vinegar process. It will be asked then, Where does Pasteur's discovery of the acetic fermentation come in, when this discovery was already a *fait accompli* at the time when Pasteur was catching fish and drawing caricatures as a schoolboy at Arbois?

It is, however, one thing to dream of empire and another thing to actually found one; so it is one thing to make a discovery, and often a very different thing to make the world accept it.

It is here that Pasteur stands out in such bold relief from so many other distinguished *savants* of the century. Just as in connection with the alcoholic fermentation the pioneering work of Cagniard Latour and Schwann was of such a character that it was practically effaced at one fell swoop by the edict of Liebig, so here again the structure raised by Kützing was within two years demolished by the same autocratic mandate.

But whilst the houses built by Cagniard Latour, by Schwann, and by Kützing were only founded on sand, and therefore destined to fall almost with the first winter's blast, Pasteur was an architect who built only on the solid rock of experiment, and the many mansions which he has raised on the sites where lie the shattered and almost forgotten ruins of his predecessors have invariably withstood the whips and scorns of time, becoming only more mellow with advancing age.

It is in this connection that we realise that Pasteur was not only a *savant* content to seek the truth and find it, but that when he had in any matter succeeded in the difficult task of convincing himself, he was impelled with almost a fanatic's zeal to force his conviction on the world, nor did he put up his sword until every redoubt of unbelief had been taken, every opponent converted or slain. Of this uncompromising spirit in his championship of what he believed to be the truth he was himself conscious, as is seen from the following passage, which occurs in the short reply which he made at that supreme hour of his life when, on attaining the age of seventy, he enjoyed a triumph such as had probably never been accorded before to a man of science.

"Si parfois j'ai troublé le calme de nos académies par des discussions un peu vives, c'est que je défendais passionnément la verité."

In perusing the terse summaries in which Pasteur's labours on the acetic fermentation are recorded in the *Comptes rendus,* the reader cannot fail to be struck with the breadth and scope of the view which he takes of the phenomena before him, and the manner in which he shows, by a pregnant word here and there, the alertness of his mind to developments which even now are only partially realised. Thus he points out that these organisms are not only endowed with the power of producing acetic acid from alcohol, but that they can impose the oxidising action of the air on a multitude of organic substances, the sugars, the organic acids, divers alcohols and albuminoids, giving rise in some cases to intermediate products of which he had already detected some. Here, then, we have indicated those beautiful transformations, carried into execution many years later by Mr. Adrian Brown, in which, by the agency of the acetic bacteria, normal propylic alcohol was made to yield propionic acid, *d*-glucose to give *d*-gluconic acid, mannitol to produce lævulose, and glycol, glycollic acid; whilst methylic, isobutylic, and amylic alcohols, as well as cane sugar, milk sugar, starch, and dulcite, remained unaffected. He further points out the oxidising action possessed in varying degrees by the family of moulds, and thus shows the path subsequently travelled along by Le Bel and many others in what may be called the *mould-combustion* of racemoids, as well as by Wehmer in the mould production of oxalic and citric acids from carbohydrates. The same few pages indicate the necessity of reopening the investigation of the process of nitrification, and thus suggest the subsequent successful researches of others in this field.

It was thus that by a long line of monumental researches Pasteur had established the vitalistic theory of fermentation, which may be expressed in the words, *No fermentation without organisms; in every fermentation a particular organism.*

It was hardly, however, to be expected that Pasteur's opponents would allow this theory to triumph without striking a last blow in defence of the chemical or molecular vibration theory, which had enjoyed such a long supremacy over the vitalistic theories of thirty years before.

Accordingly, in 1869 we find Liebig making a lengthy communication to the Munich Academy on fermentation and the source of muscular power.

These papers are of psychological rather than scientific interest, the reader having little difficulty in discerning that the great chemist, in the winter of his brilliant career, is trying to retreat in good order before the irresistible advance of the younger man with his improved weapons of precision, and to cloak his defeat by endeavouring to show that there is but little real difference between the two interpretations put upon fermentation phenomena.

But towards the close there is a sudden change of tone, for the author, doubtless so well satisfied with his execution of the retrograde movement, has deceived himself as to the real nature of his position, and when he should have been content to decently bury an obsolete cause he becomes once more aggressive and contemptuous. He denies the activity of the *mycoderma aceti* on the beechwood shavings used in the German vinegar process, and calls to his assistance in this weighty charge the *ipse dixit* of a worthy Munich vinegar manufacturer of the name of Riemerschmied.

He challenges the accuracy of Pasteur's observation, that yeast can find its nitrogenous nutriment in ammonia, and suggests that his results are due to analytical inaccuracy. In support of his disbelief in the assimilability of ammoniacal nitrogen he invokes the assistance of that weak but blustering ally, vegetable physiology, which at that time denied to all but green plants the power of building up albuminoids from ammonia.

But the scientific world had yet to learn how often vegetable physiology would have to change its foliage at the bidding of Pasteur and his successors. What would Liebig have said had he been told that the study of these micro-organisms, for which he cannot conceal that contempt which has been shared by so many chemists even up to within the last few years, would, within the century, reveal the fact that carbonic acid can serve as a source of carbon to plants without chlorophyll, and that albuminoids can be synthesised from the free nitrogen of the air?

Liebig's memoirs were exhumed from the obscurity of the journals in which they had appeared, and were in 1871 translated and published in the *Annales de Chimie et de Physique.* Pasteur was thus obliged to take notice of them, and replied in the *Comptes-rendus* of the French Academy.

To us this reply appears a masterpiece of selfrestraint, written as it was after the great *débâcle* of 1870, the effect of which on Pasteur, who was perhaps a yet greater patriot than *savant*, cannot be realised by Englishmen, who for generations have not seen an enemy on their own soil.

Terse and to the point, the few pages of Pasteur's reply form a most welcome contrast to the verbose and unwieldy document of the Teutonic veteran. Wasting no time on the sterile disquisition, of which Liebig's paper is mainly composed, he hastens to fall like a sledge hammer on the two direct negatives with which he had been challenged—viz. (1) the assimilability of ammoniacal nitrogen by yeast, and (2) the participation of the *mycoderma aceti* in the German vinegar process. After reasserting the correctness of his previous statements, he exclaims—

"Mais comment éclairer le public ? Comment sortir de l'embarras que soulèvent ces affirmations contradictoires également honorables ?"

Then he has recourse to those tactics which he found so effective in the case of his dispute with Pouchet. He called upon Liebig to submit their difference to the arbitration of the Academy, he (Pasteur) undertaking to prepare several kilograms of yeast from purely mineral materials, and also to satisfy by ocular demonstration both Liebig and the Academic Committee that the beechwood shavings in Herr Riemerschmied's vinegar factory were covered with growths of the *mycoderma aceti* which Liebig had been unable to discover.

Liebig, however, did not accept the challenge or renew the attack, and his submission had a touch of melancholy about it which is apparent from the following letter, addressed during the ensuing year (1872) to Duclaux, at that time an assistant of Pasteur's:—

"I have often thought during my long and practical career at my age (69 years) how much labour and how many researches are necessary to understand a somewhat complicated phenomenon. The greatest difficulty arises from the fact that we are too much in the habit of attributing to one cause that which is produced by several, and the majority of our controversies thus arise. I should be very sorry if M. Pasteur should take in bad part the remarks in my last work on fermentation. He appears to have forgotten that I only sought to sustain by facts a theory which I originated now more than thirty years ago, and which he attacked. I had, I believe, the right to defend it. There are very few men whom I esteem more than M. Pasteur, and he can rest assured that I did not dream of injuring his reputation, which is so great and so justly acquired. I assigned a chemical cause to a chemical phenomenon, and that is all that I attempted to do." (Pasteur: "Histoire d'un Esprit," E. Duclaux, Paris, 1896.)

CHAPTER VII.

THE DISEASES OF WINE.

THE researches on the acetic fermentation which we have just been considering open again a new chapter in Pasteur's career, for whilst in his previous investigations he had restricted himself to the purely scientific aspects of the problems upon which he was engaged, from henceforward we find the practical application of scientific principles occupying a large part of his attention.

The success which attended his efforts in thus applying his discoveries, doubtless soon led to the growth of a conviction within him that he was entrusted with a great mission, which embraced not only the revelation of abstract truth, but also the promotion of the material welfare both of his own beloved country and of humanity at large.

Thus his excursion into practical matters in connection with the manufacture of vinegar was at once followed by his giving similar attention to questions relating to the production of wine. In placing the vinegar process on a sound scientific basis, Pasteur had obviously in reality broached the subject of the "maladies des vins," for that the souring of wine is one of the most widespread ills to which it is subject is surely well known to all. What more natural, therefore, than that Pasteur should conceive that those other and more mysterious deteriorations which wines so frequently undergo might receive a rational explanation by the application of those same methods which had so effectually elucidated the vinegar process?

He was not long in putting his ideas to the test of scientific experience, and we find him installed at Arbois in a hastily improvised laboratory, submitting to a minute microscopic examination wines of all kinds, which had been gladly placed at his disposal by many of the old comrades of his youth.

From the outset success followed his efforts, and whenever a sample was presented to him defective in some respect or other in taste, he discovered, mingled with the yeast cells, a distinct microscopic form. So skilful did he become in the detection of these various germs, that he soon was able to predict the particular flavour of a wine from an examination of the sediment. In healthy wines, these foreign forms were absent and yeast cells alone were discovered.

Although a number of different bacteria connected with these several maladies of wine were described and figured by Pasteur, it must not be supposed that the mechanism of these processes was investigated with anything like the completeness which characterised his researches on the acetification process. The chemical changes taking place in the production of wine are of a much more complex nature than in the case of vinegar manufacture, and a large amount of work is being done and still remains to be accomplished in connection with these more obscure difficulties which attend the preparation of sound wine. To Pasteur, however, is due the broad explanation of these phenomena as dependent on foreign organisms, and the further elaboration of the subject is chiefly a matter of laborious detail.

Pasteur, however, did not rest content with having established the source of the disturbances which so long had troubled the wine industry; he at once proceeded to direct his attention to the possibility of effectually guarding against them. The commercial importance of this undertaking to the country may be conceived when we remember that at this time, 1867, a rough estimate of the capital absorbed by the French wine industry is given as 500 millions of francs.

Pasteur's first experiments were made to discover, if possible, a substance which, whilst inimical to bacterial life, would not, when added to the wine, impair its flavour and bouquet. Various antiseptics were tried, but the results were not encouraging, and Pasteur determined then to have recourse to heat. He had, however, scruples in applying such severe treatment to so delicate an article as wine, a prejudice which was shared later by manufacturers even after Pasteur had demonstrated beyond all question its beneficial effect upon wine.

He had, however, previously very carefully studied the relationship of wine to oxygen, and he did not anticipate that any evil would result, provided that the wines were only heated after they had finished absorbing oxygen.

Moreover, he foresaw that a comparatively low temperature—far below the boiling point—would suffice, as from his experiments on spontaneous generation he was well aware that the acid reaction of the wine would facilitate the sterilisation, whilst he had further reason to believe that it would not be necessary to actually destroy all micro-organisms, and that it would be quite sufficient only to so paralyse their activity as to prevent their inducing prejudicial changes in the wine.

This simple process of partial sterilisation is now generally known by his name as "*Pasteurisation*," and has already proved of enormous value to man, having been employed with the greatest success in connection with wine, beer, milk, cream, and other food materials of a perishable nature, whilst in the future there can be no doubt that it is destined to become of ever increasing importance, and to largely take the place of those chemical preservatives or antiseptics which at present are employed in such an excessive and altogether reckless fashion.

Thus, Pasteur found that by heating wine for a short time to a temperature of from 55 to 60 degs. Centigrade it was effectually protected from subsequent deterioration, whilst it suffered no alteration in taste or bouquet. As mentioned above, however, wine growers were far from feeling convinced that by venturing upon the adoption of this method they would not be damaging their stock to a much greater extent than by leaving them to the operation of natural causes. But another circumstance contributed not a little to the tardy acceptance of Pasteur's discovery, and this was the appearance about this time of that scourge of vineyards, the phylloxera, which led to the attention of the whole wine world becoming centred upon this disease, which subsequently wrought such terrible havoc in some of the fairest and most favoured provinces of France.

Convinced himself of the efficacy of his process for preserving wines, Pasteur was determined to also convince the public, and after having privately submitted samples of heated and unheated wine respectively to the severe testing of skilled connoisseurs, and obtaining in each case favourable reports, he approached the principal wine merchants of Paris, and induced them to organise a committee which should pronounce an impartial opinion upon the relative merits of treated and untreated wines. This committee was formed without difficulty, met in November, 1865, at the Ecole Normale, where, after the most searching tests which could be devised and applied, it was unanimously stated that if any difference did exist between the heated and the unheated wines it was so insignificant as to be practically imperceptible.

Thus one of the most important economical problems of the day was solved, solved, as Dumas so aptly described it, not through chance experiments but by means of researches directed by a profound knowledge of the laws of nature, and aided by an exquisite appreciation of the methods which science possesses for their revelation.

Pasteur was attacked somewhat virulently more than once on the ground that this idea of heating wines was not original, and he was accused amongst other things of having resuscitated, without acknowledgment, some experiments made long ago by Appert. It, is, however, only just to Pasteur to say that he was not aware of these investigations when he carried out his experiments, and that as soon as his attention was directed to them, he at once publicly acknowledged and described them in a memoir which he communicated to the Academy of Sciences. In this he mentions how Appert had sent bottles of Beaune from Havre to Saint Dominique, the bottled wine having been previously heated in a water-bath to 70 degs. Centigrade, and that on its return to Havre he compared two bottles of this wine with some which had not been heated. Appert apparently laid great stress upon the fact that the heated bottles were markedly superior to the others, and had, moreover, suffered no damage from the process either in taste or bouquet.

It was, moreover, urged that this heating of wine had for some time past been carried on extensively at Mèze in the South of France. In order to meet this attack, Pasteur went to Mèze and inspected the process in vogue there; he returned triumphant, remarking "that they do certainly heat their wine at Mèze, but it is to age it more rapidly. To bring this about they heat it exposed to the air for a long time, in such fashion that the taste is altered, and sometimes unpleasantly so, and immediate steps have to be taken to correct it; this clumsy proceeding shows that the merchants of Mèze are not too well up in what they are doing, and have not read my book. It would be to their interest to do so, for I supply the theory of their practice. Meanwhile, however, what is there in common between this long and perilous heating of wine in the presence of air and the rapid heating to 50 degs. Centigrade in the absence of air which I recommend? Far from having received any suggestions from the Mèze methods, I rejoice that I was ignorant of them. They might have deterred me from employing heat, for whilst I aimed at producing no change in taste, their one object is to secure such an alteration."

CHAPTER VIII.

RESEARCHES ON SILKWORM DISEASES.

During the progress of his researches on fermentation, Pasteur had exchanged his official appointment of Director of Scientific Studies in the Ecole Normale for the Professorship of Geology and Chemistry at the Ecole des Beaux-Arts, which post he held from the year 1863 to 1867.

It was during the latter part of his tenure of this office that he entered upon an entirely novel line of investigation, which, although belonging in point of time to what may be described as the "fermentation period" of his researches—for the *Etudes sur la Bière* followed later—yet had nothing whatever to do with it, but was, on the other hand, a sort of prophetic incursion into that region of viruses and vaccines where later the climax of his fame was to be reached.

At this time a portion of France was experiencing one of those waves of industrial calamity which periodically overwhelm communities, and cause distress and suffering hardly less acute than those which are consequent on war. The helplessness even of modern civilisation in stemming these disasters must have impressed all who have witnessed such industrial disturbances as the phylloxera, the potato disease, or the rinderpest, which are the nineteenth-century counterparts of some of the plagues of Egypt. It was with a great national calamity like any one of these that Pasteur was to be called upon to cope single-handed, and the eyes of the world were naturally fixed —in many cases, no doubt, with scepticism and distrust—on this new Bellerophon and his winged Pegasus of modern science.

The monster which he was challenged to overcome and destroy with the resources of science was a disease called "*pébrine*," which, having already attacked the silkworms in 1849, had by this time so crippled the silk industries of the country that the annual revenue to the State from this source had been reduced in the course of twelve years from 130,000,000 to 8,000,000 francs. The value of the cocoons produced, in normal years reaching more than 100,000,000 francs, fell in the years 1863 and 1864 to 34,000,000 francs. From this last figure 10,000,000 must be deducted, this sum representing the extra cost of purchasing foreign "graine"* instead of the cultivators raising it themselves.

Some idea of the epidemic proportions which this disease had assumed amongst all European countries may be gathered from the fact that whilst in the year 1853 France was able to import healthy silkworms' eggs from Spain and Italy, ten years later there was not a corner of Europe which was free from the disease, and recourse had to be had to Japan, where alone non-infected eggs were procurable.

A silkworm cultivator, writing already in 1862, gives a graphic picture of the distress which the

* A technical expression for the eggs of the silk-moth.

disease had brought about in his district:—"The traveller who some fifteen years ago traversed the Cevennes mountains and retraces his steps to-day, would be astonished and deeply moved by the changes of all descriptions which have taken place in so short a space of time in the district.

"Formerly he saw on the slopes of the hills active and sturdy men busy quarrying the rock, building solidly constructed walls out of the débris, destined to support fertile soil prepared with infinite labour, and carried thus to the summit of the hills in carefully laid-out terraces, upon which mulberry trees were planted. These men, despite the fatigues of such hard work, were happy and contented, for comfort surrounded their domestic hearth.

"To-day these plantations of mulberry trees are completely abandoned; 'the golden tree' no longer enriches the country, and there, faces formerly radiant, are now melancholy and sad; where before plenty reigned, now misery and poverty prevail."

So acute a stage had matters reached in the year 1865 that a great petition was forwarded to the Senate with 3,600 signatures attached of the mayors, municipal councillors, and landed proprietors belonging to the silkworm districts, urging upon the Government the appointment of a commission to inquire into the disease, with a view to remedial measures being adopted, so that the silk industry might be saved, if possible, from the bankruptcy which was staring it in the face.

Already in 1857 the Government had instructed Dumas to visit the silkworm districts and report upon the character and distribution of the disease.

The vaguest ideas were current as to the conditions controlling its dissemination. Thus many were of opinion that the mulberry trees were the source of the evil, and the practice had arisen of treating the latter with sulphur; others, again, attributed the plague to atmospheric conditions, and had proposed the use of disinfectants such as chlorine or carbolic acid, Some cultivators had even suggested making the worms take rum or absinthe, and then a disinfectant in the shape of a dose of nitrate of silver or creasote. Dumas, however, examined the mulberry trees and could find nothing to justify their being held responsible for the calamity; the state of the air in the *magnaneries*, or breeding rooms, he also regarded as incapable of solving the mystery. He succeeded, however, in indicating the external signs of disease in the affected worms, but he was quite unable to suggest any remedial measures.

When the nomination of a commission of inquiry was forced upon the Government they once more approached Dumas; his previous knowledge of the subject, his great scientific reputation, and his well-known sympathy with the widespread distress produced by the disease, combining to render his presidency of the commission satisfactory to all parties.

With admirable sagacity, Dumas, instead of turning to some distinguished zoologist, entomologist, or other authority learned in the ecdyses and metamorphoses of the insecta in general and of the lepidoptera in particular, at once singled out Pasteur as the man who of all others was most capable of being entrusted with the difficult task of searching out the hidden mysteries of this disastrous silkworm disease.

Pasteur was, however, loth to leave his investigations on fermentation, which had now begun to open up vistas of work the interest and importance of which seemed well-nigh inexhaustible. To abandon a field of research which he had conquered after so much toil and trouble, and to embark upon a fresh voyage of discovery the issue of which was highly doubtful, and upon which years of valuable time might be vainly expended, was indeed an enormous sacrifice to demand of any scientific man.

"Considérez je vous prie," urged Pasteur in response to Dumas' pressing request, "que je n'ai jamais touché à un ver à soie."

"So much the better," replied Dumas; "for just by knowing nothing of the subject you will import no ideas but those which you derive from your own observations."

But coupled with his reluctance to interrupt the work upon which his whole thoughts were at this time concentrated, Pasteur was himself diffident about his powers of carrying such an undertaking to a successful issue.

Dumas was, however, obdurate in his insistence that Pasteur should devote himself to the question, and at length persuaded him to overcome his scruples and accept the task entrusted to him. Thus Pasteur, who had never made a dissection in his life—who had never seen or handled a silkworm, and knew nothing of physiology—suddenly found himself precipitated headlong, as it were, into an investigation the very importance and publicity of which would in themselves have been sufficient to deter other men from running the risk of failure.

M. Duclaux describes how, after Pasteur had finally accepted the mission entrusted to him, he, with characteristic enthusiasm, endeavoured at once to obtain some knowledge of the larvæ of insects in general by watching the dissection of worms, etc. He attends meetings of the Imperial Commission on Silk Culture, from which, however, he returned more discouraged than enlightened; he rapidly peruses some of the latest publications on the subject, and leaves for Alais on June 6th, 1865, accompanied by Duclaux, Gernez, Raulin and Maillot, all assistants of his at the Ecole Normale, hardly three weeks having elapsed since he first wrote placing himself at the disposition of Dumas.

M. Gernez tells us how, on his arrival at Alais, Pasteur at once made himself accessible to one and all. Full of consideration, he would thoughtfully listen to everything, taking, however, little part in any ordinary conversation, but full of interest and life immediately any scientific subject was discussed. His simple and incisive language displayed his clear grasp of the question, whilst the spirit and animation of his address, combined with the restraint imposed by a rigid adherence to strictly logical reasoning, rendered him a most eloquent and impressive speaker.

The outward and visible signs of this *pébrine* are variously exhibited, sometimes at the time of hatching already, a mass of *graine* or eggs proves sterile, or a great mortality takes place amongst the worms during the first few days of their existence.

Sometimes all goes well until the first moult, when many worms begin to eat very little and become blackish in appearance, and a number die off. In some cases, again, no trace of disease is visible until the third or even the fourth moult, but frequently, instead of assuming the proper white tint, the skins remain yellow, and the worms eat less and less and die off, or their bodies become gradually covered with black marks. Frequently the silkworm breeder is deprived of every single insect before the chrysalis stage has been reached.

An even more tragic exhibition of the disease, however, is to be found in those cases where nothing has occurred to interrupt the normal succession of stages in the life of the worms, and the latter have arrived at the period characterised by voracious feeding which precedes the chrysalis condition. It is at this period that in the silkworm chambers the peculiar noise of the mandibles busy at work, resembling the sound of rain falling on the leaves of trees, rejoices the heart of the proprietor, for he knows that the time is now approaching when *la bruyère** will be covered with silk of the colour of gold and silver.

The dismay can be pictured when an inspection of the silkworm tables suddenly at this period reveals the fact that numbers of these full-grown worms are failing to eat, and that numbers are either dead or dying. Pasteur has himself vividly described this tragedy in the following sentences:—"After having bestowed his time and his labour upon his dear *bétail*, dispensed his leaves, paid his workpeople, the

* Branches of brushwood in which the mature caterpillars ascend to spin their cocoons.

unfortunate breeder gathers nothing but putrefying bodies. Formerly the period of collecting the cocoons was a season of *fêtes* and rejoicings. In spite of the labours of the last days, when the appetite of the worms cannot be appeased except at the expense of attention which knows no pause either day or night, joyous songs resound throughout the country, on the trees where the gathering of the leaves is going on, near the tables where the precious insect, the body full of silk, is hastily mounting to the *bruyère*, there to construct its golden prison. A single incident will convey an impression of the important part which the harvesting of the precious textile plays in the life of the people, in these districts : The payments of the whole year, all the arrangements of business turn around the completion of the silkworm culture. This custom, so ancient and respected, is to-day nothing more than a memory."

As has before been mentioned, numerous works and pamphlets had been published, and quite a mass of literature already existed upon the subject when Pasteur entered the field.

A great number of careful observations had been made by various observers. Thus microscopic corpuscles had been seen in the diseased silkworms by Guérin-Méneville ; their pathological import had been suspected by Cornalia ; their abundant presence in all the diseased larvæ and moths had been observed by Lebert and Frey ; whilst Osimo of Padua had even found them in the eggs. Vittadini, moreover, in 1859, had suggested that these eggs should be submitted to a microscopic examination to ensure that only healthy ones should be preserved.

Various endeavours at isolation and other methods of compassing the plague had been resorted to, but so far nothing had availed, and the disease was as rampant as ever when Pasteur and his assistants took up their abode in the little house in the environs of Alais and started the culture of silkworms.

Pasteur's first efforts were directed to searching out the corpuscles which had figured so prominently in the reports of his predecessors in this field of inquiry, and he had but little difficulty in discovering them, for all the silkworm nurseries in the neighbourhood were infected with disease. A few hours after his arrival he was able to show the famous corpuscles to many members of the Agricultural Society who had never before set eyes on them. An examination of sickly worms and moths revealed the presence of thousands of these same corpuscles; all the so-called *pébrine* worms appeared to be invaded by masses of these little oval, luminous bodies.

The question was, What connection had these corpuscles with the disease with which the worms were afflicted? And now the work began in real earnest. Pasteur's plan was to initiate all the experiments himself, carrying them out personally even in the minutest details, only calling in his assistants to repeat them and control their accuracy. His energy was boundless; he would frequently rise at five in the morning so as to be present at the first feeding of the silkworms, and not retire to rest until eleven, after their last meal. At the end of his long day's toil, instead of taking his much-needed repose, he would commence on the mass of correspondence of all kinds with which he was inundated, and which more frequently than not involved replies to hostile critics. Theories and ideas poured in upon him from France and all parts of the world; and in order to clear the way for work, he was obliged to sift carefully and place on one side those which appeared to have any semblance of value, whilst he felt it incumbent on him to test with the utmost care and accuracy before pronouncing an opinion upon methods which were stated to be capable of "infallibly" curing the disease. The amount of work which this involved is more easily imagined than described. Often of an evening, M. Gernez tells us, Pasteur, broken down with fatigue and worry, would exclaim to his assistants: "Hélas! nous n'avançons pas!"

This was in 1866, and Madame Pasteur determined to leave Paris and come with her two daughters to Alais, to help to cheer and help him during this terribly trying and anxious time. Unfortunately, before reaching Alais the elder of the two children developed typhoid fever at the house of one of Madame Pasteur's sisters. Having already lost their eldest child from the same disease, the anxiety of the parents can be readily conceived, and for five weeks Pasteur, heroically abstaining from forsaking his work, was a prey to the most acute mental suffering. At length, yielding to the entreaties of his assistants, he left Gernez in charge, and joined his wife in time only to spend a few days with his child before a relapse brought about a fatal termination of the malady. Pasteur's grief was pathetic to witness, for he was a most devoted father; but he returned to Alais with his wife and little daughter, and patiently and bravely took up his work once more.

We have seen that the first problem awaiting solution was to ascertain the connection, if any, which the bright oval bodies or corpuscles already referred to, found in the bodies of afflicted silkworms, had with the disease of *pébrine.*

All the previously ascertained facts concerning them were confirmed by Pasteur, but nothing in the whole course of this most interesting inquiry is more remarkable than that Pasteur, who in his fermentation experiments had been guided so successfully by the conviction that the living organism was the cause of the chemical process, should have failed for so long a time, in spite of his intimate contact with the disease in all its various phases, to recognise that these living corpuscles were the real *materies morbi* of the *pébrine.*

For more than two years Pasteur held the opinion that these corpuscles were only the consequence of, or the visible witnesses, as it were, to a disease which had already invaded the worm. It was only towards the close of the year 1867 that he recognised that these living particles were parasitic to the worm and the *fons et origo* of the disease. The history of Pasteur's misconception in this important matter is very interesting and extremely simple.

Soon after he had commenced his studies at Alais, he came across two sets of silkworm cultures, one of which had apparently succeeded very well, so much so that the proprietor had already decided to preserve all the chrysalides for the future supply of eggs, considering them perfectly healthy, whilst the other culture had a bad appearance and showed unmistakable signs of being infected. Now Pasteur examined chrysalides and moths from the culture which had raised such buoyant hopes in the heart of the proprietor, and discovered masses of corpuscles; in worms taken from the unpromising nursery he, on the contrary, only discovered a few here and there. Nor was this an isolated observation, for Pasteur confirmed it over and over again. How was this to be interpreted? To all appearance the presence of corpuscles and disease were two distinct phenomena. Worms could seemingly be perfectly healthy and yet give rise to chrysalides swarming with corpuscles, whilst worms could be severely and visibly afflicted with disease and yet possess hardly one of these suspicious particles.

Pasteur, before venturing to draw a definite conclusion from these most puzzling and to all appearances contradictory observations, waited to see what would be the condition of the chrysalides derived from the unpromising but comparatively corpuscle-free nursery. He studied these chrysalides day by day, and he found that in proportion as they developed the corpuscles became more and more abundantly present, whilst finally not a single moth was without them, and they were, moreover, demonstrable in great numbers.

Another most striking observation contributed to conceal the real character of the corpuscles from Pasteur at this time. With the object of ascertaining what part, if any, was played by the dust and refuse in the infected silkworm nurseries, he collected and microscopically examined *débris* and rubbish which had been left lying from the previous year's cultures, for at this time the incredibly dirty custom prevailed of leaving the nurseries untouched, and only cleaning them up a few weeks before the new season's work commenced.

Pasteur was amazed at the enormous numbers of the corpuscles which he found mixed up with this dust, looking as distinct and as well defined as he was accustomed to see them in the tissues of the worms themselves. In order to find out if this dust served to spread the disease, Pasteur took some perfectly healthy worms and fed them on leaves sprinkled over with it. The mortality which followed this dust repast was very great, but on examining the dead worms he was immensely surprised to find no corpuscles. Thus again Pasteur was confirmed in his idea that the corpuscles were not the agents but rather the results of *pébrine.*

Later observations, however, enlightened him upon this as on other perplexing difficulties, for he discovered that these corpuscles lose their pathogenic or disease-producing power when they have been kept, as the above had been, for a long time in a dry condition in contact with air. The corpuscles he saw in the dust were the corpuscles of *pébrine*, but they were dead and incapable of provoking disease. The death of the worms, he discovered later, was due to another disease altogether, to which we shall have to refer presently. It was in the spring of the year 1868 that Pasteur found conclusively that it was possible to infect worms with *pébrine* by feeding them with *freshly* collected dust containing *living* corpuscles.

Now we come to the point where Pasteur took the wrong turning, as it were. He first concluded that in both the nurseries above referred to the same disease had infected the worms, and that the only difference in the two cases was its greater severity in the one than in the other. He secondly was led, as we have before mentioned, to believe that the corpuscles were only a delicate means of diagnosing the existence of disease, but were not themselves the cause of the malady. Nevertheless, his observations of the apparent preference exhibited by the corpuscles for establishing themselves in the chrysalis and moth stage of the worm's life, caused him to recommend the wise plan of microscopically examining chrysalides and moths for corpuscles with a view to their preservation or destruction, as the case might be, and so avoiding the employment in the subsequent year of infected *graine*, and the consequent waste of labour and money in rearing diseased worms.

We know now, for Pasteur himself has shown us, that he was wrong in his conclusions, that the corpuscles are the cause and not the consequence of *pébrine*, that in the sickly worms where he failed to find them, or only in small numbers, the worms were suffering at the time from a totally distinct disease, although later falling victims to *pébrine* as well.

But Pasteur's erroneous reasoning led him also to make mistakes in his method of examining the moths for the presence of corpuscles. Convinced that these particles were the later signs of a pre-existing disease, he considered that they would be omnipresent in the insect's body, and hence he pronounced a moth infected or not infected according as he discovered corpuscles in a small portion of the skin of the abdomen. Had he been impressed with the parasitic nature of the corpuscles he would have realised, as he did later, that such an examination was not sufficient, that the corpuscles might be absent in some organs and present in others.

Thus his method of endeavouring to insure only the eggs of healthy moths being employed sometimes succeeded and, naturally, sometimes failed. It was only when he adopted the plan of pounding the body of the moth in a mortar with a little water and examining a drop of the emulsion under the microscope, that he was able to pronounce with certainty upon the presence or absence of corpuscles, and hence presence or absence of disease in the insect, and the consequent value to be attached to its eggs.

When Pasteur had at last succeeded in unravelling the mystery of *pébrine*, his endeavours were at once directed to persuading silkworm proprietors to adopt the method just mentioned for the separation of good from bad *graine*, and foreseeing that the use of the microscope might prove an impediment to its being employed by these good people, he anticipates their objections by saying: "If you tell me that you are afraid of the microscope and that its management does not appear easy, know that I have a little girl but eight years old who makes very good use of it."

The systematic examination of the moths recommended by Pasteur is now universally adopted, and hundreds of women and girls may be seen every year at the period of "grainage" pounding up moths, making microscopic examinations, and sorting the eggs from the healthy and unhealthy moths respectively.

Once convinced of the parasitic character of *pébrine*, Pasteur proceeds to make elaborate investigations showing its communicability, whilst he also indicates the precautions which should be observed to keep it within bounds and circumvent its dissemination. He had already shown how the dust of infected nurseries was capable of propagating disease, and he impresses upon the proprietors the necessity of cleanliness, of observing far greater precautions than had hitherto been customary, to insure the requisite hygienic conditions for the protection of the worms from disease. He demonstrates how one worm in an infected litter can infect another by crawling over its body and inflicting small wounds with its feet, the latter being shown in many cases to have the fatal corpuscles attached, collected there by the worm in the course of its wanderings amongst its dead companions or over the excrements of *pébrine* victims.

He presents the silkworm proprietors with an easy method of distinguishing healthy from infected eggs, which while saving the trouble and expense of rearing sickly worms, would also materially assist in diminishing the proportions of the epidemic by banishing bad *graine* and employing only that certified as free from disease.

The victory seemed complete, the triumph certain, and Pasteur awaited with confidence the result of the cultures with the *graine* which he had collected and certified as pure by his method the previous year. His intense disappointment and mortification may be imagined when he received along with letters testifying to the complete success of the cultures raised from his *graine*, numerous complaints of silkworm disease. He became more and more depressed, but did not communicate his fears and anxiety to his assistants until one day, coming into the laboratory almost with tears in his eyes, he sank disconsolately into a chair and exclaimed, "Il n'y a rien de fait ; il y a deux maladies !"

Yes, there were indeed two silkworm diseases, and it was their superposition which was largely responsible for the circumstance that Pasteur had so tardily arrived at the truth with regard to the corpuscular cause of *pébrine.*

It will be remembered how Pasteur had come across this other disease already on several occasions, but he had, in common with many other authorities, regarded it as but a part, a different symptom, of this same *pébrine* upon the elucidation of which he had concentrated all his efforts.

He tells us frankly himself how, up to the year 1867, he had put this interpretation upon the facts which he had observed, which, he goes on to say, "je considère aujourd'hui comme tout-à-fait erronée . . . le progrès de mes études vint jeter de nouvelles lumières sur le sujet, et étendre le cercle des difficultés à vaincre et des expériences à tenter."

From this time onwards he realised that the cause of the disastrous condition to which the silkworm industry had been reduced was attributable not to one disease alone, but also to a second, totally distinct and independent from the other, a disease the appearance of which was familiar enough to silkworm cultivators, although its origin was as great a mystery as had been that of *pébrine.*

This disease was known as the *maladie des morts-blancs, morts-flats,* or more commonly called *la flacherie.*

This disease generally attacks silkworms after they have completed their fourth moult. To all outward appearance the worms are in excellent condition, but their movements are languid, and their death follows quickly, their bodies becoming black after an interval of from twenty-four to forty-eight hours. If they manage to creep on to the twigs they remain for days before they complete *la montée,* and so familiar is this condition of the worms to the cultivator that an old custom prevails of burning incense, or thyme, or perfumes, or raising the temperature of the nursery to rouse them from this state of lethargy.

Pasteur points out how important it is that this phenomenon should receive careful attention from silkworm cultivators, and that the resulting chrysalides should be destroyed and not preserved for purposes of grainage for the following year; unless this precaution is observed the nurseries will be decimated by *flacherie.*

Careful investigation convinced Pasteur that this disease is due essentially to a disturbance in the digestive functions of the worm; this disturbance he moreover discovered to be akin to a process of fermentation set up by particular vibrios or bacteria, which he describes as *vibrions de la flacherie,* and by a series of skilful experiments he demonstrates beyond question the contagious character of the disease. His remarks on this micro-organism and its appearance are of great interest in connection with the history of the discovery of the hardy or spore form of bacteria in disease. That he really observed spores in these bacilli we know from a remark which he makes in a foot-note, where he points out how the supposed identity of *pébrine* with *flacherie* by many observers may have been materially assisted by the similarity in appearance of the *pébrine* corpuscles "avec les petits corps brillants que l'on voit souvent dans l'intérieur des vibrions."

Again, that this micro-organism was endowed with the power of existing in this spore and hardy form, we have evidence from the fact that worms succumbed to *flacherie* from swallowing infected dust more than a year old, for we know now that the fragile or rod form could not have survived this length of time under such conditions, but that in the spore form a micro-organism can retain its vitality and virulence for long periods of time under apparently most trying and disadvantageous circumstances. Pasteur was, therefore, the first to discover the spore form in a pathogenic or disease-producing micro-organism.

Whilst predisposition, such as eggs derived from chrysalides infected with *flacherie*, plays an important part in determining the appearance of this disease, yet its occurrence may often follow from accident due to inattention to details of management. Thus overcrowding in the litters, too high a temperature in the nurseries, bad ventilation, the use of wet leaves, are all fertile sources of *flacherie*, inasmuch as they affect the vitality and health of the worms. As long as the worms are vigorous, these vibrios or microscopic organisms, which are derived from the mulberry leaves themselves, are kept in abeyance by the secretions of the intestine, but if adverse circumstances arise, depressing the vitality of the insects, the digestive functions become disorganised, the vibrios get the upper hand, and the symptoms of *flacherie* declare themselves.

One circumstance which promotes *flacherie* is the use of mulberry leaves from trees which are regularly pruned each year. Such leaves are larger and coarser and more indigestible than those gathered from trees allowed to grow wild.

The custom of pruning the trees is not surprising, for, whereas it requires one man per day to gather sufficient leaves from a pruned tree, to provide food to satisfy the inordinate hunger of the worms just before the chrysalis state is reached for a nursery supposed to yield 100 kilogrammes of cocoons, it involves the labour of four men per day to collect sufficient food material at this busy time from unpruned or wild trees.

Of so much importance is the character of the mulberry leaf in the feeding of worms, that it is recommended to start the cultures as early as possible, so that the leaves are younger and more digestible at the critical and last stage of the worm's life. An enthusiastic valet attached to the person of Henry IV. of France was ennobled and appointed controller of commerce and of mulberry trees in France by his master, on account of the zeal and intelligence which he displayed in the culture of silkworms. Many of the observations on silkworm culture made by this Laffémas on the advantages of cultivating the mulberry tree in the centre and north of France, in a work published in 1604, are, Pasteur points out, full of wise advice which silkworm proprietors would do well to follow at the present day. Thus, amongst other things, cleanliness is insisted upon, too high temperatures are condemned, and the use of coarse and wet leaves proscribed.

In studying this second silkworm disease, Pasteur was brought in contact for the first time with a number of phenomena akin to those which obtain in the infectious diseases of man and the higher animals. It was in investigating this bacterial disease of *flacherie*, that he acquired that great store of ideas which he afterwards so successfully deployed into line in his brilliant attack upon those subtle maladies which absorbed the later years of his life.

That he himself was deeply conscious of the educational value which these researches on *pébrine* and *flacherie* had possessed for him, is shown by the fact that in after years, when young medical men were aspiring to undertake researches in his renowned laboratory at the Institute bearing his name, he never failed to say to them, "Lisez les études sur les vers à soie; cela sera, je crois, une bonne préparation aux travaux que nous allons entreprendre."

Meanwhile his arduous toil and brilliant investigations had not passed without recognition from foreign countries. In the year 1868 the honorary degree of Doctor of Medicine was conferred upon him by the University of Bonn; the prize of 5,000 florins, offered by the Austrian Government in 1868 to whoever should succeed in discovering the best means of compassing the disease of pébrine in silkworms was awarded to Pasteur also in this year; whilst in 1869 he was elected a foreign member of the Royal Society of London. In the market-place at Alais a fine statue of Pasteur has recently (1896) been erected, in which he is represented standing, gazing fixedly at a sprig of mulberry covered with cocoons, which he is holding in his left hand; at his feet is a young girl in a graceful attitude handing him other cocoons, whilst close by a microscope and a box of scientific instruments are to be seen.

M. Berthelot, who in company with Dr. Roux carefully inspected the statue, is said to have exclaimed, so struck was he with the likeness, "Je revois Pasteur tel qu'il était il y a vingt-cinq ans!"

But if Pasteur had conquered his difficulties, he had not vanquished all his opponents, and he was continually harassed by attacks of sceptics, and constantly occupied in exposing the imperfect manipulations and false conclusions of his detractors. During these years he was leading a life not only of unremitting activity but of great mental tension. The strain and anxiety told terribly upon him, and in the autumn of the year 1868, at a critical moment, before he had had time to convince his opponents of the truth of his hypotheses and efficacy of his methods, he was struck down by an attack of paralysis. The severity of the attack was such that his recovery was at first regarded as hopeless, and Pasteur himself was despondent. "Je regrette de mourir," he said to a friend, "j'aurais voulu rendre plus de services à mon pays." His brain, however, was never affected, and his one absorbing idea was the thought that he had not been able to complete his researches on silkworm diseases. One evening, Gernez tells us, how he was watching beside Pasteur's bed all alone, and after in vain endeavouring to distract his thoughts from his work, allowed him to have his own way and unfold the ideas of which his mind was full. To his great astonishment, Gernez found that they were all definitely and clearly formulated, and he therefore fetched pen and paper and wrote down, word for word, what Pasteur dictated to him, without altering a single syllable. The next day he took the manuscript to Dumas, who could scarcely believe his eyes, it having been produced exactly eight days after Pasteur was seized with paralysis. This memoir of Pasteur's is the note which appeared in the *Comptes rendus de l'Académie* on October 26th, 1868, and contains suggestions for an extremely ingenious method of ascertaining in advance whether *graine* is predisposed or not to the disease of *flacherie*.

Although Pasteur's physical condition became less critical, he remained for two months completely paralysed, and never in after-life recovered the full use of his limbs.

In the beginning of the year 1869, in January, stung to the quick by the hostile criticism with which his investigations and remedial measures were being received, he determined, although he could not yet even move across his room, to go back to Alais and superintend further experiments. "A scientific principle was at stake, and an element of national wealth," he urged upon those who endeavoured to dissuade him from undertaking so risky an enterprise.

His son-in-law, M. Vallery-Radot, has vividly described this painful expedition, so fraught with anxiety to his family and those who accompanied him. "Il fallut céder à son désir. Ah ! le terrible voyage plein d'anxiétés ! C'était a quelques lieues d'Alais, a Saint-Hippolyte-du-Fort, que se faisaient les essais précoces. M. Pasteur s'arrêta là. Il s'installa, il campa pour mieux dire, avec sa famille et ses préparateurs dans une maison plus que modeste, une de ces maisons mesquines, froides et carrelées de province. Du fond de son fauteuil, M. Pasteur dirigeait les expériences, contrôlait l'exactitude des observations qu'il avait faites l'année précédente."

His indomitable courage and energy were rewarded, and he had the immense joy and satisfaction of confirming at every point and in every detail the truth of his predictions and the efficacy of his preventive methods. The noisy opposition of his adversaries, however, continued; and the French Government hesitated, in the face of such tenacious and clamorous contradictions, to give official recognition to his method of grainage.

The Emperor Napoleon, however, came to Pasteur's assistance, and proposed that he should visit a villa near Trieste, belonging to the Prince Imperial, where the cultivation of silkworms was carried on, which, however, during the past ten years had failed utterly. Pasteur accepted the offer with gratitude, and at once started for Trieste, and so great was the success which followed the application of his methods that the sale of the cocoons realised a profit to the estate of 26,000 francs.

This signal success so impressed the Emperor that he nominated Pasteur a Senator in July, 1870. There was not time, however, for his promotion to be gazetted before the Franco-German war was declared. Pasteur, a patriot before all else, completely crushed by his country's misfortunes, for the first time felt powerless to do any work, and he retired to his old home at Arbois.

The splendid volumes containing the history of

Pasteur's researches on silkworm diseases were published in 1870, and in the preface Pasteur writes:—

"Although I devoted nearly five consecutive years to the laborious experimental researches which have affected my health, I am glad that I undertook them, and that august words* gave me the courage to persevere. The results which I have obtained are perhaps less brilliant than those which I might have anticipated from researches pursued in the field of pure science, but I have the satisfaction of having served my country in endeavouring to the best of my ability to discover a remedy for great misery. It is to the honour of a scientific man that he values discoveries which at their birth can only obtain the esteem of his equals, far above those which at once conquer the favour of the crowd by the immediate utility of their application; but in the presence of misfortune it is equally an honour to sacrifice everything in the endeavour to relieve it. Perhaps, also, I may have given young investigators the salutary example of lengthy labours bestowed upon a difficult and ungrateful subject."

* "Les maladies des vers à soie" is dedicated to the Empress ("Hommage de profonde reconnaissance et d'une vive admiration pour son esprit élevé et son grand cœur") in recognition of the gracious interest taken in his researches and the encouragement given to continue them.

CHAPTER IX.

STUDIES ON BEER.

THE condition of melancholy depression into which the war of 1870 plunged Pasteur, and the intense patriotism which his country's misfortunes roused in him, may be gathered from the following letter which he addressed from Arbois in January, 1871, to the Dean of the Medical Faculty at the University of Bonn:—

"In 1868 the Faculty of Medicine of the University of Bonn did me the honour of bestowing upon me the title of Doctor of Medicine, in recognition of my researches on fermentation and on the part played by microscopic organisms.

"Of all the distinctions brought me by the discoveries which I have been permitted to carry out since my entrance upon a scientific career, now twenty-two years ago, there is not one, I assure you, which gave me greater satisfaction It was, in my eyes, the public recognition of a secret thought, the truth of which I felt was asserting itself more and more, that my investigations had opened new horizons for medicine. Indeed, I eagerly framed the diploma of honour conveying the resolution of your Faculty, and ornamented my study with it.

"To-day the sight of this parchment is odious to me, and I feel insulted to see my name, with the designation of *Virum clarrisimum* with which you endowed it, placed under the auspices of a name since devoted to the hatred of my country —that of Rex Guilelmus.

"Whilst expressing sincerely my deep respect towards you and towards all the distinguished professors who appended their signatures to the decision of the members of your Faculty, I obey the cry of my conscience in begging you to erase my name from the archives of your faculty and to take back this diploma, a marking a sense of the indignation inspired in a French savant by the barbarism and hypocrisy of one, who to satisfy a criminal ambition, persisted in the massacre of two great peoples."

It will be remembered by many that this feeling of antipathy and patriotic resentment never wore off; for, on the recent occasion of the festivities which attended the opening of the Kiel canal, the Berlin Academy of Sciences, at the instigation of the Emperor, offered Pasteur, in the most flattering terms, a Prussian distinction, but only to find that the deep wound received more than twenty years before was still unhealed. Pasteur replied that, whilst appreciating the honour as a savant, he could not as a Frenchman forget the war of 1870, and that he would never be able to accept a German decoration.

That Pasteur's old energy was returning, and that he was growing restless and anxious to be once more up and doing, assisting by some means or other to retrieve the misfortunes which had fallen on his country, we learn from a letter addressed about a couple of months later to his old assistant and friend, Duclaux:—

"My head is full of the most beautiful plans for work. The war has let my brain lie fallow. I am ready for fresh undertakings. Alas! perhaps I am deceiving myself. Come what may, I shall try. Ah! if I only were rich—a millionaire! I would say to you, to Raulin, to Gernez, to Van Tieghem, etc., 'Come, we will transform the world by our discoveries!' How happy you are to be young and strong! Oh, if I only were so, to start afresh a new life of study and work. Poor France, dear country, could I but help to raise you from your disasters!"

Just as Pasteur was starting for Paris, full of energy, and impatient to carry out the investigations which he had been planning with so much enthusiasm in his retirement, the Commune was declared, and he accepted instead Duclaux's invitation to come and work in his laboratory at Clermont-Ferrand, where he was at this time professor in the Faculty of Sciences.

It was natural that Pasteur should once more turn to those studies on fermentation to which he had devoted so many years of labour, and which he had so reluctantly abandoned when he consented to undertake the investigation of the silkworm disease. Even during his researches on pébrine and flacherie, which we have seen he pursued with so much enthusiasm and energy, he had room for a regret that he had been obliged to sever himself from his former investigations. In his preface to the splendid volumes in which he has brought together his studies on the diseases of silkworms, he writes:—

"One day—it was, I think, at the beginning of the month of October, 1868—encountering Dumas as I was coming out from one of the meetings of the Academy of Sciences, I said to him, 'Ah, I made a very great sacrifice for you in 1865.' A discussion had just taken place at this meeting on various questions relative to fermentations and contagion, and it had roused up afresh all my regrets."

But another and very different consideration also led Pasteur to return to his old subject, and this was the hope that, by investigating the fermentations incidental to the brewing of beer, he might be able to succeed in so improving the manufacture of French beers that they should be in a position to compete with those so successfully produced in Germany, and that he might thus secure some commercial advantage for his now over-burdened country.

"L'idée de ces recherches m'a été inspirée par nos malheurs. Je les ai entreprises aussitôt après la guerre de 1870 et poursuivies sans relâche depuis cette époque, avec la résolution de les mener assez loin pour marquer d'un progrès durable une industrie dans laquelle l'Allemagne nous est supérieure." These words figure on the first page of that monumental work "Etudes sur la bière," in which he has collected the numerous researches with which he was occupied between the years 1871 and 1876.

It must not, however, be supposed that this volume constitutes in any sense a handbook to the practice of brewing; of breweries there is hardly any mention, and but little space—a single chapter only—is devoted to the description of the methods recommended by Pasteur for the improvement in the manufacture of beers.

The following terse summary of the practical results of his investigations, given by Pasteur himself, will afford the reader an idea of the general direction which his researches took in endeavouring to substitute a scientific basis for the empirical methods which, previously employed, dominated the production of beer.

"We have shown, firstly, how the changes which are produced in the beer-yeast, in the wort, and in the beer itself are due to the presence of microscopic organisms of a totally different nature from those belonging to the so-called yeast proper. These organisms, by the correlative products resulting from their multiplication in the wort, in the beer-yeast, and in the beer, denaturalise the properties of the latter and militate in consequence against its preservation.

"We have further demonstrated that these organisms responsible for such alterations, these disease-ferments, do not appear spontaneously, but that on every occasion when they exhibit themselves in the wort or in the beer it is because they have been brought thither from without, either by dust in the air, or by the vessels, or by the raw materials which the brewer's art employs.

"We also know that these disease-ferments or their germs perish in malt-wort when the latter is raised to the temperature of boiling, and, as a necessary consequence of this fact, we have seen that malt-wort exposed to pure (sterile) air undergoes no sort of fermentation after having been boiled.

"Since all the disease-germs of wort and beer are destroyed in the copper in which the wort is heated, and that the introduction of yeast from a pure beer cannot import into the latter any foreign ferment of a detrimental nature, it follows that it ought to be possible to prepare beers incapable of developing any mischievious foreign ferments whatever, provided that the wort coming from the copper is protected from ordinary air, or only brought in contact with pure air during the cooling and further manipulations, and that it is then fermented with pure yeast, and that the beer, after the completion of the fermentation, is placed in vessels carefully freed from disease ferments."

That Pasteur's patriotic ambition to serve his country by his researches was fulfilled, we know from the graceful tribute which was accorded to his "Etudes" by French brewers at a congress held in the year 1889, whilst the power they have wielded in stimulating and suggesting scientific researches in the domain ot brewing is recognised all over the world.

The important work on the study of pure yeast so splendidly inaugurated by Pasteur has been nowhere more fully appreciated than in Copenhagen, where Jacobsen erected and endowed the now world-famed Carlsberg experimental laboratory for the study of fermentation problems, and which, under the able direction and guidance of Hansen, has produced such valuable scientific and practical results. In the hall of this Carlsberg Institution Jacobsen has placed a bust of Pasteur, as a tribute to the genius of the man whose labours threw such important light on the difficult and so long concealed problems of fermentation.

We have already pointed out that the portion of this famous volume devoted to the consideration of the practice of brewing is comparatively small, only a few out of the 383 octavo pages of which it is composed being directly occupied with the manufacture of beer. A closer inspection of its contents shows us that it contains an account of the numerous and varied subjects attacked by Pasteur, and a record of the original and laborious experiments which he made in elucidating them during these years. We find him carrying out experiments to prove the freedom from micro-organisms of urine and blood in their normal condition and collected with proper precautions. He is embroiled in a discussion with Frémy on spontaneous generation. He carries out a number of comparative examinations of air in different localities, and maps out their distribution in greater detail than he attempted in the original experiments on the presence of germs in air already referred to (*see* p. 59). He takes for example a series of thirty flasks containing sterile grape-must. Ten he opens in the garden of the Ecole Normale, ten on a landing of the second floor within the building, ten in the principal room of his laboratory, where a short time previously the dust had been purposely disturbed. Of the first series opened in the garden only one flask underwent alteration, of the second series four broke down, whilst of those flasks opened in the dust-laden air of the laboratory not a single one escaped infection.

The centre of gravity of this volume is, however, undoubtedly the new theory of fermentation which it contains, and which may be summarised in the words, "Fermentation is life without oxygen."

To the enunciation of this theory Pasteur was led by a careful study of the phenomena exhibited on the one hand by the life of aërobic organisms in the absence of air, and, on the other hand, of anaërobic organisms in the presence of air.

It had been asserted since 1857 by Bail that the mould *Mucor mucedo,* which is so common on horse manure, becomes transformed into brewer's yeast if grown out of contact with air by immersion in a saccharine liquid, and that the latter under these conditions suffers the ordinary alcoholic fermentation. Pasteur repeated this experiment, using special precautions, and was able to confirm the apparent transformation and the alcoholic fermentation consequent thereon. He, however, showed that the round or oval cells obtained were not veritable yeast, but that they only simulated the latter, and that the change in form was only a concomitant of the change in function under the altered conditions of life, for on bringing these yeastlike cells to the surface they again gave rise to an ordinary mould mycelium which destroyed the sugar by oxidation. The power of decomposing the sugar into alcohol and carbonic anhydride is thus only possessed by the *mucor mucedo* so long as it is growing in the absence of air, or, in other words, the *mucor mucedo* becomes a ferment when deprived of oxygen.

Pasteur endeavoured to trace the counterpart of these phenomena in the behaviour of ordinary yeast when grown in the presence and absence of air respectively.

Thus he found that yeast could grow in the absence of air, and although the growth was a very feeble one and the absolute amount of sugar transformed into alcohol and carbonic acid very small, yet the weight of sugar so transformed per unit weight of yeast present was very large indeed (150 to 200 of sugar : 1 of yeast).

On the other hand, by admitting a small quantity of oxygen, the growth of yeast is more abundant and the fermentation accelerated, but the transformation of sugar for unit weight of yeast present is less than in the entire absence of oxygen (67 of sugar : 1 of yeast). By further increasing the quantity of oxygen, the disappearance of the sugar is still more rapid and the growth of yeast still more abundant, but there is hardly any alcohol formed, the sugar having principally suffered oxidation instead of decomposition; moreover, the amount of sugar which has disappeared per unit weight of yeast present is still lower than in the previous case (4 to 5 of sugar : 1 of yeast).

It would be out of place here to discuss the criticisms to which this theory of fermentation has given rise—criticisms which at the present day are being actively carried on ; one of the principal objections to the acceptance of Pasteur's views being the omission of all consideration of the element of time in estimating the fermentative power of yeast.

Before, however, leaving this fermentation theory of Pasteur's, which it is to be hoped will still continue to stimulate research in the future, as it has done in the past, we would point out two very remarkable confirmations which this theory receives: first, in connection with industrial practice, where the production of yeast is the object of the manufacturer, the liquids in which the yeast is grown are kept as fully aërated as possible, experience showing that thus the maximum transformation of sugar into yeast cells is secured. On the other hand, the discovery in 1869 by Lechartier and Bellamy that the vegetable cells present in ripe fruits transform a part of the sugar which they contain into alcohol if the fruits in question are preserved in an atmosphere of carbonic anhydride, would tend to show that the production of alcohol from sugar is a more or less general property of vegetable protoplasm when deprived of free oxygen, irrespectively of the nature of the cells in which this protoplasm is contained.

Within the present year the discovery has been made by E. Buchner that a soluble principle giving rise to the alcoholic fermentation of sugar may be extracted from yeast cells, and for which the name *zymase* is proposed. This important discovery should throw a new light on the theory of fermentation, as it will now be possible to attack the problem in a new and much more decisive manner. Thus it is presumably very improbable that the action of this soluble zymase is influenced by the presence or absence of air, but it is very possible, on the other hand, that the amount of zymase produced in a given yeast cell may depend largely on whether the latter is supplied with, or deprived of, free oxygen.

Of great interest is Pasteur's excursion, arising out of his studies of aërobic and anaërobic organisms respectively, into the question of the transformation of one species of micro-organism into another. The idea had become current amongst certain German and French biologists that moulds could give rise to alcoholic fermentation, that the spores of these little vegetable growths could produce real beer yeast; an opinion already expressed, as we have seen, by Bail in 1857 with respect to the mould *mucor mucedo.* Now, however, we find a certain M. Trécul affirming positively in 1872 that "*all* varieties of *penicillium* moulds, especially when young and vigorous, will exhibit this transformation into yeast."

Pasteur, although he publicly controverted the assertion that yeast could change into *penicillium glaucum*—such a statement being entirely at variance with his own experience—was not really in a position absolutely to repudiate the doctrine of the transmutability of species, for at this time he was under the firm conviction that the *mycoderma vini* could change under suitable conditions into an alcoholic yeast.

More extensive investigations, however, convinced him that the yeast cells which he discovered in his solutions sown with *mycoderma vini* did not owe their source to the latter, but to the outside air, and by elaborate precautions to exclude this chance of error Pasteur tells us that, "Never again did I see yeast or an active alcoholic fermentation follow the submersion of the flowers (*mycoderma vini*) either in the flasks themselves or in the experimental flasks connected with the former. . . . At a time when the notion of the transformation of species was so easily adopted, perhaps because it dispensed with rigorous accuracy in experimenting, it is not without interest to note that in the course of my researches on the culture of microscopic plants in a state of purity, I had once reason to believe in the transformation of one organism into another, in the transformation of *mycoderma vini* or cerevisiæ into yeast, and that at this time I was in error: I did not know how to avoid the very cause of illusion in my own case which the confidence in my theory of germs had so often enabled me to discover in the observations of others."

Still occupied with this subject of the supposed transmutability of moulds into yeast, we find him asking himself, Where do these ferments themselves come from? what is the origin of the grape yeast, for example? To answer this question he visits vineyards and makes careful microscopic examinations of the dust obtained from the surface of grapes; he inoculates some of this dust into sterilised grape-must and observes the growths which ensue, and describes the appearance of the yeast cells which make their appearance. By making examinations of grape-dust collected during different stages in the development of the fruit, he ascertains that whilst the latter is green, between the end of July and middle of August, no yeast cells are present on their surface, that later and during September the number continually increases, whilst in the subsequent months of the year they are only discoverable with difficulty.

He, however, still leans towards the idea that these yeasts may have their origin in a mould called *dematium*, abundantly present on the surface of leaves and especially prevalent on the wood of the vine at the time of the vintage, for he distinctly says, p. 177: "All conduces to the belief that at this period of the year (autumn) one or more of these dematiums furnish yeast cells."

In 1879 Pasteur carries out further experiments, the results of which led him to abandon this view of the origin of yeast cells, whilst he makes it an opportunity of exhibiting once more the truth of his vitalistic principle of fermentation phenomena.

A posthumous essay by Cl. Bernard raised once more objections to the acceptance of Pasteur's dictum that "A ferment is a living form which originates from a germ"; and the day after the appearance of this essay of Bernard's, Pasteur, bethinking himself of his investigations on the presence of yeasts on grapes at different periods of their development, plans a new experimental campaign, and, armed with a supply of small greenhouses, which he had had constructed, he remarks "sans trop de souci de la dépense," he starts at the beginning of August for the Jura, where he possessed a small vineyard of his own.

Here he erects his greenhouses, covering up portions of the vines, whilst at the same time, fearing lest any defect in the fitting up of his glass houses should permit the access of air from without, he also takes the precaution of wrapping up some specimens of grapes in sterilised cotton-wool. Meanwhile he had satisfied himself that at the time when he, as it were, imprisoned the fruit there were no yeasts present on their surface. Towards the commencement of October the greenhouse grapes were ripe, and on the tenth of the month he made his first comparative examination of the condition, as regards yeast cells, of the covered and uncovered grapes respectively. He found that in no single instance could he obtain alcoholic fermentation by means of the grapes protected from the access of air; on the other hand, when he uncovered the fruit and allowed it to remain unprotected in the open air, so that the yeast cells could settle upon its surface, he was subsequently easily able to induce fermentation by means of the grapes. In the case of the protected or non-fermenting grapes no yeasts were present: in the case of the unprotected or fermenting fruit, yeast abounded. Thus by a most original experiment did Pasteur once more illustrate the truth of his views on the dependence of fermentation phenomena upon life.

We remarked above that in these experiments Pasteur had effectually disposed of his original idea as to the supposed connection existing between the common mould *dematium* and the origin of yeast cells, and it was the repetition of his experiments which demolished this theory completely when recently resuscitated.

During the last two years the question of the derivation of yeasts from moulds has been energetically revived by more than one accomplished investigator and well-known authority on fermentation phenomena. Dr. Jörgensen, of Copenhagen, has been especially associated with this revival of ideas so prevalent at the time when Pasteur was carrying out the above investigations. The relationship, however, which Jörgensen, Juhler and others have endeavoured to establish between *dematium* and yeast cells has not borne the test of the rigorous and critical examination to which it has been submitted by several other investigators, and at present we have no experimental justification for refusing to yeasts the position of an independent group of organisms.

As regards the dissemination of yeasts, we may refer the reader to some very interesting investigations just published by Dr. Berlese in an Italian scientific journal, on the part played by insects in the distribution of alcoholic ferments. From these researches it appears that ants, in the course of their journeyings over grapes in search of food, deposit large quantities of yeast cells, the number and variety of the latter depending, seemingly, upon the source from which the ants were originally obtained. Thus when these insects were derived from vineyards, and made to crawl over sterilised grapes, the germs they conveyed were found to be chiefly moulds, together with some varieties of yeast known as *Saccharomyces apiculatus* and *ellipsoideus*. When the ants were collected from the trunks of oak-trees, they brought an abundance of *S. apiculatus*, with some *S. ellipsoideus* and *S. pastorianus*. If these insects, however, were transferred from olive-trees to grapes, no yeasts whatever were subsequently found on the latter. Berlese has also shown that flies materially assist in the process of infecting grapes with yeast cells, as well as with *dematium* and other moulds. This is effected by means of the excreta of flies, the yeast cells being able to pass uninjured through the digestive tract of these insects. Not only, however, are yeasts able to live within the bodies of flies, but it has been shown that they can also multiply in a very remarkable manner under these circumstances. Thus a fly originally fed with a small drop of must containing about 500,000 yeast cells (*S. apiculatus*), and subsequently only fed with *sterilised* must, emitted in the course of the eight days during which it received no further supply of yeast about 35,000,000 of such cells. It would appear, therefore, that not only may ants and flies distribute alcoholic ferments, but that these insects may actually furnish such micro-organisms with a nursery in which their vitality is so promoted that they are able to thrive and multiply abundantly.

* * * * *

Throughout this volume of Etudes, Pasteur shows unmistakable signs that his thoughts and ideas were leaning in the direction of the applications which his methods and discoveries might have in the interpretation and treatment of the phenomena of disease.

For five years he was, we have seen, investigating the diseases of silkworms, and although to all appearances he abandoned this direction of research, when he again took up the more prosaic study of yeasts, yet in reality he was becoming more and more deeply engrossed with the prospects which were gradually unfolding themselves before him of the far-reaching and beneficent results which might follow from a more intimate and extended knowledge of the nature and character of these microscopic forms of life.

CHAPTER X.

INTRODUCTION TO THE STUDY OF INFECTIOUS DISEASES.

ALREADY in his studies on silkworms, Pasteur's first experience in the domain of disease, the dawn of a new era in the contest of man with contagion, opens up before him. "Il est au pouvoir de l'homme," he writes, "de faire disparaître de la surface du globe les maladies parasitaires, si, comme c'est ma conviction, la doctrine de la génération spontanée est une chimère."

Again, in his "Etudes sur la bière," he makes the significant suggestion that "L'étiologie des maladies contagieuses est peut être à la veille d'en recevoir une lumière inattendue."

Indeed, his researches *had* already borne fruit in many of the directions indicated by the above words, for Rayer and Davaine were encouraged to once more approach the investigation of anthrax; "les petits corps filiformes," which they had observed in the blood of animals infected with this disease as far back as the year 1850, becoming endowed, as they acknowledge, with an entirely new significance and importance since the publication of Pasteur's researches on the butyric ferment in 1861.

But amongst a number of achievements in medicine and surgery, which their authors gratefully ascribe to the inspiration and suggestion which they had received from a study of Pasteur's brilliant researches of this period, by far the greatest and most important development is that which is universally associated with the name of Lister, and which has revolutionised the practice of surgery by introducing the antiseptic and aseptic treatment of wounds.

That this outcome of his researches was viewed with special satisfaction and pride by Pasteur we may gather from the fact that he reproduces in full in the pages of his "Etudes sur la bière," the letter addressed to him in 1874, "par le célèbre chirurgien d'Edimbourg, le Dr. Lister," who in forwarding Pasteur a memoir on the lactic ferment, takes the opportunity of sending him his most warm thanks "for having, by your brilliant researches, demonstrated the truth of the theory of putrefactive germs, and having thus given me the only principle which could lead to the success of the system of antiseptics."

Many years later, on the occasion of Pasteur's jubilee celebration, Lister, who was present as representative of the Royal Society, embraced the opportunity of again publicly referring to the debt of gratitude which the art of surgery owed to Pasteur's researches, and, rising and addressing M. Pasteur, pronounced the following words—as remarkable for their impressive truth as for their beautiful modesty:—

"Truly, there does not exist in the entire world any individual to whom the medical sciences owe more than they do to you.

"Your researches on fermentation have thrown a powerful beam, which has lightened the baleful darkness of surgery, and has transformed the treatment of wounds from a matter of uncertain and too often disastrous empiricism into a scientific art of sure beneficence. Thanks to you, surgery has undergone a complete revolution, which has deprived it of its terrors and has extended almost without limit its efficacious power."

Indeed, as Dr. Roux has recently so aptly stated: "C'est grâce à une expérience bien faite sur la fermentation que Pasteur, qui de sa vie n'a tenu un bistouri [dissecting knife], ni fait un pansement [bandage], a sauvé plus de blessés que tous les maîtres de la chirurgie."

Later on, in the year 1876, Pasteur received a letter from Professor Tyndall, in which the latter refers to the revival of the idea of spontaneous generation by Dr. Bastian in this country, which had induced him (Professor Tyndall) to take up the defence of Pasteur's position, to repeat his experiments, and to vindicate afresh the "inattackable exactitude of your conclusions." "For the first time," continues Professor Tyndall, "in the history of science we have the right to indulge the hope sure and certain, with regard to epidemic disease, that medicine will soon be delivered from empiricism and placed upon a sound scientific basis. When this great day shall come, humanity, in my opinion, will know how to recognise that to you is owing the greater portion of its gratitude."

Pasteur has himself described the "vive satisfaction" which this letter gave him, on learning that his researches had received the support of investigations made by a "savant, renommé par sa rigueur expérimentale autant que par la brillante et pittoresque clarté de tous ses écrits. La récompense comme l'ambition du savant est de conquérir l'approbation de ses pairs ou celle des maîtres qu'il vénère."

The excursion thus made by Tyndall into the study of microbial life, it may be incidentally remarked, has another special interest for us, as it was undoubtedly through this master of attractive exposition that many of our countrymen received their baptism in bacteriology. Not a few workers in this field at the present day had their enthusiasm for its study aroused by his magnetic influence.

Whilst, however, following with the closest attention and deepest interest the developments of his ideas in the hands of the medical world, whilst rejoicing in the partial realisation of his dream "that his researches might prepare the way for a deeper investigation of the origin of disease," Pasteur was not altogether satisfied with the manner in which the further extension and application of his methods was being carried on.

Dr. Roux describes how at this time "the experiments published by the members of the medical profession frequently appeared to him incomplete, the methods adopted defective, and the conclusions arrived at unjustifiable, and more likely to compromise the good cause than to promote it."

Pasteur himself sounds a strong note of warning in the following interesting extract, taken from the "Etudes sur la bière":

"I am the first, however, to regret that inferences are drawn beyond the scope of the facts acquired. The exaggeration of new ideas infallibly leads to a reaction, which again over-shooting the mark, casts disfavour upon what is correct and fertile in these ideas. Already in divers ways, and as a rebound from the exaggerations to which I have referred, one can perceive a thoughtless tendency to deny that certain diseases can be due to specific ferments of the same nature as those which have been discovered during the past twenty years, ferments both organised and living. All through one ought to keep to facts, control those which are announced if one is led to doubt them, study them afresh, and only deduce from them those ideas which, so to speak, can be regarded as justified, for the exploration of the subject has as yet hardly begun.

"Unfortunately, doctors delight in premature generalisations. Many amongst them are men of rare distinction either natural or acquired, endowed with lively intelligence, with a ready flow of elegant phrases, but the more distinguished they are the more they are absorbed by their craft, and the less leisure have they for the labour of research. Urged on, nevertheless, by that passion for knowledge belonging to men of distinction and which is fostered by the increasing scientific interest manifested by the upper classes, they eagerly get hold of easy, specious theories, the more general and appropriate to vague explanations as they are more weakly founded on facts.

"When we see beer and wine undergoing profound changes because these liquids have furnished a refuge for microscopic organisms which have there established themselves by some sort of mysterious chance, and have subsequently multiplied, how can we avoid being possessed by the thought that phenomena of the same order can and must of necessity be found sometimes in the case of men and animals?

"But if we are inclined to believe that this is so, because we consider it likely and possible, let us before asserting the same, recall the motto on this book* : 'The greatest distortion of the intellect is to believe things because one wishes them to exist.'"

Yet Pasteur still hesitated himself to undertake the responsibility of pursuing these investigations. "I am neither a doctor nor veterinary surgeon" he declared with modest diffidence. The world knows, however, now how the prophetic words written by Boyle two

* "Etudes sur la bière."

centuries before—"The man who shall probe to the bottom the nature of ferments and of fermentations will, doubtless, be much more capable than any other of giving a true explanation of the divers morbid phenomena, both of fevers as well as of other affections"—have been fulfilled in the person of Pasteur.

The long apprenticeship which he had served in the elucidation of abstruse chemical problems, and in the revelation of the functions of micro-organisms in the economy of nature, had equipped Pasteur, as no man before him had ever been, not only with the power of comprehending the complex problems of disease, but also with the means for their successful solution.

During his laborious researches on the maladies of beer, Pasteur had not only accumulated an immense amount of experience, but he had introduced extremely important improvements in his methods of investigation. Thus he had succeeded in obtaining for the first time cultivations of micro-organisms in a state of purity or freed from all foreign germs, by conducting a series of successive inoculations from one liquid medium to another, or by what is now known as "selective cultivation." By this method he isolated a number of different varieties of yeasts and bacteria, and submitted them to minute and careful observations. He had abandoned the exclusive use of mineral solutions for the cultivation of germs, and had introduced the important step of ascertaining the medium most suitable to the vitality and growth of each variety of micro-organism, and of then adopting the same as its food-material. Not only was his knowledge of the physiology and morphology of micro-organisms more profound than that of any of his contemporaries, but the refined technique of his methods, in the development of which he had been so ably assisted by his faithful assistants Joubert, Chamberland, and Roux, placed Pasteur in an unrivalled position to commence his attack upon the etiology of infectious diseases.

Thus Pasteur, almost in spite of himself, was hurried on from being a simple spectator of the labours of others, prompted by his researches, into becoming the inspired leader in whose footsteps a generation of ardent disciples have since trodden; and from this time onward down to the day of his death Pasteur never swerved from the pursuit of those researches by the light of which the principles of contagion were first revealed, and from which the revolution now slowly gaining ground in the treatment and prevention of disease has directly arisen.

Indeed, the hope is justified, in the words of a modern French writer, that "When man learnt how to protect himself from the wild beasts he made the first step in civilisation. To-day man is learning how to defend himself from the microbes—it is a step of equal importance. A day will come when in Berlin, in London, in Paris, man will not die of diphtheria, of typhoid, of scarlet fever, of cholera, or of tuberculosis, any more than he dies in these cities to-day from the venom of snakes or from the tooth of wolves."

CHAPTER XI.

RESEARCHES ON ANTHRAX.

AT the already ripe age of fifty-five, then, we find Pasteur devoting himself with all the energy and enthusiasm of youth to the study of pathological phenomena, and perhaps in the whole career of this remarkable man there is no spectacle which is more striking or instructive.

The best years of his life had, we have seen, been spent in studying the crystalline forms of obscure chemical compounds, in unravelling the chemical changes taking place in the brewer's vat, in the wine cask, in the vinegar factory; he had devoted years to discredit and overthrow the doctrine of the spontaneous generation of life—all of them subjects entirely outside the perspective of the medical practitioner or of afflicted humanity in general; and yet at a period of life when too many scientific men are contemplating repose and escape from their laboratories, Pasteur plunged into an entirely new sphere of research, in which he was not only to win his most glorious laurels but to fight his fiercest battles.

The malady which first attracted the attention of Pasteur was the infectious cattle disease called anthrax, a disease known and dreaded all over the world, and which in France alone in some years had meant a loss to the country of from fifteen to twenty millions of francs.

For centuries this scourge had been wrapped in mystery, and assuming as it did different guises according to the class of victims it attacked, the discovery of its essential character had been rendered yet more difficult and perplexing. It was only in the year 1850 that any real light had been thrown upon its nature by the discovery that it was communicable from one animal to another, and that although exhibiting different symptoms in different animals as well as in man, it was in each case one and the same agent which was responsible for the various morbid phenomena. At the time when the commission of inquiry appointed by the medical association of Eure and Loir was carrying on the investigations which had resulted in the above important conclusions, Rayer and Davaine published the now classical memoir on the etiology of anthrax, in which they call attention to the "small, thread-like bodies about twice as long as a blood corpuscle" found in the blood of anthrax infected bodies. This observation, the importance of which impresses us so forcibly at the present day, recognising in it as we do the original centre from which all the subsequent researches on the etiology of infectious diseases have sprung, received, however, but little attention at the time of its publication.

In fact, the discovery by Rayer and Davaine of these filiform bodies in anthrax blood, like the previous revelations of Latour and Schwann concerning the yeast cells in fermenting liquids, fell upon irresponsive soil. Both were opposed to the scientific *Zeitgeist* prevailing when they were published, and both announcements were stifled and prevented from bearing fruit for many years, through the opposition which they encountered from the leaders of science of the time.

This indifference is perhaps not so astonishing if we remember, that at this period leading scientific men, like Helmholtz, Ludwig, Brücke, Dubois Reymond, and their numerous followers, regarded the complete explanation of the phenomena of life on a physico-chemical basis as assured, and merely a question of time. Observations, therefore, which tended to shift the weighty responsibility of such complex phenomena as infection and disease upon minute parasitic organisms in the blood and tissues, appeared not only inadequate but almost ridiculous.

It was the particular mission of Pasteur, with his well directed and irresistible energy, to remodel this *Zeitgeist*, to overthrow the oligarchical sway of these captains of science, and so clear the way for a new order of things.

Notwithstanding the unsympathetic attitude of the leaders of science, this new line of research was silently proceeding. These filiform bodies, discovered by Rayer and Davaine, were again seen and emphasised in 1855 by Pollender, but immediately afterwards brought into discredit by Brauell, only to be again rehabilitated in 1860 by Delafond, who first succeeded in cultivating them in blood outside the body.

We have seen (*see* p. 123) how Rayer and Davaine were themselves unconscious of the epoch-making nature of their original discovery of the "petits corps filiformes" in cases of anthrax, until their interest and attention was again aroused in the matter by the researches of Pasteur on fermentation. Davaine returned with renewed energy to the re-investigation of anthrax, and in 1863 he was able to cite hundreds of experiments in which he had discovered these particular parasites in the blood of animals infected with anthrax, whilst he also demonstrated beyond question the contagious character of the disease by taking a small drop of blood from one infected animal and inoculating it into another healthy animal, and producing thereby the same disease in the latter, and so on through a series of eleven animals, with invariably the same result, that the blood became invaded with myriads of these same small rod-like bodies. In the course of his researches Davaine discovered an extremely interesting fact, *i.e.* the dependence of the course of the disease upon the number of bacteria originally introduced. He counts the individual rods present in a drop of anthrax blood, and estimates that from eight to ten millions are congregated together in this small space. He dilutes this drop of blood a million times without depriving it of its lethal properties; but he finds that although the morbid material is still present, its great dilution modified to a certain extent the course of the disease, that whereas an animal inoculated with undiluted blood succumbed to anthrax in twenty-three hours, when infected with the same blood diluted, it died in from forty-eight to fifty-three hours. Davaine had in reality by his researches conclusively shown that the blood of animals affected with anthrax could only communicate the disease when these rod-like bodies were present in it, and this discovery was again confirmed by Klebs, who, in 1871, filtered anthrax blood through porous earthenware cells, and showed that infection only followed when the solid residue left on the filter was inoculated, no symptoms of disease whatever resulting from the injection of the blood which had passed through the filter, and from which all the rod-like forms had thus been removed. Davaine, however, even after all his brilliant researches, was unable to convince the scientific world of the dependence of this disease upon living rather than chemical or physical processes; and the vitalistic theory of infectious diseases so eloquently revived by Henle already in the year 1840, was destined to languish until it received the support of Pasteur, who brought all the force of his genius and indomitable energy to bear upon its detractors and opponents. Davaine's researches, moreover, at this time, had been dimmed and questioned by the publication of some investigations made by Jaillard and Leplat, in which they claimed to have repeated his experiments, to have inoculated the blood of an animal certified to have succumbed to anthrax into rabbits, and to have failed, although inducing death, to find any symptoms of anthrax or any traces of the so-called anthrax bacteria in the blood.

When Pasteur entered the field in 1876, Robert Koch, then a humble *Kreisphysikus* in an obscure part of Germany, had already announced that he, likewise, had seen these rod-like forms described by Davaine in anthrax blood, and had succeeded in cultivating them through a number of generations in blood serum and in aqueous humour, and, most important of all, had observed their mode of multiplication under the microscope, and had seen that they effected their reproduction not only by fission, but also by the formation of spores, the incredible vitality of which he had demonstrated by actual experiment, showing—to quote his own words—that they "in kaum glaublicher Art und Weise ausdauern." Koch further indicated the importance of these spores in the etiology of anthrax by showing that they could lead to the infection of animals through the alimentary tract.

But convincing as the proofs furnished by Davaine and by Koch appear to us to-day, they stood in much need of corroboration and extension at the time; for twenty years ago it was with principalities of prejudice and with mighty powers of darkness that the new views concerning the bacterial causes of disease had to contend. It required a man of Pasteur's fearless originality and keen penetration to comprehend how order might be created out of disorder, to discern the truth which lay all but stifled under the *débris* piled up by prejudice and misconception, to rescue this truth, increase its brilliancy, and maintain it unsullied in the face of adverse scientific opinion based upon tradition and ignorance. To successfully accomplish such a task was indeed a mission for a master mind and will, and not without reason did his disciples and fellow workers speak reverently of him in after years as "Le Grand Maître."

Pasteur's first efforts were directed to dispose of the view so current amongst medical men that the virus of anthrax was distinct from the bacilli, which Davaine and Koch had laboured so zealously to prove were alone responsible for the disease. "In anthrax blood," it was urged in the medical world, "Davaine's rodlets are not alone present; side by side with them there are globules and plasma which contain the real amorphous virus. The cultures of Koch do not succeed in convincing us. He introduces into the drop of aqueous humour which he sows with anthrax blood not only bacteria, but also the virus contained in the plasma, and the series of successive sowings* which he carries on in drops of liquid only bring about a dilution of this virus. Now, is it not well known to us that the property of a virus is to act in infinitely small doses, and that it may be enormously diluted without losing any of its activity?" (Roux, Agenda du chimiste, 1896.)

Pasteur, like Koch, cultivates the anthrax bacilli, but instead of using for this purpose single drops of a culture liquid, he takes a flask containing some hundreds of cubic centimètres of a sterilised organic infusion such as urine rendered slightly alkaline, and inoculates it with anthrax blood collected with all the precautions which his previous researches had shown him would ensure his obtaining it free from all other organisms but those present in the blood itself, *i.e.* the bacilli of anthrax.

Having obtained a vigorous growth of the bacilli in this flask, he takes a trace of this liquid and inoculates a second flask, and continues until he has reached the hundredth generation. A trace of this hundredth generation, he showed, induced anthrax

* Koch in his original memoir describes how he made eight successive cultures from drop to drop of anthrax bacteria, and the latter taken from the last or eighth generation and inoculated into animals induced their death from anthrax.

as readily as if a drop of the original anthrax blood had been used for inoculation.

Pasteur had thus successfully disposed of the objection raised to Koch's results, for here could be no question of the disease being attributable to a diluted virus, for the original material employed was, as compared with the volumes of culture liquid into which it was introduced, like a drop in the ocean. No, here there could be no longer any doubt that it was the work of a living ferment capable of growth and self-propagation. That the disease of anthrax is not due to the chemical substances which are found along with the bacilli in the culture flasks, but to the action of the latter alone, Pasteur further showed by keeping the vessels containing the cultures at a low temperature, and allowing the bacilli in suspension to settle to the bottom, leaving the liquid in the upper layers clear. This clear liquid inoculated into animals had not the power of inducing anthrax, whilst a trace of the bacillar-sediment invariably ensured their death from the disease.

As is so frequently the case, in repeating and perfecting the experiments of other investigators, new discoveries of the highest importance are made; this was strikingly exhibited by Pasteur and Joubert in the course of their studies on anthrax. It has been previously mentioned (*see* p. 134) how Leplat and Jaillard had not only questioned the results obtained by Davaine, but had succeeded in exciting considerable distrust in his bacillar theory of the origin of anthrax through the circumstance that the animals which they had inoculated with blood derived from anthrax victims had indeed been killed by the inoculation, but that not a single anthrax bacillus could be found in their blood. In vain Davaine urged that the animals inoculated by Leplat and Jaillard had not succumbed to anthrax but to some other disease, for his efforts to find definite proofs that the disease was not anthrax failed completely. The refutation was left to Pasteur, who not only confirmed Davaine's opinion that the disease was not anthrax, but succeeded in showing what the other disease was, and to what it was due.

Pasteur made a number of examinations of anthrax blood and discovered that when the latter is collected immediately after the death of the animal and before putrefactive processes have commenced, it contains anthrax bacilli, but if some hours have elapsed since the death of the animal and the collection of its blood, the latter does not only contain anthrax bacilli but another micro-organism, which is normally present in the intestine and can only get into the blood after death. In many cases it completely overwhelms the anthrax bacilli present, for it flourishes abundantly in the absence of air, whilst the former cannot exist without oxygen, and hence the blood of an anthrax carcase frequently may contain no anthrax bacilli, whilst this other anaërobic bacillus obtains complete possession of the field.

Pasteur further showed with what virulent pathogenic properties this bacillus was endowed when it obtained access to the blood, for rabbits into which it was inoculated died even more rapidly than when infected with the fatal authrax bacilli themselves.

This micro-organism, which gives rise to a deadly septicæmia, is known commonly as the *bacillus of* *malignant œdema*, but it was called by its discoverers —Pasteur, Joubert, and Chamberland—*le vibrion septique*, and it was to the presence of this lethal vibrio in the putrid anthrax blood employed by Jaillard and Leplat that the death of their animals was due.

Pasteur makes a number of most interesting investigations as to the character of this new micro-organism, and points out that it is an anaërobic germ resembling in this particular the butyric ferment he had discovered in 1861 (*see* p. 46); he ascertains also that, although in its rod form it is destroyed by the oxygen present in the air, it can give rise to *spores*, which are capable of resisting the action of air. We are thus presented for the first time with a pathogenic anaërobic micro-organism, and the methods adopted by Pasteur for its cultivation have been since employed for other anaërobic micro-organisms associated with disease, such as the bacillus of tetanus or lockjaw.

The memoir in which Pasteur and his assistants communicated their investigations on anthrax and septicæmia to the Academy of Sciences in 1877 is famous not only on account of the successful manner in which they mastered the etiology of these diseases, but also for the extreme fertility and originality of the ideas and experiments which it records. Thus we have the first suggestion of the association of microbes in disease, a subject which is being vigorously pursued at the present day, and upon which we have by no means heard the last word. Pasteur was led not only to speculate but to experiment in this direction: he introduces ordinary aërobic organisms into infusions along with anthrax bacilli, and finds that the former, growing more rapidly than the latter, get possession of the oxygen and consequently succeed in starving their rivals. To this observation he imparts practical importance by showing that "anthrax bacilli may be introduced into an animal with impunity when the liquid inoculated contains also along with the former an abundance of ordinary harmless bacteria."

Another instance of the fertility of Pasteur's ideas and the prodigality of his experimental resources during these classical studies on anthrax, is to be found in his investigations on fowls in respect to this disease.

Pasteur was confronted by the fact that although he inoculated anthrax bacilli all equally virulent into various kinds of animals, some of the latter failed to develop anthrax. Thus whilst he was easily able to communicate anthrax to oxen, sheep, rabbits, and guinea pigs, he rarely succeeded in infecting either dogs or pigs, whilst he was never able to produce the disease in fowls.

To what could this failure be attributed? Obviously some circumstances of which Pasteur was ignorant operated against the development of the anthrax bacillus in these animals. Nothing daunted, Pasteur and his assistants set to work to study more closely the idiosyncrasies of this microbe, or in other words, the conditions which affected its vitality in artificial cultivations outside the body. These investigations revealed the interesting fact of the sensitiveness of anthrax bacilli to even such a slightly elevated temperature as is possessed by the blood of fowls, and the idea immediately occurs to Pasteur of artificially reducing the temperature of these birds and seeing if inoculations with anthrax would take effect under these circumstances. A fowl was inoculated with anthrax and subsequently made to stand with its feet in cold water, so that its temperature was reduced from 42 degrees C. to from 37 to 38 degrees C. At the end of forty-eight hours the bird was dead, and on examination its blood was found to be teeming with anthrax bacilli. Another variation of the experiment was made by infecting the fowl, reducing its temperature, and then on the first sign of anthrax disease making its appearance, the fowl, instead of being further submitted to the cooling process, was carefully wrapped in cotton wool and kept at a temperature of 35 degrees C. Under this fostering care the bird gradually regained its vitality, and when it was completely restored to health it was killed, but on now examining its blood not a single anthrax bacillus was discovered.

An interesting confirmation of these experiments in the opposite direction has been furnished by Gibier in respect of the susceptibility of frogs to anthrax. These amphibians are normally unsusceptible to anthrax infection, their temperature being too low to admit of the growth of the anthrax bacilli within their system; but by gradually accustoming them to live in warm water their body temperature becomes sufficiently raised to permit of the development and multiplication of these bacilli within them, and by these artificial means they can be made to contract anthrax.

Engrossed with the interest of these pathological researches Pasteur casts about him in all directions for material; he walks the hospitals armed with sterile vessels to collect morbid products, heroically overcoming the natural antipathy of a sensitive nature to the sight of suffering and distress; he cultivates the *staphylococcus pyogenes* from boils on the person of one of his assistants, and from its appearance and character boldly asserts its identity with the organism found in cases of osteomyelitis; he visits the Maternity Hospital and discovers the *streptococcus pyogenes*, asserting it to be the cause of puerperal fever.

In connection with this discovery an instructive incident is related by M. Roux. One day at a discussion on puerperal fever which was taking place at the Academy of Medicine, whilst one of the most distinguished authorities was eloquently descanting on the causes of epidemics of this disease at Maternity Hospitals, he was suddenly interrupted by Pasteur: "ce qui cause l'épidemie, ce n'est rien de tout cela; c'est le médecin et son personnel qui transportent le microbe d'une femme malade à une femme saine." And when the speaker replied that he was much afraid that they would never discover that microbe, Pasteur rushed to the blackboard and drew the streptococcus, exclaiming, "Tenez, voici sa figure." The surprise, the stupefaction which this assurance of a novice in pathological study caused amongst the assembly of learned doctors, is more easily conceived than described.

There can be no doubt that the great fertility of Pasteur's researches in so many different departments of science was due to his at once seizing upon the essential point of a question, and that he always directed his attention to the main line of an inquiry without allowing his time and energies to be frittered away by side issues and considerations of secondary importance. Thus, as we have so frequently seen, whilst there was no detail insignificant enough to escape his observation, yet these details were at once sifted by him, and only those which were of importance to his train of thought utilised. In fact he entered the most widely different departments of knowledge, not because of his special interest in them, but only because the continuous course of his ideas led from the one to the other.

Thus in his biological studies he was utterely indifferent to the purely morphological questions in which so many investigators in this branch of science appear to find a permanent anchorage. He never bestowed, for example, botanical names upon the micro-organisms which he discovered. The microbe which he isolated from boils was sufficiently endowed with the title "microbe en amas de grains," whilst that of puerperal fever he recognised as "microbe en chapelet de grains," names which have long since been exchanged for *staphylococcus* and *streptococcus pyogenes* respectively.

M. Duclaux relates how an able morphologist came to the laboratory one day and explained to Pasteur in the most courteous terms that a particular organism which the latter had described as a micrococcus was in reality a small bacillus, information which only evoked the brusque reply, "Si vous saviez combien cela m'est égal," a remark which very clearly indicates his attitude of mind and his power of dissociating the essential from the non-essential, his discrimination between the things which belong to nature and the things which are the outcome of the vanity of man.

Before following Pasteur into his further progress in the domain of pathology, a few words are necessary to convey some idea of the conditions under which these and other bacteriological researches were being pursued. When he first entered upon the study of bacteria he was met in every direction by difficulties which were occasioned through the absence of reliable methods and a technique based on experience. We have seen how he overcame all these obstacles, how he contrived the means of procuring sterile culture media, how his intimate study of bacteria induced him to devise various kinds of culture materials according to the individual requirements of the organisms which he was handling, how he was able to separate out by skilful methods numbers of different varieties of yeasts and bacteria, how in fact he had elaborated with his own efforts and those of his assistants a complete scheme, as it were, by means of which the pursuit and accurate study of bacteria could be carried on. Whilst, however, Pasteur by his teaching and example was stimulating bacterial researches in all directions, Robert Koch had still further facilitated such investigations by the beautiful improvements which he had introduced into microscopic technique.

In 1875, a red-letter year in the annals of microscopy, Weigert discovered the method of staining bacteria with aniline colours, and in the hands of Koch this discovery led to the most brilliant results. In 1877 appeared his masterly treatise on the investigation, preservation, and photography of bacteria, which was followed in the next year by his classical investigations on the etiology of the infectious diseases of wounds. What had before been wrapped in mystery or seen with difficulty was now for the first time placed within the easy reach of every investigator; bacteria could be discovered with the greatest facility, their appearance studied, and their presence in the various tissues demonstrated with a precision which was altogether unprecedented.

Robert Koch's services to bacteriology did not, however, stop here; for with his name is associated that great advance which introduced transparent solid media for the isolation and cultivation of bacteria.

Already, as far back as the year 1872, solid media had been employed by Schroeter, who observed and recorded the growth and appearance on slices of cooked potatoes of the *bacillus prodigiosus* and other pigment-producing bacteria. Schroeter used also white of eggs, meat, and white bread for cultivating bacteria, but he does not appear to have employed gelatine in any of his investigations, although undoubtedly to him belongs the credit of having first isolated bacteria by means of solid culture media.

Gelatine was originally introduced for the cultivation of bacteria by Vittadini, Klebs, and Brefeld. Klebs, in a memoir which he published in 1873, describes how he endeavoured to "fix" a micrococcus under the microscope in order to watch its division, and he relates how, in order to overcome the difficulties, such as movement and evaporation, attending the use of liquid drops, he substituted melted gelatine, which solidified when cold.

Brefeld, in 1881, to continue the history of the introduction of gelatine for the cultivation of bacteria, employed this material, which, he says, he "added to culture fluids in order to prevent evaporation." He also mentions that this addition of gelatine favoured rather than damaged the development of moulds, whilst such culture material placed on cover-glasses enabled the latter to be turned upside down, so that the organisms present could be studied with high powers. So far, therefore, the addition of gelatine to culture media had been made with the object of facilitating microscopic observations; no idea was entertained of separating out or isolating individual bacteria by its means; and it is to Robert Koch that we owe this apparently simple but so profoundly important step. Since the adaptation by Koch of transparent solid media for the cultivation of bacteria in 1881, and the introduction of his method of isolating bacteria by means of gelatine plate cultures in 1883, the study of micro-organisms has advanced by leaps and bounds, and the facilities which it has offered for the examination of air and water are but a few of the benefits which gelatine plate culture have bestowed upon bacteriology.

* * * *

Before leaving the classical researches of Pasteur and his assistants on the etiology of anthrax, we are tempted to give the reader an extract from the interesting account of some of the circumstances under which they were carried out, which has been furnished by Dr. Roux:—

"For many years the laboratory in the Rue d'Ulm was abandoned towards the end of July for Chartres. Chamberland and I took up our abode here, and were joined by a young veterinary surgeon. Every week Pasteur came to superintend and to inspect our investigations. What happy memories those campaigns against anthrax in the Chartrain country have left us! The visits early in the morning to the sheep-folds scattered over the great plateau of Beauce, which lay basking in the August sun; autopsies carried out at Sours or on the farms, and in the afternoons the recording of the results in the note-book, letters to Pasteur, the starting of fresh researches.

"The day was well filled up, and how absorbing and how health-giving was this bacteriology carried out in the open air! The days when Pasteur came to Chartres the déjeuner was hurried over, and quick into a carriage to drive to Saint Germain, where M. Maunoury had willingly placed his farm and his herds at our disposal. During the drive we discussed the experiments of the past week, and planned fresh ones to be under taken. As soon as he arrived, M. Pasteur hurried, without losing a moment, to the enclosures. Motionless he would stand close to the hurdles, inspecting with the minutest attention the animals which were specially under observation, not a detail escaping him. For hours he would watch over a single sheep which he believed to be ill, and it was necessary to remind him of the hour, and to point out to him that the towers of the Cathedral of Chartres were fast growing dim in the dusk, before we could persuade him to return.

"He would interrogate the labourers as well as the farmers, and he gave much weight to the opinions of the shepherds, who, in their lonely life, concentrate all their attention upon their flocks and frequently become the most sagacious observers. Nothing seemed insignificant to Pasteur; from the smallest circumstance he knew how to derive some unexpected clue.

"The original idea of the possible part played by worms in the distribution of anthrax was started one day during a walk he was taking in a field belonging to the St. Germain farm. The harvest was over and only the stubble was left. Pasteur's attention was attracted to a particular portion of the field on account of the different colour of the soil. M. Maunoury explained that the previous year they had buried sheep which had died of anthrax in that place.

"Pasteur at once went and examined the ground more closely and noticed immense numbers of worm-castings scattered over the surface. The idea occurred to him that these worms, in their repeated journeys from the depth to the top, must bring up the rich soil which surrounds the carcases, and with it possibly the spores of anthrax which must be present in their vicinity.

"Pasteur never stopped at ideas; he passed directly on to their verification, and the germs of anthrax were actually discovered in the intestines of worms, taken from a ditch in which several years previously anthrax carcases had been buried.

"His researches on the etiology of anthrax" (continues Dr. Roux) "remain as a model. Medicine had never before witnessed such perfection in experiments, such rigour in deductions, such certainty in application.

"Pasteur felt indeed that a decisive battle was being fought, and he neglected nothing to ensure for himself the victory."

A yet greater victory was, however, awaiting Pasteur, and in a direction moreover towards which he had for some time past been slowly though surely drifting.

CHAPTER XII.

FIRST RESEARCHES IN THE DOMAIN OF IMMUNITY.

PASTEUR'S mind was gradually becoming more and more occupied with the idea of utilising the knowledge of viruses which he had obtained, for inducing in some manner, as yet unknown to him, immunity from the diseases of which these viruses were the active principles.

"Il faut immuniser contre les maladies infectieuses dont nous cultivons les virus," was Pasteur's constant cry to his assistants at this time. Haunted by this idea Dr. Roux tells us how, during the busy period which preceded the discovery of the attenuation of viruses, numbers of impossible experiments were gravely discussed amongst them, to be only laughed over the following day.

In order to follow all the steps which led to this truly epoch-making discovery, yet another living virus, viz. that of fowl cholera, must be mentioned, which Pasteur already identified in these earliest days of his pathological researches.

"A bird afflicted with this malady," writes Pasteur, "is weak and tottery, its wings droop, its feathers become ruffled, giving it the appearance of a round ball. It is overcome by an invincible somnolence. On being forced to open its eyes it appears to be waking from a profound sleep. The eyelids rapidly close again, and most frequently death supervenes after a dumb agony without the animal having ever moved from the spot."

The dependence of this disease upon a micro-organism was first suspected by an Alsatian veterinary surgeon, whilst an Italian, one Peroncito of Turin, actually described this micro-organism in 1878, and his discovery was confirmed in the following year by Toussaint, a professor at the veterinary college of Toulouse.

But although this particular microbe had been seen and had been seriously suspected of being responsible for this disease, the irrefutable proof of its connection with fowl cholera was wanting, and Toussaint, stirred up by the brilliant success of Pasteur's researches on anthrax, determined to consult the latter on the results which he had obtained and to ask him to fully investigate the matter.

Pasteur eagerly embraced the opportunity thus afforded to him of extending his knowledge of diseases, and converted part of his laboratory into what was practically a poultry-yard, and the systematic study of this new malady was vigorously pursued. Like his predecessors, Pasteur observed the presence of the microbe described by them in the blood of infected birds, but he went a great and important step farther; he succeeded in cultivating it outside the animal's body, and in artificially inducing the disease in other fowls by the inoculation of such cultivations. He found, moreover, that this micro-organism, which is now known as the bacillus *choleræ gallinarum*, so lethal in its effect on fowls, produced only a passing and slight abscess when inoculated into guinea pigs, although when taken from such abscesses and again introduced into fowls it was found not to have parted with one jot of its original virulence in respect of the latter. The contagious character of this disease was further shown by the fact that healthy fowls placed in the same cage with guinea pigs suffering from such abscesses became infected and rapidly succumbed to fowl cholera. Pasteur discovered in this manner that rabbits were also extremely sensitive to the lethal action of this microbe, and some ten years later he utilised this fact in suggesting to the Government of New South Wales that the Australian rabbit plague should be combated by the artificial dissemination of this bacterial virus amongst these destructive rodents. The suggestion was not accepted by the Government, chiefly on account of the reluctance which was felt to introduce what, at that time, was looked upon as a new disease into the colony. The idea, however, has recently been revived, as it has been since discovered that fowl cholera has existed there for many years past, its presence having been formerly ignored, owing to imperfect knowledge of the nature of the disease and inability to diagnose it in afflicted birds.

But this year, 1880, which had thus seen another disease tracked to its source, which had thus furnished new important evidence as to the vital cause of contagious disease, was also to witness a discovery, the far-reaching application of which we are only now beginning to appreciate, and which has opened up an entirely new field of investigation, and promises to change the whole aspect of modern medicine.

This great discovery was the attenuation of virus and the artificial production of immunity, and was led up to by one of those events which when occurring singly appear as wholly the work of chance, but which, when recurring again and again in connection with one and the same individual, are the most unmistakable evidence of genius.

The investigations on fowl cholera had been commenced in the year 1879, and had been vigorously and uninterruptedly pursued until they had to be temporarily suspended owing to the vacation. All who have seriously worked with bacteria must have experienced the difficulties which stand in the way of taking any prolonged holiday. To the chemist the vacation often comes as a welcome assistant in his researches; refractory oils and unpromising syrups, which are set aside almost in despair at the end of the term, often greet us on our return to work with crystalline forms which gladden the eye and make the heart beat with redoubled vigour at the prospect of renewing our labours; but the bacteriologist returns after a hardly earned holiday only to find that the cultivations, which have perhaps taken him months or even years to obtain, are either languishing or even defunct through the want of that maternal solicitude which he was wont to lavish on them, or that they have suffered contamination while consigned to the stepmotherly care of some unworthy assistant.

On the reopening of the laboratory, the dismay of Pasteur may be imagined when he found that nearly all his cultures had in the interval died off or become sterile. Numerous efforts were at once made to revive those which still showed signs of life; they were transplanted into fresh culture material, and fowls were inoculated, but in many cases no evidence of life was displayed in the tubes, and the animals remained provokingly healthy. There seemed to be no alternative but to discard all the old series of cultures and start *de novo*, when the idea occurred to Pasteur to infect these same fowls, which had so effectually resisted the previous inoculations, with a young and vigorous growth of the microbe. To the astonishment of all, Pasteur included, nearly all these fowls survived the inoculation, whilst other fowls, similarly infected, but which had not previously been experimented upon with the weakened cultures, died, exhibiting the usual typical symptoms of the disease. Convinced that this was no chance circumstance, but that he was here face to face with an entirely new phenomenon, Pasteur repeated the experiment in various ways, and found that he had indeed realised his great ambition of "immunising against an infectious disease of which they cultivated the virus," and the microbe, which hitherto had only proved a malignant foe, was constrained to become the beneficent protector of its prey.

Numerous investigations were now carried out to ascertain upon what factors this conversion of the virus into a vaccine was dependent, and before long Pasteur was able to announce the methods by which this transformation could be effected with certainty. The secret lay in the prolonged action of the air upon the culture at a suitable temperature. Whereas, a young growth of the microbe is extremely lethal in its action, if it be kept at a temperature of 37 degrees C. in a tube plugged with cotton wool, to which, therefore, air has free access, it gradually loses its virulence in proportion to the length of time it is preserved under these conditions. If, on the other hand, the cultivation is carried on in a closed tube from which air is excluded, it will retain its virulent properties.

Pasteur also discovered that this attenuated or weakened fowl-cholera virus retained its modified character in subsequent generations, that this protective power or immunising property was transmissible or hereditary. By suitable cultivation a permanently modified race of bacilli had been raised, and we shall see later how this principle was applied for the elaboration of other vaccines. With what confidence and rejoicing this great discovery of Pasteur's was received by the Academy of Sciences we may judge by the spontaneous eloquence of a member who was present when the communication was made. "Ce n'est là qu'un commencement. Une doctrine nouvelle s'ouvre pour la médecine, et cette doctrine m'apparaît puissante et lumineuse. Un grand avenir se prépare; je l'attends avec la confiance d'un croyant et le zèle d'un enthousiaste."

It was in 1881, on the occasion when the International Medical Congress met in London, that Pasteur, discussing his latest discoveries in the domain of immunity, paid a graceful tribute to his great predecessor nearly a century before him, in this direction: "J'ai prêté à l'expression de vaccination une extension que la science, je l'espère consacrera comme un hommage au mérite et aux immenses services rendus par un des plus grands hommes de l'Angleterre, Jenner."

Pasteur's attention, indeed, had long been riveted on that great achievement of Jenner's which towers in royal isolation above the plains of the medical history of centuries, an achievement which, as Herbert Spencer has pointed out, a grateful country has, up to the present, rewarded by a begrimed statue hidden away in an obscure corner of Kensington Gardens, frequented chiefly by nursemaids and perambulators.

CHAPTER XIII.

DISCOVERY OF ANTHRAX VACCINE.

From this time onwards Pasteur's attention became riveted upon the artificial production of attenuated viruses or vaccines. Stimulated and encouraged by the extraordinary piece of good fortune which, as we have seen, had launched him on his first voyage into those regions which had so long appeared only as the shadowy illusions of a vivid imagination, he now set to work with all his customary zeal and enthusiasm to prepare the vaccine of anthrax.

The virus, we have seen, was to hand; for months past Pasteur and his assistants had been busily engaged in studying its character, and it was only natural, therefore, that this disease should be the next to furnish material for further investigations on the artificial production of immunity.

At the very outset, however, the experiments met with a serious check from the fact that the virus of anthrax differs in a very important particular from that of chicken cholera. We have seen that to elaborate a vaccine in the case of the latter disease, it was only necessary to allow the bacterial cultures to age considerably in the presence of air; but this simple method was found to be quite inapplicable to anthrax, for this micro-organism, unlike the bacillus of fowl cholera, multiplies not only by fission, but also by the production of spores.

Now, the preservation of anthrax cultures over prolonged periods of time neither weakens nor destroys these spores, so that the virus after ageing has lost nothing of its virulence.

It was obvious, therefore, that the method so simple and effective in the case of fowl-cholera virus, could not be applied without important modifications to the attenuation of the virulence of anthrax cultures. Pasteur then planned a scheme of experiments based upon the assumption that in its simple bacillar form anthrax would be as sensitive as the bacilli of fowl cholera to those conditions of environment which had so profoundly modified the virulence of the latter.

"Let us find out how to prevent the corpuscular germs (spores) of anthrax from being produced," argued Pasteur, "and we shall have surmounted the difficulty; for once freed from these corpuscular germs, the anthrax threads (bacilli) can be kept in contact with air during a given time, and we shall then have possibly secured the conditions which led to the attenuation of the fowl-cholera microbe."

Innumerable were the experiments which Pasteur and his two assistants, Chamberland and Roux, carried out. Pasteur became more and more pre-occupied, and wore that air so familiar to those around him, and which his daughter used to designate as "la figure à découverte prochaine"—a state of mind of intense nervous tension and excitement, which, however, was only evident to those in his immediate surroundings by his abstraction and silence, a condition which has again been well described in the following graphic manner by Dr. Roux:—

"Of Pasteur it may be said that he has made his discoveries by continually thinking over them. His thoughts attached themselves obstinately to the difficulties, and ended by solving them, just as the intense flame of a blowpipe constantly directed upon a refractory substance ends by melting it. During these moments of great pre-occupation Pasteur remained silent, even in his own family circle. Nothing was able to smooth the determined lines in his face until the solution was found. Then his countenance became illuminated, and this reserved man allowed his joy to overflow around him, and he described what he had planned and what he hoped. For Pasteur's surroundings were associated with his scientific life; they submitted to the *contre-coup* of his pre-occupations and shared in the rejoicing of the savant."

At length the day arrived when, hastily leaving the laboratory, he announced to his family the success which had at length crowned the long and patient labours which had cost him so much mental and physical strain—the discovery of a vaccine for anthrax. "Jamais," writes his son-in-law, M. Vallery-Radot, referring to this incident, "je n'ai vu sur une physionomie un plus grand rayonnement de toutes les émotions hautes et généreuses que peut contenir l'âme humaine."

But even at these moments of supreme scientific triumph the patriotic sentiment asserted itself, and showed what a large place it occupied in the savant's heart; for says the same family biographer: "'Je ne me consolerais pas,' nous dit-il en nous embrassant, 'si une découverte comme celle que nous venons de faire, mes préparateurs et moi, n'était pas une découverte française!'"

By cultivating anthrax in the presence of air at

42 degrees to 43 degrees C. it does not form spores. It is found, after being kept for two, four, six, or eight days, to have abated its original virulence according to the length of time it has been preserved in these unfavourable conditions, thus affording a series of vaccines of different degrees of strength. These attenuated anthrax bacteria retain, moreover, their enfeebled character in subsequent generations, and thus the production of a graduated series of attenuated vaccines offers no difficulty and becomes a mere matter of laboratory routine.

Thus to confer immunity from anthrax it is only necessary to select from the series of vaccines one which, whilst sufficiently virulent to induce a passing manifestation of the disease, is not strong enough to destroy the animal, and yet by reason of the modified symptoms engendered suffices to protect the latter from the subsequent lethal effects of anthrax virus possessing its full complement of toxicity.

In actual practice it is customary to make two vaccinations at an interval of twelve days, the first with a very weak virus, the second with a stronger virus which completes the immunity.

It was on the 28th of February, 1881, that Pasteur communicated to the Academy of Sciences, in his own name and in that of Chamberland and Roux, the famous memoir on the attenuation of anthrax virus; and hardly had the results been made known when Pasteur was approached by the President of the Agricultural Society of Melun, with a view to the organisation of a public demonstration of the value attaching to these new protective methods. Pasteur gladly accepted the challenge, and the details of the programme to be followed were drawn up and arranged between him and the Melun Agricultural Society just two months after he had first communicated his results to the French Academy.

Dr. Roux has described the details of this remarkable performance, in which he took a prominent part, in such a vivid manner that we cannot do better than quote the account of it which he has given.

"Chamberland and I were on our holidays. Pasteur wrote to us to return immediately, and when we were once more together in the laboratory, he gave us an account of what had been agreed upon. Twenty-five sheep were to be vaccinated and afterwards inoculated with anthrax at the same time as twenty-five non-vaccinated sheep; the first set would resist infection, the second would succumb to anthrax. The terms were precise, no place was reserved for the unexpected. When we remarked that the programme was a severe one, but that there was nothing left but to carry it out since it was signed, Pasteur replied: 'What has succeeded with fourteen sheep in the laboratory, will succeed equally well with fifty at Melun.' The animals were brought together at Pouilly-le-Fort, near Melun, on the estate of M. Rossignol, a veterinary surgeon, who first originated the idea of the experiment, and who was entrusted with its superintendence. 'Above all do not get your flasks mixed up,' said Pasteur gaily, when on the 5th of May we left the laboratory to make the inoculations with the first vaccine. Those with the second vaccine were carried out on the 17th May, and every day Chamberland and I went to inspect the animals.

"During these journeys from Melun to Pouilly-le-Fort, many remarks came to our ears which showed that it was not everyone who believed in the success of the undertaking. Agriculturists, veterinary surgeons, doctors, followed the experiment with the greatest interest, some even with feelings of the keenest excitement.

"In 1881, the science of microbes had hardly any partisans many considered the new doctrines as pernicious, and the fact that Pasteur and his assistants had been drawn beyond the precincts of the laboratory was regarded as an unexpected opportunity for their open discomfiture in a public trial. These novelties so compromising for medicine would be swept away at one stroke, and the safety of wholesome traditions and ancient practices, menaced for a moment, would be restored !

"In spite of all the passion and prejudice which surrounded it, the trial followed its course. The experimental inoculations were made on the 31st May, and a meeting was arranged for the 2nd June for the verification of the results.

"Twenty-four hours before the decisive day, Pasteur, who had anticipated the public trial with such perfect confidence, began to regret his boldness. For a few moments his faith wavered, as if the experimental method might betray him. A too continuous mental tension had brought about this reaction, which, however, did not last long. The following day, more confident than ever, Pasteur was able to confirm the brilliant success which he had predicted. In the eager crowd assembled that day at Pouilly-le-Fort, there were no more unbelievers, only admirers."

The immediate result of this magnificent triumph was a pressing demand from all parts of the country for vaccine, numerous agricultural societies were fired with ambition to repeat the celebrated experiment of Pouilly-le-Fort, and Pasteur was besieged with correspondence. A small additional laboratory was hastily improvised where the preparation of vaccines was carried out, and already by the end of the year no less than 33,946 animals had been vaccinated.

The burden of work which all this meant for Pasteur may be imagined, as he personally superintended the production of the vaccine and its dispatch to its various destinations, whilst he invariably followed the course of the inoculations, which alone involved a mass of letters dealing with the various details of the process, replying to complaints, and answering adverse critics, amongst whom in those days were ranged Koch and Loeffler.

In spite, however, of prejudice and hostile opinion, the protective inoculation against anthrax grew more and more in public favour, and in a report drawn up by Chamberland in 1894, who, after the first demonstration at Pouilly-le-Fort, was made responsible by Pasteur for the production of the vaccine, we learn that in the preceding twelve years 3,296,815 sheep were vaccinated, with a mortality of about one per cent., and 438,824 oxen and cows, with a mortality of about 0·34 per cent.

The mean annual mortality from anthrax amongst sheep not vaccinated is given in France as 10 per cent., and amongst horned cattle 5 per cent.

Chamberland in his report further points out that the saving to French agriculture which has accrued from the use of Pasteur's vaccine may be estimated as at least five millions of francs with regard to sheep and two millions in respect of oxen and cows.

But, as Dr. Roux has well said, the immediate results are the least merit of the Pasteurian vaccinations; they have imparted an immense public confidence in the science which has achieved such great triumphs and aroused so much interest. Above all, they have inaugurated that series of researches on immunity which at last is leading us towards an efficacious therapy for infectious diseases.

Pasteur, however, having succeeded in artificially controlling the degree of virulence possessed by anthrax and fowl cholera cultures, set to work to ascertain whether and to what extent such attenuated races of bacteria could be re-endowed with lethal properties. The short note which contains the account of these most original and suggestive investigations was communicated to the Academy of Sciences early in the year 1881, and bears also the names of Roux and Chamberland.

Although anthrax reduced to the condition of a vaccine is incapable of procuring the death of an adult animal, yet if these weakened anthrax bacilli be inoculated into extremely susceptible animals, such as mice and guinea-pigs but one day old, the latter succumb to its action, and the blood of these animals introduced into rather older mice and guinea-pigs succeeds also in fatally infecting these, and so on until the stage has been reached, when, through the successive passage of the virus through the bodies of animals, the original attenuated race of anthrax bacilli has regained its full complement of virulence and can once more destroy large animals, such as sheep and oxen.

Similar results were obtained with the vaccine or weakened bacilli of fowl-cholera, their lethal effects on fowls themselves being gradually restored by passing the attenuated microbes through the bodies of small birds, such as sparrows, canaries, and pigeons, until their virulence was fully regained and fowls once more fell victims to their action.

Pasteur points out that what has thus been successfully accomplished in the laboratory may not unreasonably be conceived to take place in nature—that just as the action of the atmosphere may weaken a virus and so bring about the extinction of an epidemic disease, so the impression of virulence upon an otherwise harmless microbe by its passage through the system of an animal, or by other means yet unknown to us, may possibly account for the origin, in past ages, of infectious diseases.

But besides increase of virulence we may also obtain diminution of virulence by passing the virus through the bodies of suitable animals, and this was done by Pasteur and Thuillier in the course of their investigations on the disease known as swine measles or *rouget des porcs.* By successively passing the virus of this disease on from pigeon to pigeon the virulence is so greatly augmented towards these animals, that they succumb far more rapidly to its effects than when the virus is taken direct from a pig suffering from the disease ; moreover, this pigeon-treated virus is even more rapidly fatal to pigs than in its original condition.

If, however, instead of pigeons, rabbits be employed, the virus instead of increasing in virulence becomes less fatal in its effects, until finally it is incapable of killing pigs, and only renders them ill, leaving them, however, vaccinated against a fatal attack of the disease.

We shall see later how Pasteur utilised these principles in the methods he was led to adopt for the attenuation of another virus.

In connection with the researches on swine measles published in conjunction with Thuillier, a young, extremely able and enthusiastic student and assistant of Pasteur's, we find a pathetic little communication from Pasteur a couple of years later to the Academy announcing his death: "La science perd en Thuillier un de ses courageux représentants et du plus grand avenir. Je perds un disciple aimé et dévoué, mon laboratoire un de ses principaux soutiens. Je ne me consolerai de cette mort qu'en pensant à notre chère patrie et à ce qu'il a fait pour elle."

CHAPTER XIV.

RABIES.

It must not be supposed that, absorbing and laborious as these investigations on vaccines were, they represent by any means the whole extent of Pasteur's activity at this time, for simultaneously experiments were being carried on in quite another direction, the study of hydrophobia having been already commenced in the year 1880.

In extending his beneficent investigations to the study of rabies, Pasteur thus finally devoted his energies to combating disease in man himself. These last labours, moreover, display in the highest degree those remarkable qualities which had characterised his whole career, and for the performance of these labours the powers and experience gained during nearly forty years of ceaseless scientific activity were called into requisition and submitted to the severest strain.

It has appeared a most unaccountable circumstance to many that in approaching the diseases of man Pasteur should have made the selection which he did in taking hydrophobia as the first human malady to which he was determined to apply those prophylactic measures which had been found so successful in combating some of the diseases of animals. Thus, terrible as hydrophobia may be to the individual affected, it is of little absolute importance to the human race as a whole, claiming as it does perhaps a smaller number of victims annually than almost any other well-recognised malady.

In making this selection Pasteur was doubtless guided by that instinct which leads the experimental genius to choose those subjects of research which are ripest for attack at the time, and quite irrespectively of their immediate practical importance to the world in general. Experience has, in fact, fully justified the selection of this comparatively obscure human disease as the one on which to make the first assault with the scientific weapons which his researches on fowl-cholera and anthrax had created.

The wisdom of Pasteur's selection doubtless depends on rabies being a well-defined disease in both animals and man, and that it can therefore be fully investigated by direct and real experiment on animals, and not merely by those statistical methods which have in general to pass muster as experiments in medicine.

We venture to think that there is the more force in these remarks from the fact that so much success has attended this attack on hydrophobia, in spite of our being even still in complete darkness as to the real nature of the exciting cause of the disease; for not only has, up to the present day, the microbe of rabies remained undiscovered, but it is not even known with certainty whether it is a microbial disease at all. At the very threshold of this investigation, then, was the obstacle of the exciting cause of the disease being unknown, and although this obstacle still remains, it has no more blocked the way to the discovery of preventive measures than did the same obstacle in the case of small-pox so many years before.

The fact that rabies is transmissible from animal to animal and from animals to man, not unnaturally led Pasteur and his assistants to believe that they had in this virus an active agent probably resembling in character the other viruses which had been so successfully tracked out by them, and there seemed every justification in presuming that here again they had to reckon with a bacterial transmitter of disease.

But, in spite of the most laborious microscopic examinations, and the application of all the subtlest devices for the staining and cultivation of bacteria, as has been already mentioned, the microbe of rabies has until now successfully eluded all attempts at its detection. It would be impossible to enumerate the countless cultivations and experiments which were made with the saliva of rabid animals in the hope of isolating the bacterium of rabies, nor the host of inoculations carried out to secure the artificial infection of animals with rabies.

That Pasteur did not despair in the presence of such overwhelming difficulties can only be attributed to the fact that " la génie c'est la patience," and it was the possession of such unconquerable energy and determination which enabled Pasteur to calmly encourage his assistants when on the brink of despair by saying: " Refaisons la même expérience, l'essentiel est de ne pas quitter le sujet."

The important step to be secured was the discovery of a method whereby rabies could be with certainty communicated to an animal. Inoculations in the first instance were invariably made with the saliva obtained from a rabid animal, and every case of hydrophobia in Paris was at once notified to Pasteur.

It is not often that the scientific man of to-day has an opportunity of displaying personal courage, but the vivid description given by M. Vallery-Radot of how he accompanied Pasteur on one of his expeditions to inspect a rabid dog and collect its saliva, shows that Pasteur had inherited the same fearless *élan* which had doubtless gained for his father the decoration on the field of battle. They started, taking six rabbits with them in a basket. The rabid beast was in this case a huge bull-dog, foaming at the mouth and howling in his cage. All attempts to induce the animal to bite, and so infect one of the rabbits, failed; "but we *must*," said Pasteur, "inoculate the rabbits with this saliva." Accordingly, a noose was made and thrown, the dog secured and dragged to the edge of the cage, and his jaws tied together. Choking with rage, the eyes bloodshot, and the body convulsed by a violent spasm, the animal was stretched on a table, and kept motionless whilst Pasteur, leaning over this foaming head, sucked up into a narrow glass tube some drops of the saliva.

Actions such as these should make the British public remember that there are some who, in the obscurity of the laboratory, exhibit the same heroism which is rewarded by the Victoria Cross when displayed on the veldt of South Africa or in the passes of Afghanistan.

Unfortunately, however, inoculations made with the saliva of rabid animals did not invariably produce hydrophobia, and even when they succeeded, the symptoms frequently did not declare themselves for months. This method had, therefore, to be abandoned; and as it was evident that rabies was essentially a disease affecting the nervous system, it was thought probable that the virus was located in the nerve centres of the body—a suggestion already made by Dr. Duboué, of Pau.

Experience soon verified the truth of this hypothesis, for nervous tissue inoculated subcutaneously into an animal did excite rabies. But even this mode of infection proved in practice hardly more reliable than had the saliva inoculations, and so far, in spite of all efforts, no trustworthy means of transmitting rabies with certainty and within a reasonable time had been discovered.

Now, however, an important departure was made. Bearing in mind the fact that the seat of the disease in rabies is located in the nervous centres, Pasteur conceived the idea of communicating it by taking the nerve tissue of an animal which had died of rabies and introducing it into the central nervous system—the brain—of the animal to be infected.

This mode of procedure, it should be pointed out, was not based on any pathological considerations, but was simply an adaptation of the principle which Pasteur had followed in all his researches both on fermentative and other micro-organisms—namely, to provide for each microbe that nutritive medium which was best suited to its particular requirements. To Pasteur, therefore, the nervous tissue of the rabid animal appeared as a pure cultivation of the rabies virus, and in this material he now endeavoured to induce attenuation on the lines which had proved so effective in the case of fowl-cholera and anthrax.

"Usually," Dr. Roux tells us, "when an experiment was planned it was carried out without delay; but this one, from which we anticipated so much, was not at once put in operation. Pasteur, although obliged to sacrifice so many animals in the course of his benevolent researches, had a real repugnance to vivisection. He took part in a simple operation, such as a subcutaneous inoculation, without much distress, but if the animal cried out a little, Pasteur was at once full of pity for it and gave the victim sympathy and encouragement which would have appeared comic had it not been touching.

"The idea of perforating the skull of a dog was repulsive to him. He ardently desired that the experiment should be carried out, but he dreaded seeing it done.

"I did it one day when he was absent. The next day when I informed him that the intra-cranial inoculation offered no difficulty, he was moved with pity for the dog. 'Poor beast! his brain is doubtless injured: he must be paralysed.' Without replying, I went down to the basement to fetch the animal and let it come into the laboratory. Pasteur did not like dogs, but when he saw this one, full of life, inquisitively rummaging about in all directions, he exhibited the greatest delight, and lavished most charming words upon him.

"Pasteur was infinitely grateful to this dog for having borne the trepanning so well, and thus causing all scruples as regards such operations in the future to disappear.

"This first trepanned dog exhibited characteristic rabies in fourteen days. The experiment repeated many times gave the same results: it was thus possible to communicate rabies with certainty and in a relatively short time; after that it was easy to experiment.

"The inoculation of the virus by trepanning succeeds also in the case of rabbits, and it is easy to transmit in this manner rabies from rabbit to rabbit. In the course of these successive passages of the virus the latter increases in virulence, and the time of incubation is diminished until it lasts no longer than six days. In this way the virus of rabies was actually cultivated within the skull. Instead of carrying on the cultivations as in the case of other viruses in artificial media, the virus of rabies is cultivated in living material. These cultures in nerve tissue can be modified just as the culture of anthrax or fowl-cholera.

"Rabid marrows, exposed to the action of the air, in a dry atmosphere become desiccated and lose their activity. After fourteen days the virus is attenuated to such an extent that it is harmless, even in the largest doses. A dog receiving this fourteen-days-old marrow, then on the following day thirteen-days marrow, then that of twelve days, does not take rabies, but has become immune to it. Inoculated in the eye or in the brain with the strongest virus, it remains well. In fifteen days, therefore, it is possible to confer immunity upon an animal from rabies. Now, human beings bitten by mad dogs do not usually develop rabies until a month or even longer after the bite. This time of incubation can be utilised to render the person bitten refractory."

In these few concise words Dr. Roux has summarised the results of years of work, and still the most difficult, the most perilous task remained to be accomplished—the application of the knowledge and experience thus acquired to the prevention of rabies in man. This momentous step was taken by Pasteur, encouraged by the support of Vulpian and assisted by Grancher.

Dr. Grancher, who undertook the onerous task of performing the inoculations, was already distinguished in his profession when he entered Pasteur's laboratory to fill up, as he said, a blank in his scientific education.

The first human being to undergo the treatment was a young boy from Alsace. It was in July, 1885, that Joseph Meister arrived in Paris, his body literally covered with wounds from the bites of a rabid dog. Vulpian and Grancher both urged Pasteur to apply his treatment to this poor child, whose life already was so seriously threatened, and Pasteur, yielding to their solicitations, gave his consent.

As, however, the series of inoculations drew to a close, Pasteur became terribly uneasy. He passed days of anxiety and sleepless nights, and was a prey at once to the wildest hopes and to the most cruel fits of depression.

Meister returned to Alsace on the 27th of July, and was instructed to supply Pasteur with a daily bulletin of his health. With the forgetfulness, however, of a child, often five or six days would pass without any news of him reaching the laboratory, and Pasteur suffered torments of anxiety. On being reproached by Pasteur for his long silence on one of these occasions, the lad wrote towards the end of

August: "It is indeed ungrateful in me not to send you news of how I am, since you, my dear Monsieur Pasteur, are so concerned about my health. I thank you, as also do my parents, a thousand times. It is with delight that I tell you that I am well and eat well."

It was on the 26th October, 1885, that Pasteur communicated that celebrated memoir to the Academy of Sciences in which he described the results of what he modestly designated a "tentative heureuse." A profound impression was produced by this successful result, and true indeed were the words with which his colleagues greeted this great achievement: "Ce nouveau travail met le sceau à la gloire de M. Pasteur et jette un éclat incomparable sur notre pays."

Wounded persons soon streamed in from all parts, the laboratory becoming transformed into a veritable clinic, and the resources of the staff were taxed to the utmost during the next year to keep pace with the inoculations alone, as many as 2,682 individuals being treated, each of whom, on an average, received between fifteen and twenty inoculations.

Nearly 20,000 persons have now undergone Pasteur's anti-rabic treatment at the Paris Institute, and the mortality has been less than 5 per 1,000.

But this magnificent triumph was not easily secured. At the time when Dr. Grancher first accepted the responsibility of conducting the inoculations, one of Pasteur's most determined opponents—M. Peter—reiterated his request to the Academy of Sciences almost weekly, that they should order the laboratory in the Rue d'Ulm to be closed, where, he declared, instead of curing rabies they were, in reality, communicating the disease.*

Tempora mutantur! On the outer walls of this same laboratory, now known as the Pasteur Laboratory and occupied by the Ecole Normale, the Municipal Council of Paris have recently (1897) placed a bronze medallion of Pasteur. It surmounts a slab of black marble bearing in letters of gold the following inscription:

ICI FUT LE LABORATOIRE DE PASTEUR

1857.—Fermentations.
1860.—Générations spontanées.
1865.—Maladies des vins et des bieres.
1868.—Maladies des vers à soie.
1881.—Virus et vaccins.
1885.—Prophylaxie de la rage.

It was amidst the most determined opposition at home and abroad that Pasteur had to fight over two years for the public recognition of this great discovery,

* In this country public opinion was so divided as to the value attaching to the new treatment, that the Local Government Board was induced to take up the matter, and in April, 1886, at Sir Henry Roscoe's suggestion, a committee was appointed to inquire into the efficacy of Pasteur's methods, and into any dangers which might be connected with their application. The committee was a representative one, and consisted of Sir James Paget (Chairman), Dr. Lauder Brunton, Dr. George Fleming, Sir Joseph Lister, Dr. Richard Quain, Sir Henry Roscoe, Professor J. Burdon Sanderson, and Professor Victor Horsley. Professor Horsley, who acted as secretary, subsequently visited Paris in company with Dr. Brunton, Sir Henry Roscoe, and Professor Sanderson, in order to study Pasteur's methods on the spot. Numerous investigations were carried out by Professor Horsley on his return, with the result that in their report to the Government the committee unanimously expressed confidence in Pasteur's system for the treatment of hydrophobia.

and it was in connection with these inoculations that we have handed down to us an incident which exhibits at once the courage as well as the unselfish devotion of this great man. At a time when scepticism was rife, and when attacks were raining down upon him, a little child was brought to Pasteur which had been bitten thirty-seven days previously by a rabid animal. His assistants pointed out to him that to treat a case, already practically hopeless by reason of the long interval which had elapsed since the infliction of the wound, would, in the almost certain event of failure, endanger the reputation of the treatment and expose him to fresh opposition from a public at that time both unfavourable and unsympathetic. But Pasteur, in spite of arguments which he could not but admit were both legitimate and forcible, was not to be deterred from making the attempt. "If the child has but one in ten thousand chances of recovery I ought to try everything," was his reply. The result was not successful and the child died, and the attacks and discussions were renewed with increased bitterness and animosity.

The effect of this constant strain told terribly upon Pasteur's health. Dr. Roux tells us how, "from time to time, when the preventive inoculations were applied to man, all repose was lost for him. Each bitten individual brought fresh pre-occupation to him. The sight of the wounded children caused him especially the most vivid emotion, which he could not control.

"When desperate cases were brought in for which there was no remedy, Pasteur shared all the sufferings of his patients. Every visit he made to them was torture to him, and yet he could not help going to see them. It was necessary to take him away from Paris. He was in Italy when those attacks were brought against the antirabic inoculations which made so much stir at the time but have been completely forgotten to-day. He was deeply distressed by them, and from this time onwards Pasteur was obliged to give up his life in the laboratory, and to a worker such as he had been, *l'inaction c'était la tristesse.*"

All these researches on anthrax, the attenuation of virus, swine measles, and rabies were accomplished by Pasteur in less than ten years, between 1876 and 1885. His assistants during that time were Joubert, Chamberland, Thuillier, and Roux. To Roux we owe the following vivid account of the life which was led by the great master and his collaborateurs during this period of concentrated scientific activity :—

"These years passed in the laboratory of the Rue d'Ulm, remain ever present before me as the best of my life.

"In order to be nearer our work, master as well as disciples lived at the Ecole Normale.

"Pasteur was always first on the spot. Every morning at eight o'clock I heard his hurried and slightly dragging footstep pass the window of the room which I occupied at one extremity of the laboratory. Hardly had he entered, than he went, paper and pencil in hand, to the incubator to note down the condition of the cultures, and then descended to the basement to inspect the animals under experiment. After this we made the autopsies, the culture-inoculations, and the microscopic examinations.

"One ought to have seen Pasteur at his microscope to obtain an idea of the patience with which he examined a preparation. But, in fact, he looked at everything with the same minute care; nothing escaped his short-sighted eyes, and we used to say jokingly that he saw the microbes growing in the broth tubes.

"Afterwards Pasteur wrote down what had just been observed. He permitted no one else to keep these laboratory note-books, he himself recorded every detail of the information which we gave him.

"What numbers of pages he thus covered with his small, irregular, and cramped writing, with drawings on the margin and back, the whole mixed up, difficult to read to those without practice, but kept, all the same, with extraordinary care! No fact was registered which was not fully confirmed; once written down, the observations became incontestable truths to Pasteur. When, in the course of our discussions, the words 'C'est sur le cahier' were heard, not one of us dreamt of replying.

"The notes taken, we then discussed what experiments should be made. Pasteur sat upright at his desk, ready to write down what should be decided upon, Chamberland and I in front of him, leaning against a glass cupboard. It was the important moment of the day; each one gave his opinion, and often an idea, at first confused, became clear during discussion, and ended by leading up to one of those experiments which dissipated all doubts. Sometimes we did not agree, and our voices became raised; but to Pasteur one could freely express one's thoughts. I have never known him oppose a sound argument.

"A little before twelve, Pasteur was called to his déjeuner; at half-past twelve he came down to the laboratory, and oftenest on our return we found him motionless, near a cage, observing with unwearying attention a specially interesting guinea-pig or rabbit.

"Towards two o'clock, Madame Pasteur sent to fetch him, for otherwise he would have forgotten to go to the Academy and various committees of which he was a member.

"We then employed the afternoon in carrying out the experiments previously arranged, only interrupting our work to permit of Chamberland's smoking a pipe, for 'le Maître' had a horror of tobacco, and we only smoked in his absence.

"Pasteur returned about five o'clock; he at once made himself acquainted with what had been done and took notes. His notebook in his hand, he would check the labels fastened on to the cages; and then he would tell us about any interesting communications he had heard at the Academy, and chat about the various papers. It was at such a time that Pasteur opened out most willingly, especially if we roused him with some objections. Then his eye, so clear, became yet brighter; his speech, a little slow to start with, became more and more animated and fascinating. He developed the most profound and the most unexpected ideas; he proposed experiments of the most audacious description. This rigorous experimenter possessed a powerful imagination; for him nothing was *à priori* ridiculous. But his most enthusiastic outbursts always led him to try some experiment, and in the end he only retained that which was proven.

"His zeal was so infectious that, after listening to him, the mind became crowded with experimental projects.

"When we got him on to the subject of his early researches, he would descant like a poet on molecular dissymmetry and its relation to the dissymmetric forces of nature.

"On such days as these Pasteur forgot all about his dinner-hour. Madame Pasteur was obliged to have him called two or three times, or came to fetch him herself; then he left us laughing, saying: 'It is your fault that I shall be scolded.'

"The laboratory was *très fermé;* no one could penetrate into it without first ringing at the entrance door, which was always kept shut. Visitors hardly ever got beyond the waiting-room. When M. Pasteur was working, he was not in a humour to receive even his friends; an interruption made him wretched.

"I see him turning round to the bore, waving his hand as if to send him away, and saying, in a pleading and despairing voice: 'No, not now; I am too much occupied.' He was, nevertheless, the simplest and most accessible of men, but he could not understand how anyone could disturb a *savant* when he was writing down his laboratory notes. When Chamberland and I were busy over some interesting experiment, he mounted guard round us, looked through the glass door when our comrades came to call upon us, and went himself to receive them and to politely show them out.

"These freaks of Pasteur's showed so naïvely his entire preoccupation with his work that no one ever felt hurt by them.

"Pasteur was always plotting out experiments, and he jotted down his ideas on the leaves of a little notebook, or on pieces of cardboard, which he carefully preserved.

"His left hand having remained awkward since the attack of paralysis which he had in 1868, he entrusted the carrying out of his experiments to his assistants; an irreproachable experimenter himself, he was very exacting in what he demanded of others. For him no experiment was impossible. When we remarked that what he expected of us presented particular difficulties, he would reply, 'That is your affair; arrange it as you like, provided it is done, and well done, too.' And he always ascertained for himself whether it was well done, separating out what was strong and what was weak with admirable sagacity.

"A communication of Pasteur's to the Academy of Sciences or to the Academy of Medicine was an event; for he never published anything which was not finished. Each one of his memoirs only occupies a few pages of the *Comptes rendus,* but it contained the results of hundreds of experiments. One can read and re-read them, one always finds something fresh to learn; often a simple phrase opens up a new path, and many such which have been thus indicated have not yet been traversed. Pasteur's whole individuality comes out in his writings; his imagination is revealed in them by the depth and audacity of his generalisations, the vigour of his mind by the correctness of his views and the strength of his conclusions, his enthusiasm by the emotion of his language.

"Before writing, Pasteur read and re-read his experimental notebooks, then he dictated to one of us, or more frequently to Madame Pasteur. He kept the manuscript sometimes for weeks, constantly retouching it; when he was satisfied, he communicated it to us and discussed the mode of expression with us; often he received observations with impatience, but he always valued them if they were correct.

"Madame Pasteur recopied it in her beautiful handwriting, so easy to read; Pasteur never would send a manuscript scored with erasures to the printers; if he altered some passage he stuck some gummed paper, cut to the right size, over the lines and wrote it afresh. During all this work of editing, the subject treated of developed wonderfully, and we, the assistants of the Master, who knew how far the experiments had carried it, were astounded to see how it had grown and become transformed in the final memoir."

Before closing this chapter on rabies, it is of interest to glance at the report which M. Henri Pottevin has just published of the antirabic inoculations which have been carried out in Paris during the past ten years (1886–1896), the greater number of which have been performed in that now world-famous building the Institut Pasteur, the foundation of which afforded such immense gratification to its great namesake, and was the public expression of gratitude for the countless benefits its first great director had bestowed upon his country.

The following table shows the number of persons treated and the mortality in the various years:—

Years.	*Persons treated.*	*Deaths.*	*Mortality per cent.*
1886	2,671	25	0·94
1887	1,770	14	0·79
1888	1,622	9	0·55
1889	1,830	7	0·38
1890	1,540	5	0·32
1891	1,559	4	0·25
1892	1,790	4	0·22
1893	1,648	6	0·36
1894	1,387	7	0·50
1895	1,520	5	0·33
1896	1,308	4	0·30

It will be observed that there were fewer cases treated at the Institut Pasteur in 1896 than in any previous year. This is attributable to the fact that similar institutes, where anti-rabic inoculations are carried out, have been started in increasing numbers not only in France but all over the world; hence districts and countries which used to send a considerable contingent of cases each year to the Paris centre are now in a position to carry out the inoculations on the spot.

The following table shows the nationality of the 18,645 persons treated at the Institut Pasteur during the past decade :—

Germany ...	44	India	95
England ...	870	Morocco ...	2
Austria ...	94	Portugal ...	333
Belgium ...	429	Roumania ...	53
Brazil	13	Russia	194
Egypt	45	Servia	1
Spain	353	Switzerland ...	82
United States ...	33	Turkey	31
Greece	175	Bulgaria ...	1
Holland ...	87	Monaco... ...	2
Italy	159		

Thus 3,096 were foreigners, and 15,549 Frenchmen.

These figures show that of the foreigners treated at the Institut Pasteur by far the largest contingent came from England, a circumstance which can be regarded only as a national disgrace. Amongst the civilised countries of the world, we are indeed almost unique in obstinately neglecting to provide this benefit of modern science for those of our unfortunate countrymen who stand in need of it. This omission means, of course, that whilst the well-to-do who have the misfortune to be bitten by a rabid dog can and do largely avail themselves of the hospitality and scientific skill which is to be obtained at the Institute on the banks of the Seine, the poor, when falling victims to the same misfortune, have to forego the consolation which is afforded by the costly trip to the French capital. It is to be hoped that the British electorate, composed, as it now is, mainly of those who would thus be deprived of the benefits of modern science, will before long insist upon the reform of that legislation which owes its existence to the noisy and misdirected energy of a group of influential persons who, actuated, as the case may be, either by a misguided sentimentalism based on ignorance or by a wicked and selfish hypocrisy, are most dangerous enemies of the human race and of that scientific progress upon which the continued welfare of the latter depends.

Thus it is that the British Institute of Preventive Medicine, established in London in 1891 with infinite difficulty, and mainly through the strenuous efforts of Lord Lister, Sir Henry Roscoe, and other leaders of science in Great Britain, has made but little progress compared with the magnificent sister institutions which have been founded in the other great European capitals.

We must, in fact, recognise that in the matter of bacterio-pathology the British Empire counts now for little more than a cipher, and has to summon outside aid in almost every emergency—Koch, of Berlin, exposes the bacterial nature of cholera in India; Haffkine, of the Pasteur Institute, devises a method of contending against it by protective inoculation; it is Koch, again, who is called upon to combat the rinderpest in South Africa; it is Yersin, of the Pasteur Institute, who discovers the plague bacillus at Hong Kong, and it was to him and to the Institute that has produced him that we appealed for assistance during our recent embarrassment in Bombay. How long is "the greatest empire the world has ever seen," to use the phrase which statesmen in the Jubilee year of 1897 kept dinning into our ears, to occupy this degrading position of dependence? In this matter, indeed, we can learn from almost every other country in the civilised world, for hardly anywhere is this department of science at such a discount as in this globe-girdling empire of which we are so proud. To give the most recent instance that comes to hand of the value set upon researches in this branch of science by other countries, we hear of a Bill having just been introduced into the Legislature of Brazil offering a prize of £44,000, to be divided into two equal parts, which are to be awarded to the author of a work demonstrating the existence of a bacillus of yellow fever and the method of recognising it, and to the discoverer of an efficacious means of treating the disease. The Medical Institute of Rio Janeiro, the Hygienic Institute of Berlin, and the Pasteur Institute of Paris are to decide as to the award of the prizes. Where, we should like to ask, is a British Institute to be found capable of adjudicating on such claims? The Bill further provides for the reservation of a sum of £22,000, to be applied to the creation of an establishment for the preparation of a curative serum, the discoverer of which will be appointed organising director of the Institute. The former of these prizes will probably be awarded to Dr. Sanarelli, who has already discovered a bacillus supposed by him to be the cause of yellow fever, and the claims of which are at present being investigated by the authorities of the Institut Pasteur. In the meantime, the Legislature of Uruguay has conferred honorary citizenship on Dr. Sanarelli in recognition of his discovery, and has voted him a grant of £2,000.

CHAPTER XV.

THE INSTITUT PASTEUR.

In an unfrequented part of Paris, far removed from the busy haunts of its citizens, there existed for upwards of a century and a half a large market garden. The few pedestrians who by chance found their way to this remote district were rewarded by the opportunity of feasting their eyes on no less than eleven thousand square mètres of vegetables!

Towards the end of May, in the year 1887, however, the whole prospect was changed. Hundreds of labourers were at work upon this "hectare de salades." "Hastily they dug to great depths, to establish the foundations of a monument which it was desired should be indestructible"; for here was the site upon which the Institut Pasteur was to rise up—that splendid national tribute to a man of genius whose name was now a household word in all parts of the land, in all classes of society.

The extraordinary enthusiasm which accompanied the foundation of this great Institution has certainly not been equalled in our time. Considerable sums of money were subscribed in foreign countries, whilst contributions poured in from every part of France.* Even the inhabitants of obscure little towns and

* The total sum subscribed and announced by the treasurer of the fund at the opening ceremony amounted to 2,586,680 francs.

villages organised fêtes, and clubbed together to send their small "cadeau de la misère"; and we read of the workpeople employed in a glass factory approaching M. François Coppé, the poet, and begging from him some verses, so that their gift might be accompanied by a suitable tribute to the genius of Pasteur.

Collective subscriptions were started, amongst which that offered by the Trocadéro will be specially remembered as having received from Pasteur the following felicitous acknowledgment:—"Les grands charmeurs de l'humanité heureuse apportèrent leur glorieux concours à ceux qui veulent servir l'humanité souffrante."

But perhaps the contribution by which Pasteur, with his intense patriotism, was most deeply moved was that forwarded from Alsace-Lorraine. It was, as we have seen, from Alsace also that Pasteur received his first patient; and the young Alsatian has ever since remained one of his most devoted and grateful adherents. Enthusiasm was, however, not confined to offerings of money; valuable services were ungrudgingly given by those entrusted with the designing and carrying out of the plans for the building up of this remarkable edifice.

"La voilà donc bâtie, cette grande maison dont on pourrait dire qu'il n'y a pas une pierre qui ne soit le signe matériel d'une généreuse pensée. Toutes les vertus se sont cotisées pour élever cette demeure du travail."

It was on the 14th November, 1888, that the President of the Republic, supported by the great officers of State, representatives of various foreign Governments, and a brilliant gathering of distinguished members of both the artistic and scientific worlds, formally opened the Institut Pasteur. Amongst the great crowd present on that day were past and present pupils of Pasteur's, and deputations from all the students in Paris.

The proceedings commenced with a discourse by M. Bertrand, the Perpetual Secretary of the Academy of Sciences, and Member of the French Academy.

"During forty years, my dear Pasteur, you have let glory come to you without ever pursuing it. Amongst all the paths where often one seeks for it, there was but one known to you—that of truth. . . . The date of the 14th November, 1888, will remain immortal in the history of medicine. . . . I cannot yield to the temptation of reviewing the long series of your researches, admired by such great judges as Claude Bernard, Balard, Dumas. On every road of science we meet you. . . . It is to thank you in the name of science, to rejoice in the name of humanity, and to triumph in the name of France, that we are all met here to-day."

In an able speech, Dr. Grancher next addressed the assembly, reviewing the history of the difficulties, the trials, and the triumphs which had accompanied the discovery and practice of the new treatment for rabies.

"You must know, gentlemen," he remarked in conclusion, "that the Institut Pasteur has been not alone founded for the treatment of rabies, but also for the scientific study of means practically to compass diseases which decimate the human race—diphtheria, typhoid fever, phthisis, etc. The large laboratories which are to be opened to French and foreign doctors will thus become a source of benefit to the whole of humanity, as well as a powerful means of diffusing and spreading abroad French science."

The treasurer of the fund, M. Christophle, next rose, and, in a graceful and picturesque speech, referred to the financial and other support which the Institute had already received.

"Certainly it is for you, Sir" (addressing Pasteur), "a happiness rare and hardly hoped for, which may console you for the passionate struggles, the keen emotions, and the crises, sometimes so terrible, through which you have passed. When I think of this past, so full of trouble and of danger, in spite of myself I recall also the irony of those ready made phrases which speak of the serenity of science and the peace of laboratories."

Pasteur's emotion was too great to permit him to deliver the address he had prepared, and his son, therefore, read his discourse, from which the following extracts have been taken:—

"Never has a Frenchman addressing himself to other Frenchmen been more profoundly moved than am I at this moment. . . . But, alas! I have the poignant melancholy of entering this house of work as a man 'vaincu du temps,' who has no longer around him any of his masters, nor even any of his comrades in past contests—neither Dumas, Bouley, Paul Bert, nor Vulpian—who, even like you, my dear Grancher, was my adviser in early days, and became the most convinced adherent and the most active defender of my method! . . . Our Institute shall become at once a dispensary for the treatment of rabies, a centre of researches for the study of infectious diseases, and a centre for the teaching of subjects relating to microbiology. Born but yesterday, but born completely armed, this science draws such strength from its recent victories that it entices all intellects.

"This enthusiasm, which has been kindled in you when young, keep it, my dear colleagues, but give to it, as an inseparable companion, unflinching self-control. Advance no theories—nothing which cannot be proved in a manner at once simple and conclusive. Cultivate the spirit of criticism. By itself it is neither a generator of ideas nor a stimulus to great things. Without it nothing can avail. With it will always remain the last word.

"This that I ask of you is what you again, in your turn, will demand of the disciples who gather round you; and for the investigator it is the hardest ordeal which he can be asked to face—to believe that he has discovered a great scientific truth, to be possessed with a feverish desire to make it known, and yet to impose silence on himself for days, for weeks, sometimes for years, whilst striving to destroy those very conclusions, and only permitting himself to proclaim his discovery when all the adverse hypotheses have been exhausted. Yes, that is a difficult task.

"But when, after many trials, you have at length succeeded in dissipating every doubt, the human soul experiences one of the greatest joys of which it is capable. . . .

"If it be permitted to me, Monsieur le Président, to conclude with a philosophical reflection, suggested by your presence in this hall of labour, I would point out that two contrary laws appear here to-day to be in conflict—a law of blood and death, which, conceiving each day some new mode of warfare, compels the people to be ever ready for the field of battle; and a law of peace, of labour, and of health, which cherishes no other dream than the delivery of man from the plagues which besiege him.

"The one seeks only violent conquests, the other nothing but the alleviation of humanity. The latter law places a human life above all victories; the former sacrifices hundreds of thousands of lives to the ambition of a single life. The law of which we are the instruments seeks, even amidst carnage, to cure the bleeding wounds wrought by this law of war. The dressings suggested by our antiseptic methods may preserve the lives of thousands of soldiers.

"Which of these laws will finally prevail? God alone knows. But what we may be assured of is that French science will strive, in obeying this law of humanity, to extend the frontiers of life."

At the close of this fine oration enormous enthusiasm prevailed, and the President of the Republic, rising, said: "M. Pasteur desires no other recompense but that which we can bestow on his collaborateurs. M. Grancher and M. Duclaux are herewith created Officers and M. Chantemesse Chevalier of the Legion of Honour."

And so closed a ceremony perhaps unique in the annals of science. That the Institute inaugurated under such auspicious circumstances has withstood the attacks and machinations of its opponents and enemies, and has so far fulfilled the high promise with which it entered upon its career no one at the present day questions; that it will continue to uphold and cherish the lofty standard set by its great namesake is sufficiently guaranteed by the active presence within its walls of men such as Duclaux, Roux, Metchnikoff, and other disciples and workers bequeathed to it by its first organiser and director.

M. Duclaux, upon whom, since 1895, has fallen the responsibility of directing the Institute, was, we have seen, for years intimately associated with Pasteur and his work. He it was who first conceived the idea of bringing out the *Annales de l'Institut Pasteur*, a journal which, under his able editorship, is second to none amongst all the new bacteriological publications of recent years. In 1888 he was appointed Professor at the Sorbonne, but, by special arrangement, his work is conducted entirely at the Institute.

It is with the chemical aspects of bacteriology that M. Duclaux is chiefly concerned and has done his best work, and it is stated that he hopes to still further extend the usefulness of the Institute by establishing a school for the study of industrial fermentations, and that he is anxious to work out scientifically the principles which underlie the manufacture of wines, beer, dairy produce, etc.

In carrying out this scheme M. Duclaux will be taking up again the threads of those classical researches which Pasteur was constrained to abandon for the study of diseases, and in the ardent pursuit of which he was reluctantly compelled to let his earlier work remain uncompleted.

The Pasteur Institute has been so inseparably associated, in the public mind, with the prevention of disease that this new departure, which its present Director is anxious to inaugurate, may come as a surprise to many; but that the original conception of the Institute as a centre for the study and prevention of disease will not suffer is assured by the fact that Dr. Roux will continue to preside over the department in which he has achieved such signal success in the new treatment of diphtheria,* and that Dr. Grancher remains at the head of the anti-rabic department.

The personality of Dr. Roux, now Sub-Director of the Institute, with whom and the other Professors gathered round M. Duclaux the fortunes of the Pasteur Institute now rest, has been recently so vividly portrayed by M. de Fleury that it is impossible to resist conveying to the reader some impression of so remarkable an individuality. Originally a student at Clermont-Ferrand under M. Duclaux, who did not fail to notice a pupil "si taciturne et si studieux," Roux followed his teacher to Paris, where the latter procured for him a minor appointment at the Hôtel Dieu. Here Roux exhibited that independence of character, that almost imperious demand for liberty

* In this connection it is of interest to note the report of the medical superintendents to the Metropolitan Asylums Board, London, on the use of antitoxin in the treatment of diphtheria during the year 1896. It confirms and extends the favourable conclusions reached in the previous year, when antitoxin was first used. The statistical results with regard to mortality are compared with those for 1894, the year immediately preceding the introduction of antitoxin and the one in which the lowest mortality had been recorded up to that time; they show a marked improvement in all classes of cases, and especially in the severer ones. The more important facts may be tabulated thus:—

PERCENTAGE OF MORTALITY TO CASES.

	All Cases.	*Under 5 Years.*	*Laryngeal Cases.*	*Tracheotomy Cases.*
1894	29·6	47·4	62·0	70·4
1896	20·8	30·2	29·6	41·0

of judgment, which never forsook him even in the presence of his deeply venerated and much-loved master, Pasteur, when he chanced not to be in complete accord with him on some matter of detail. His insight, unbounded patience, and his most scrupulous scientific conscientiousness soon obtained for him the respect of all with whom he came in contact on entering Pasteur's laboratory. Since then his splendid investigations at the Institute have placed him in the first rank of scientific men.

For several years Roux has lectured at the Institute, and so eager is the competition to attend his courses of lectures that it is necessary to apply for a place eighteen months in advance, a circumstance which will hardly surprise those who had the good fortune to listen to the truly marvellous discourses, in his own beautiful language, which on two occasions he has delivered in this country. His audience is gathered from all parts, and it may truly be said that he it is who has initiated French scientists all over the country, and not a few foreigners, into the mysteries of bacteriological technique, and has incited them to the study of microbes and toxins.

"I do not think it is possible," writes M. Fleury, "to find a more eager worker. He takes no rest either on Sundays or *fête* days, and nothing has ever dissuaded him from the one set purpose which dominates him—to do good scientific work and make useful discoveries, not for his own reputation but for the glory of the Institut Pasteur, of that beloved *maison-mère* to which the Pasteurians belong."

In the department devoted to morphologica bacteriology, Dr. Metchnikoff continues to act as

Director. Originally a student at Berlin under Virchow, this brilliant and accomplished Russian investigator has pursued his researches on the morphology of the lowest animalculæ in all parts of the world—in Italy, in Madeira, in Odessa. It was whilst Professor at Odessa that he wrote to Pasteur and asked for a place in his laboratory, and since that time he, with his gifted wife, has worked without intermission at the Institute. Here it is that he has experimentally elaborated his celebrated theories of phagocytosis, which assign such important functions to the migratory cells of the body in the conflict of the system with disease.

This remarkable theory, which was the subject of so much discussion a few years ago, is the outcome of extended researches on the behaviour of the colourless corpuscles in the most varied forms of the animal kingdom.

An admirable outline of these laborious studies, and the conclusions drawn from the observations by their author, is given in M. Metchnikoff's work entitled "Leçons sur la Pathologie Comparée de l'Inflammation."

The Pasteurians have a profound respect and admiration for this distinguished investigator, and themselves agree that "après M. Pasteur, c'est Metchnikoff notre homme de génie."

Practical bacteriology is another department of the Institute's programme, and deals with the applications of bacteriology to questions of hygiene, under which head the preparation of the vaccines of swine fever and anthrax is included. Over this work M. Chamberland presides, whose name is so well known even to the lay public in connection with the Pasteur-Chamberland filter, and which, besides its general application, has also been of priceless value as a scientific instrument in the bacteriological laboratory for separating bacteria from their chemical products. Some idea of the labour which the elaboration of these vaccines entails may be gathered from the fact that in France alone it is stated that 900,000 sheep and from 400,000 to 500,000 oxen are annually inoculated with anthrax vaccine.

Separate departments also exist for comparative bacteriology, in which the study of bacterial diseases is pursued; and technical bacteriology, in which, as we have seen, Dr. Roux superintends the instruction of students in the technique of the subject.

But a very inadequate idea would be obtained of the splendid work which the Pasteur Institute has accomplished without a reference to the brilliant students and disciples which it has already raised and dispatched to all quarters of the globe to carry on the traditions and uphold the honour of the *maison-mère*.*

* Amongst the numerous institutions of this kind now existing, the erection of a Pasteur Institute at Athens deserves mention. The credit of founding this institution was due to Dr. Pampoukis, who studied for a time under Pasteur in Paris. On his return to Athens he started a microbiological institute on his own account, and eventually established the Pasteur Institute at his own expense. In due time the municipality and the Government granted him a small yearly allowance. The Consul, in his report, observes that it is practically impossible to overestimate the value of "such an establishment in the Levant, which is overrun with ownerless dogs. A muzzling order does exist in Attica, but it is not enforced, and the distribution of poisoned meat in the streets of Athens and the Piræus is apparently the only attempt made by the authorities to deal with an increasing amount of rabies. The lack of water and the prevailing disregard of all forms of animal suffering largely contribute to this result."

Amongst such we may mention Calmette, lately Director of a Pasteur Institute in Cochin China, Nicolle, who occupies a similar position at Stamboul, and Yersin in Annam.

Foremost among these must be placed Dr. Calmette, who, originally a student under Dr. Roux, left for Cochin China to undertake the establishment of a Pasteur Institute at Saïgon, the first to be founded in the French colonies. Here he struck out a comletely new line of investigation, and one which again indicates the extraordinary fertility of the ideas which are gathered from the study of micro-organisms. If, as had been shown in the case of tetanus and diphtheria, the serum of an animal rendered insusceptible to a particular disease can counteract the poisons manufactured by the specific bacteria of that disease, may it not also be possible to counteract in the same way poisons that have a non-bacterial origin altogether? This question was answered by the remarkable researches of Calmette on the nature of serpents' venom and the artificial production of immunity from the poisonous effects of snake-bite, researches which, admirable alike in their conception, execution, and in the results achieved, have justly made his name famous throughout both the scientific and medical worlds.

By gradually accustoming animals (horses by preference), to larger and larger doses of snake poison, he has succeeded in rendering the blood serum of such animals an antidote to the most potent serpent venom, such serum possessing the power, on being injected into other animals, of protecting the latter from the otherwise lethal effects of this poison.

Since Dr. Calmette has returned to his native country in the capacity of Director of the Pasteur Institute at Lille, he has logically pursued his ideas by extending this method to the artificial production of immunity towards *abrine*, a highly toxic vegetable poison, as well as continuing his researches on serpent venoms of various origin. Such successful results have already followed in Australia the use of Calmette's serums and methods in the treatment of snake-bites, that an official dispatch was forwarded from this colony to the French Minister of Foreign Affairs, through the English Ambassador in Paris, congratulating the Government on Calmette's discoveries, and expressing the gratitude of the colony for the services which he had rendered.

Yet another brilliant disciple of Pasteur's is Yersin, whose name will always be associated with that of Dr. Roux in the classical researches they together published on the toxins elaborated by the diphtheria bacillus; whilst his investigations on the plague bacillus have brought him still more prominently before the world.

When a youth of but twenty, Yersin had the rare good fortune to obtain an entrance to the Institut Pasteur. The extraordinary ardour with which he devoted himself to his work rapidly won for him the admiration and respect of all his colleagues. Desiring to travel, he obtained a medical appointment in the colonies, and it was whilst at Tonkin in the spring of 1894 that he received the request from the French Government to proceed to Hong Kong to study the plague which had recently broken out there. The report which he subsequently published is so interesting that it is tempting to describe in some detail the work which Yersin accomplished during his mission to Hong Kong.

Yersin arrived in the city a few weeks after the plague had commenced its terrible career there, a career which had already claimed the lives of 300 Chinese, and was yet to exact a tribute of over 100,000. Obtaining permission from the authorities, he erected a small hut within the precincts of the principal hospital; and here, in a concentrated plague atmosphere, he took up his quarters, and hastily improvising a laboratory, commenced his investigations.

So far the plague had confined itself to the insanitary Chinese quarters of the city, and Yersin mentions that the wretched cabins occupied by the natives were often not only without windows of any kind, but were sunk below the level of the ground, which, combined with the shocking overcrowding which prevailed, converted such dens into plague-incubators of the most fulsome and dangerous character. In these infected districts, one of the first things which attracted Yersin's attention was the extraordinary number of dead rats which lay about in all directions in the houses as well as in the streets; but, on inquiry, he soon learnt that this rat mortality was a well-known forerunner of the plague, that the latter usually attacks animals such as rats and mice, and in the country districts also swine and buffaloes, before it touches human beings.

An examination of these dead rats showed that the appearances differed in no way from those which characterise the plague in man; and the extreme susceptibility of these animals furnished Yersin at once with a valuable means of tracking out the virus. His first step was to make careful examinations of the bubonic material present in the tumours which accompany the disease, and here he discovered immense numbers of a short bacillus which appeared to be almost exclusively in possession of the field. These, he found, were readily stained, and could be grown with ease in the usual bacterial culture-media. Further investigation showed that these same bacilli were invariably present in the ganglia and liver and spleen of plague patients; that they were, however, rarely to be found in the blood, and then but in small numbers, and usually only in rapidly fatal cases a short time before death.

Healthy rats and mice inoculated with pure cultures of this bacillus succumbed, exhibiting the typical plague symptoms, and thus the first step was accomplished—the identification of the specific virus of plague.

Yersin was at first of opinion that rats were the principal disseminators of the disease, for healthy mice shut up with plague-stricken rats rapidly developed the disease and succumbed; but he noticed later the curious fact that, in the little room where he carried out his *post-mortem* examinations, immense numbers of dead flies were scattered about in all directions. He therefore determined to ascertain if this wholesale slaughter of flies had any connection with plague infection.

Taking some of these insects, and first removing the head, wings, and feet, he pounded up their bodies in broth. On subsequent examination the liquid thus obtained exhibited masses of bacilli closely resembling the now familiar plague microbe. To place their identity beyond doubt he inoculated some of this broth into mice, with the result that the latter died of plague. That flies may materially assist in the dissemination of the disease was thus established. With the slender accommodation and primitive means at his disposal, it was impossible for Yersin to further pursue his investigations in preparing a plague anti-toxin on the spot, and he therefore forwarded cultures of his bacillus to the Institut Pasteur, and from here in the course of the following year, under the joint names of Yersin, Calmette, and Borrel, was published the memoir describing the production of an anti-plague serum.

This new anti-toxin has been successfully employed by Yersin, now Director of a Pasteur Institute at Nha Trang, in Annam, in undoubted cases of plague at Amoy.

Pasteur has sometimes been reproached for not having opened his laboratory more freely to students, and he has been accused of desiring to keep his methods of research too much to himself and his assistants. "Nothing," remarks Dr. Roux, "is more unjust. In his scientific memoirs Pasteur disseminated new ideas with a liberal hand, and it was open to everyone to make use of them. He was indeed an incomparable master; he never brought forward any fact without supplying the means for its control; but instead of losing himself in useless detail, and in describing the arrangement of apparatus which everyone could easily imagine for himself, he confined himself to mentioning those conditions which were both necessary and sufficient.

"The laboratory in the Rue d'Ulm was not suitable for the accommodation of a large number of investigators; there was only room enough for Pasteur and his assistants. Moreover, Pasteur only worked at his ease in silence and meditation; in his vicinity he only tolerated his assistants; the presence of a stranger whilst he was occupied sufficed to disturb his work. One day on going to visit Wurtz at the Ecole de Médecine, we found the great chemist surrounded by his students, the laboratory resembling a hive full of bees in its bustling activity. 'How,' exclaimed Pasteur, 'can you work in the midst of such a commotion?'—'It stimulates my ideas,' replied Wurtz—'It would effectually banish all mine,' was Pasteur's answer."

Pasteur himself has expressed his opinion "that if primary and secondary education are to be made to flow as great rivers, it is necessary to be concerned about the source—that is to say, about higher education. Such instruction must always be reserved for a small number, but it is upon this small number and upon its elect that the prosperity, the glory, and the ultimate supremacy of a people depend."

There is no country which stands in more need of the admonition conveyed in the last sentence than our own. Indeed, it would appear that even the meaning of the words "higher education" is not understood by our legislators; thus whilst primary and secondary education have during the present generation been enormously extended, practically no provision has been made for that higher education upon which all real progress depends. In this matter, indeed, the words of John Stuart Mill apply with remarkable force.

"The general tendency of things throughout the world is to render mediocrity the ascendant power among mankind."

Such research as is carried on in our midst is almost invariably performed either by enthusiasts with private means or by persons holding appointments, in addition to or in spite of the arduous duties which these appointments entail. In the case even of the highest academic posts which we possess, it is comparatively elementary teaching which is the main duty, and capacity for which is the quality in the occupant which is most highly prized by the governing authorities. Whether the occupant of such a post carries on research or not is entirely a matter of personal inclination, and would appear to be viewed with hardly more concern by the educational authorities than whether he plays golf or rides a bicycle. Under such conditions it is surely not surprising that so little research is carried out in this country, but rather that any is carried on at all, and that some is of the very highest quality.

Shortly after the opening of the Pasteur Institute the feeling amongst scientific men in this country became more and more strongly emphasised that we, as a nation, could not, with self-respect, continue to accept the gratuitous services of its staff for the relief of the numerous English people who, bitten by rabid animals, sought relief at the hands of Pasteur and his assistants in Paris. Considerably over two hundred such cases had already been treated at the Institute; and it will be seen from the following letter, addressed by Pasteur at the close of the year 1888 to Sir Henry Roscoe, that efforts were being made in England to obtain some public recognition, in the shape of a fund, to testify in a substantial manner this country's gratitude for services received at the hands of the Institut Pasteur.

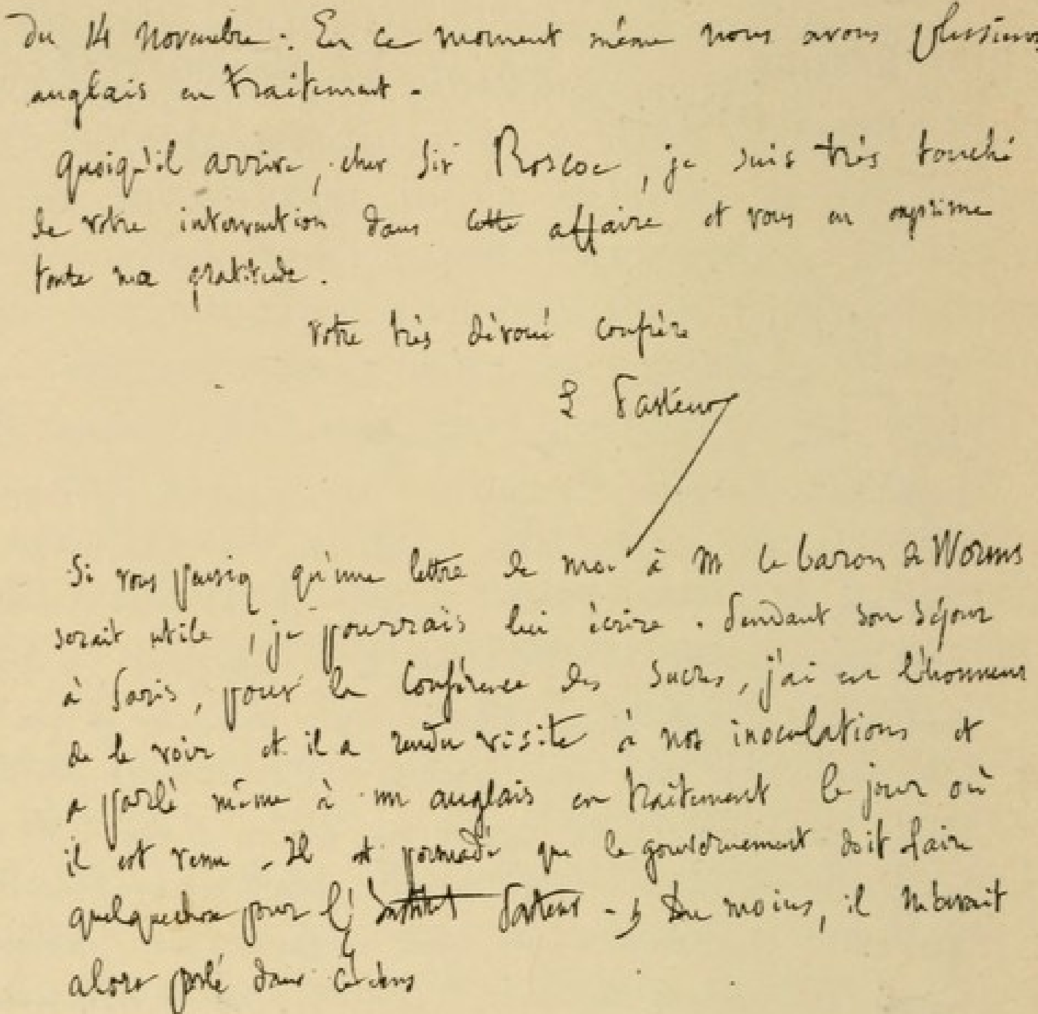
Institut Pasteur *Paris, le* 23 décembre 1888
~~25, Rue Dutot~~ 45 rue d'Ulm

Cher Sir,

Je prie M. V^r Horsley de vous faire remettre un exemplaire du Compte-rendu de notre séance d'inauguration le 14 novembre. Ce compte-rendu a paru hier seulement. Je l'attendais pour vous écrire et vous remercier très cordialement de l'initiative que vous avez bien voulu prendre en faveur de l'"Institut Pasteur."

Une réponse favorable du Chancelier de l'Échiquier, se traduisant par une participation effective du parlement ou par toute autre voie dans votre pays, aurait un effet moral considérable. Mais que penser de la réponse qui vous a été faite? Est-ce une fin de non-recevoir? Laisse-t-elle quelque espoir d'une issue favorable? Se traduira-t-elle par une souscription publique parmi les hommes de science; parmi les savants et les médecins? Quelle serait l'impression de Sir James Paget? Il n'y a rien à attendre des personnes traitées. La très grande majorité des personnes mordues par des chiens enragés sont des ouvriers ou même des indigents. Et puis, la proximité de Londres et de Paris évite au gouvernement anglais la dépense d'installation et de fonctionnement d'un laboratoire antirabique à Londres. Non seulement la Russie a fait les frais de 7 cliniques de la rage, mais le tsar a souscrit pour cent mille francs. La Turquie qui a peu de rage a fait les frais d'un laboratoire antirabique et a souscrit pour 10.000 fr. — L'Italie a cinq laboratoires antirabiques. Milan a souscrit dix mille fr. également etc... etc... Veuillez bien lire d'autres détails dans la brochure de l'inauguration

¹ Sir Roscoe


du 14 Novembre. En ce moment même nous avons plusieurs anglais en traitement.

Quoiqu'il arrive, cher Sir Roscoe, je suis très touché de votre intervention dans cette affaire et vous en exprime toute ma gratitude.

Votre très dévoué confrère

L Pasteur

Si vous pensiez qu'une lettre de moi à M le baron de Worms serait utile, je pourrais lui écrire. Pendant son séjour à Paris, pour la Conférence des Sucres, j'ai eu l'honneur de le voir et il a rendu visite à nos inoculations et a parlé même à un anglais en traitement le jour où il est venu. Il est persuadé que le gouvernement doit faire quelque chose pour l'~~Institut~~ Pasteur — du moins, il m'avait alors parlé dans ce sens

Transcription of letter from M. Pasteur to Sir Henry Roscoe.

"*Paris le* 23 *Décembre,* 1888.

"Institut Pasteur,

"45, Rue D'Ulm.

"CHER SIR,

"Je prie M. Vor. Horsley de vous faire remettre un exemplaire du compte-rendu de notre séance d'inauguration le 14 Novembre. Ce compte-rendu a paru hier seulement. Je l'attendais pour vous écrire et vous remercier très cordialement de l'initiative que vous avez bien voulu prendre en faveur de l'Institut Pasteur. Une réponse favorable du Chancelier de l'Echiquier, se traduisant par une participation effective du parlement ou par toute autre voie dans votre pays, aurait un effet moral considérable. Mais que penser de la réponse qui vous a été faite? Est-ce une fin de non-recevoir? Laisse-t-elle quelque espoir d'une issue favorable? Se traduira-t-elle par une souscription publique parmi les hommes de science, parmi les savants et les médecins? Quelle serait l'impression de Sir James Paget? Il n'y a rien à attendre des personnes traitées. La très grande majorité des personnes mordues par des chiens enragés sont des ouvriers ou même des indigents. Et puis, la proximité de Londres et de Paris évite au gouvernement anglais la dépense d'installation et de fonctionnement d'un laboratoire antirabique à Londres. Non seulement la Russie a fait les frais de 7 cliniques de la rage, mais le tsar a souscrit pour cent. mille francs. La Turquie qui a peu de rage a fait les frais d'un laboratoire antirabique et a souscrit pour 10,000 fr. L'Italie a cinq laboratoires antirabiques. Milan a souscrit dix mille fr. également, etc., etc. Veuillez bien lire d'autres détails dans labrochure de l'inauguration du 14 Novembre. En ce moment même nous avons plusieurs anglais en traitement.

"Quoiqu'il arrive, cher Sir Roscoe, je suis très touché de votre intervention dans cette affaire et vous en exprime toute ma gratitude.

"Votre très dévoué confrère,

"L. Pasteur.

"Si vous pensiez qu'une lettre de moi à M. le baron de Worms serait utile, je pourrais lui écrire. Pendant son séjour à Paris, pour la Conférence des sucres, j'ai eu l'honneur de le voir, et il a rendu visite à nos inoculations et a parlé même à un anglais en traitement le jour où il est venu. Il est persuadé que le gouvernement doit faire quelque chose pour l'Institut Pasteur. Du moins, il m'avait alors parlé dans ce sens."

In July, 1889, these efforts were so far successful that a public meeting was called at the Mansion House, under the auspices of the Lord Mayor of London, which was numerously attended by leading men of science in the country; whilst letters warmly approving of its object were read from the Prince of Wales, Professor Huxley, and other distinguished gentlemen who were unable to be present.

Huxley, after regretting his enforced absence from the meeting, writes: "I find it difficult to imagine that our wealthy country should be other than ashamed to continue to allow its citizens to profit by the treatment freely given at the Institute, without contributing to its support. The opposition . . . which is threatened . . . proceeds partly from the fanatics of *laissez faire,* who think it better to rot and die than to be kept whole and lively by State interference; partly from the blind opponents of properly conducted physiological experimentation, who prefer that men should suffer rather than rabbits and dogs."

The following are the resolutions which were moved and carried at the Mansion House:—

I. That this meeting desires to express the gratitude of the people of Great Britain and Ireland to M. Pasteur and the staff of the Institut Pasteur for the generous aid afforded by them to over 200 of our fellow-countrymen suffering from the bite of rabid dogs.

II. That this meeting, having heard the statements of Sir James Paget and others, records its conviction that the efficacy of the antirabic treatment discovered by M. Pasteur is demonstrated, and requests the Lord Mayor to establish a fund for the double purpose of making a suitable donation to the Institut Pasteur, and of providing for the expenses of British subjects unable to pay the cost of a journey to Paris when bitten by rabid animals.

III. That this meeting, whilst recognising the value of M. Pasteur's treatment, and taking steps to provide for its accessibility to Englishmen who may hereafter be bitten by rabid animals, is of opinion that rabies can easily be stamped out in these islands, and calls upon the Government to introduce at once a Bill for the simultaneous muzzling of all dogs throughout the British Islands, as provided in the measure drafted by the Society for the Prevention of Hydrophobia.

In the *Annales de l'Institut Pasteur* for July, 1889, these resolutions are reproduced in full, without comment, but the following significant lines are added at the end:—"Profitons de cette excursion en dehors de notre domaine, pour annoncer la création de deux nouveaux instituts antirabiques,—l'un à Mexico sous la direction de M. Liceaga, et l'autre à Bologne sous la direction de M. le professeur Murri."

Pasteur's letter to the Lord Mayor, acknowledging the receipt of a copy of the above resolution, is so characteristic that we have given it almost in its entirety:—

"If the aphorism that science has no country has never received authoritative sanction, it did so at this meeting, in which the leading *savants* in biological and medical science of the United Kingdom took part. I wish I could thank them individually for having attended this gathering. I was filled with gratitude on learning that the Prince of Wales himself had accorded his high approbation of your initiative. Modesty compels me to pass over in silence the kind words of which my labours and those of the Pasteur Institute have been the subject, but I have a right to rejoice with all friends of the progress of humanity at the great moral effect of the meeting. The manifestation of July 1st had not only for its object the question of the treatment and possible extinction of hydrophobia in England, but in the nature of things it was also a protest against that false sentiment which led certain persons not merely to put on the same footing the life of men and that of animals—which was already a strong point with them—but even to prefer the existence of animals to the salvation of human life. When this view is taken, what is the limit? We must become firm vegetarians. We must even extend our scruples so that no living being is sacrificed. We must endure the importunities of a mosquito, the daring of a mouse, the bite of a flea—false ideas or excuses for a tirade which one finds most often at the root of all the attacks on experimental physiology.

"Certain credulous souls—through I know not what tales—imagine that our laboratories are chambers of torture. They ignore the fact that the rabbit or the guinea-pig is rendered insensible by chloroform before it is subjected to the most insignificant operation.

"As for me personally, the suffering of an animal affects me so much that I would never shoot a bird, and the cry of a wounded skylark pierces me to the heart; but if the investigation of the mysteries of Nature and the acquisition of new truths be at stake, the sovereignty of the object justifies all.

"Who, then, having the least regard for the pursuit of the knowledge of the mysteries of Nature, would put in the balance the sacrifice of a few fowls and rabbits with the discovery of the attenuation of virus and prophylactics which have resulted from such sacrifice? No one, my Lord Mayor, will have contributed more than you have done to rectify the errors which, under a show of compassion, can only hinder the progress of science, and compromise even the most legitimate interests of humanity."

CHAPTER XVI.

CLOSING YEARS.

We have seen that the strain of work and anxiety connected with the anti-rabic inoculations told so severely upon Pasteur's weakened health that he was practically compelled to bid farewell to those studies which had for so many years engrossed his whole attention, and the eager pursuit of which, during nearly half a century, had brought that inexorable toll of physical suffering which overshadowed the later years of his life, but could not sully the brightness of his intellect or dull the keenness of his perception.

The following striking personal impression produced by Pasteur was written but a short time before his death by one intimately acquainted with him :—

"Everyone knows that Pasteur is short, that since 1870 his leg and left arm, smitten by apoplexy, are somewhat stiff, and that he drags one foot much like a wounded veteran. Age, illness, the heavy labours of so many years,* the bitterness of conflict, the intense

* It may not be without interest to briefly refer to the record of published work which Pasteur has left behind him. Besides nearly two hundred notes and memoirs inserted in the "Annales de Chimie et de Physique," in the "Comptes Rendus" of the Academy of Sciences, in the "Recueil des Savants Etrangers," etc., Pasteur published separately "Nouvel Exemple de Fermentation déterminée par des Animalcules infusoires pouvant vivre sans Oxygène Libre" (1863); "Etudes sur le Vin, ses Maladies, Causes qui les provoquent, Procédés Nouveaux pour le Conserver et pour le Veillir" (1866); "Nouvelles

passion for his work, and, lastly, that prostration which follows triumph, have combined together to make a grand thing of his face.

"Weary, traversed with deep furrows, the skin and beard both white, his hair still thick, and nearly always covered with a black cap; the broad forehead wrinkled, seamed with the scars of genius, the mouth slightly drawn by paralysis, but full of kindness, all the more expressive of pity for the sufferings of others, as it appears lined by personal sorrow; and, above all, the living thought which still flashes from the eyes beneath the deep shadow of the brow—this is Pasteur as he appeared to me: a conqueror, who will some day become a legend, whose glory is as incalculable as the good he has accomplished."

Few men have during their lifetime received the public recognition for their labours which was accorded to Pasteur. This recognition, moreover, was not confined to his own country, but honours were showered

Etudes sur la Maladie des Vers à Soie" (1866); "Etudes sur le Vinaigre, sa Fabrication, ses Maladies, Moyen de les Prévenir" (1868); "Etudes sur la Maladie des Vers à Soie, Moyen Pratique Assuré de la Combattre et d'en Prévenir le Retour" (1870, 2 vols.); "Quelques Réflexions sur la Science en France" (1871); "Une Correspondance entre un Savant Français et un Savant Prussien pendant la Guerre —M. Pasteur et M. Naumann" (1872); Etudes sur la Bière, ses Maladies, Causes qui les Provoquent" (1876); "Les Microbes organisés, leur Rôle dans la Fermentation, la Putréfaction et la Contagion" (1878); "Examen Critique d'un Ecrit Posthume de Claude Bernard sur la Fermentation" (1879); "Discours de Réception de M. L. Pasteur à l'Académie Française" (1882); "Traitement de la Rage" (1886); "Résultats de l'Application de la Méthode Pasteur prévenant la Rage après Morsure" (1886); "Discours à l'Académie Française à la Réception de M. J. Bertrand" (1887); "Discours prononcé à l'Inauguration de la Statue de J. B. Dumas, à Alais" (1889).

upon him by numerous foreign public and scientific bodies. Thus, to briefly summarise some of these distinctions, we find him a member of the Academy of Sciences in 1862; Honorary Doctor of the Medical Faculty of the University of Bonn in 1868; Foreign Member of our Royal Society in 1869; an Associé libre of the Academy of Medicine in 1873; Member of the French Academy in 1881; a D.C.L. of Oxford in 1883; Perpetual Secretary of the Academy of Sciences in 1887; whilst among the various medals and other prizes bestowed upon him we find the Rumford Medal of the Royal Society in 1856; the Copley Medal of the same society in 1874; a prize of 10,000 francs from the Austrian Government in 1868, in recognition of his researches on the diseases of silkworms; a prize of 12,000 francs in 1873 from the Société d'Encouragement; a medal from the Russian Society of Rural Economy in 1882; the Albert Medal from the Society of Arts, also in 1882; the Bressa Prize of 12,000 francs from the Turin Academy of Sciences in 1888, etc.; whilst in 1874 the French Government voted him an annual pension of 12,000 francs, which in 1883 was raised to 25,000 francs, with the further proviso that on his death it should be continued to his widow and children.

Pasteur was also the recipient of numerous orders. Thus, Chevalier of the Legion of Honour in 1853, he became successively Officier in 1863, Commandeur in 1868, Grand Officier in 1878, and Grand Croix in 1881. A large number of orders were also bestowed upon him by foreign countries, amongst which were Russia Denmark, Greece, Brazil, Sweden, Turkey, Norway and Portugal.

If his life was darkened by struggles, it was equally illuminated with brilliant victories, which Pasteur not only prized on account of the vindication of the truths for which he fought and for the love of science, but also for the lustre which they shed upon his country.

"Si la science n'a pas de patrie," has said Pasteur, "l'homme de science doit en avoir une, et c'est à elle qu'il doit reporter l'influence que ses travaux peuvent avoir dans le monde."

It was in this sense that Pasteur participated with such profound feelings of emotion and gratitude in the magnificent ceremony of his jubilee which took place on December 27th, 1892, in celebration of his seventieth birthday.

Early in the year already a committee was formed in Denmark for the purpose of opening a national subscription to present Pasteur with a medal commemorating his discoveries. The Medical Society of Christiania followed suit and organised a public subscription to enable a scholarship to be founded which should be called after Pasteur, and provide the means for a student to complete his scientific studies in some foreign institute, and preferably in France. A similar movement with a like object was started in Stockholm. Throughout France all sections of society were united in the desire to worthily honour their great countryman.

The occasion was observed in Paris as a great, almost a national festival. The President of the Republic and all the Ministers of State were present, the members of the Institute of France, innumerable delegates of foreign as well as French scientific bodies, deputations from agricultural, pharmaceutical, veterinary and other colleges, and an immense gathering of admirers, as well as students from all parts of the country. In fact the large amphitheatre of the Sorbonne, placed at the disposal of the organising committee, capable of holding 2,500 persons, was crowded to overflowing, as many as 4,000 requests for places having been received.

The list of speakers included M. Dupuy, the Minister of Public Instruction, M. d'Abbadie, President of the Academy of Sciences, M. Joseph Bertrand, the perpetual Secretary of the Academy of Sciences, Sir Joseph, now Lord Lister (representing the Royal Societies of London and Edinburgh), the perpetual Secretary of the Academy of Medicine, and the President of the Municipal Council of Paris.

After these gentlemen had delivered their various orations M. Bertrand introduced the delegates who had been entrusted with addresses of congratulation from the University of Athens; the medical faculty and the Medical Society of Berlin; the Medical Society of Berne; the Belgian Microscopical Society; the Society of the Students of the Civil Hospitals in Brussels; from Bucharest; the Academic College, and the University of Christiania; the Hygienic Association of Cologne; the Academy of Copenhagen; the Royal Irish Academy and University; the Faculty of Medicine of Ghent; the Academy of Medicine and the Medical Society of Geneva; the University and the Faculty of Genoa; the University of Lausanne; the Faculty of Sciences and the University of Liège; from Leyden; from Posen; from the School of Medicine and Faculty of Sciences of Stockholm.

Then followed delegates from the Academy of Sciences; the Medical Society and the Society of Naturalists of St. Petersburg; from the Russian Students of the Institute of Experimental Medicine in St. Petersburg; the Turin Academy of Medicine; the University of Utrecht; and the Medical Society of Warsaw.

Thus strikingly did nations forget politics, and meet together to do honour to one of the greatest men of science of the century.

After the foreign delegates had handed their addresses and had filed past the table, behind which sat Pasteur, supported by the President of the Republic, the national delegates were summoned, amongst which were representatives from the towns of Dôle and Arbois, where, it will be remembered, Pasteur was born and had passed his childhood respectively.

Then followed the Students' Association of Paris, represented by their President.

It was now Pasteur's turn to address the great assembly, but being so much overcome by his feelings, his speech was actually read by his son.

In itself a sufficiently pathetic speech, delivered in the winter of his life, though at the zenith of his fame, it assumes a yet more pathetic significance inasmuch as it proved to be the last public address which Pasteur gave before his death.

"Monsieur le Président de la République.—Your presence transforms everything: a family fête becomes a public fête, and the simple anniversary of the birth of a savant, thanks to you, will remain a date in French science.

"Monsieur le Ministre, Messieurs—My first thought in the midst of this brilliant scene carries me back with melancholy to the memory of the many men of science who have known nothing but trials. In the past they had to contend against prejudices which stifled their ideas. These prejudices vanquished, they encountered obstacles and difficulties of all kinds.

"Still but a few years since, before public authorities and the Municipal Council had given magnificent dwellings to science, a man whom I greatly loved and admired, Claude Bernard, had, only a short distance from here, nothing but a damp and low cellar as a laboratory. Perhaps it was there that he was attacked with the malady which removed him from us!

"On learning what you had here arranged for me, the thought of him arose at once before me: I salute this great memory.

"Gentlemen, through an idea, at once delicate and ingenious, it would seem that you desired that my life in its entirety should to-day pass before my eyes. One of my countrymen from the Jura, the Mayor of the town of Dôle, has presented me with a photograph of the very humble house where my father and mother lived and struggled.

"The presence of all the students of the Ecole Normale brings back to me how dazzling was my first enthusiasm for science.

"The representatives of the faculty of Lille recall to me my first studies in crystallography and fermentation, which opened up an entirely new world to me. With what hopes I was filled when I first surmised that there were laws behind so many obscure phenomena! By what series of steps it was permitted to me, as a disciple of the experimental method, to pass on to physiological studies, you, my dear colleagues, have yourselves been witnesses. If I have sometimes disturbed the peace of our Academic meetings by somewhat too lively discussions, it is because I have passionately defended the truth.

"You, lastly, delegates of foreign nations, who have come from so far to give proof of your sympathy with France, you bring me the deepest happiness which a man can experience who believes invincibly that science and peace will triumph over ignorance and war, that people will learn to agree together, not for purposes of destruction but for improvement, and that the future will belong to those who shall have done the most for suffering humanity. I address myself to you, my dear Lister, and to all of you illustrious representatives of Science, of Medicine, and of Surgery. Young people, young people, confine yourselves to those methods, sure and powerful, of which we as yet know only the first secrets. And all, whatever may be your career, never permit yourselves to be overcome by scepticism, both unworthy and barren; neither permit the hours of sadness which pass over a nation to discourage you. Live in the serene peace of your laboratories and your libraries. First ask yourselves 'What have I done for my education?' Then, as you advance in life, 'What have I done for my country?' so that some day that supreme happiness may come to you, the consciousness of having contributed in some measure to the progress and welfare of humanity. But whether our endeavours are more or less favoured by the circumstances of our life, on approaching the great end we must have the right to say to ourselves, 'I have done what I was able.'

"Gentlemen, I express to you my profound emotion and my deep gratitude. Whilst on the reverse of this medal,* the great artist Roty has hidden beneath roses the date which now weighs so heavily on my life, so you have desired, my dear comrades, to give to my old age the spectacle which is capable of once more gladdening it—this gathering of youth so full of life and affection."

Dr. Roux has told us how the never-to-be-forgotten ceremony of his jubilee, in showing Pasteur the place he held in the esteem of the whole scientific world, moved him profoundly. "Puis Pasteur ne vécut plus que par l'amour des siens; il fallait les soins et toute l'affection dont il était entouré pour prolonger sa faiblesse. Mais jusqu'à la fin sa pensée était dans les laboratoires, avec ceux qui faisaient tous leurs efforts pour que la maison qui porte son nom restât digne de lui."

It was in September, 1895, that the news of Pasteur's grave state of health gave cause for universal anxiety.

A paralytic seizure, followed by a second attack a week later, coming upon him in his already enfeebled condition, led the worst to be anticipated, and on the 28th of September he passed away at Villeneuve-l'Etang, near Garches (Seine-et-Oise).

The body was embalmed and brought to Paris on October 1st, where it was received in the name of the Government by M. Poincaré, the Minister of Public Instruction, and was placed in a room of the Institut

* A gold medal presented to Pasteur, designed by M. Roty, and the funds for which were raised by international subscriptions.

Pasteur which was temporarily transformed into a chapel.

A public funeral at Notre Dame with military honours was accorded to Pasteur by the State, and took place amidst great pomp and ceremony on October 5th. His body was, however, only temporarily placed in one of the chapels of Notre Dame, for Pasteur's final resting-place was to be in the Institut Pasteur.* Hither it was brought at the beginning of January, and was deposited in the mausoleum which was erected by the Pasteur family.

The tomb † is built at the end of a long corridor in the Institute, and is shut off by magnificent gates of wrought-iron. The archway over these gates is decorated with irises on a gold ground, and the simple words are inscribed, "Ici repose Pasteur,"

* PASTEUR'S GRAVE.

No cypress-shadowed churchyard, nor the gloom
Of haunted cloisters, doth immortalise
The dust of him whose patience proved more wise
To save than Death to slay. The busy loom
Glancing with silk, the teeming herd, the bloom
Of purpling vineyards, and the grateful eyes
Of souls reprieved at Death's most dread assize,
Shall make eternal gladness round his tomb.
Not 'mid the dead should he be laid asleep
Who wageth still with Death triumphant strife,
Who sowed the good that centuries shall reap,
And took its terror from the healer's knife;
Defender of the living, he shall keep
His slumber in the arsenal of life."

ALFRED HAYES.

† The well-known tomb of Galla Placidia at Ravenna served as the model for the mausoleum.

whilst on either side of it are recorded the dates of his birth and death—"1822-1895." Passing through the gates, the crypt is reached by a flight of nine steps of white statuary marble. The pavement of the crypt is of marble mosaic on which are represented large wreaths of laurel. The crypt itself is formed by four arches which support a cupola, and in the centre is placed the sarcophagus, which is carved out of a single block of dark-green porphyry. The arches are supported on four groups, each of three columns, two of green porphyry and one of red, with Byzantine capitals of white marble. The walls are lined with a cream-coloured marble, richly veined in black, and above it are beautifully-executed mosaics.

On the marble which fills the arches on the right and left are inscriptions indicating Pasteur's discoveries, in historical order, as follows:

PASTEUR.

1848 DYSSYMETRIE MOLECULAIRE	1871 ETUDES SUR LA BIERE
1857 FERMENTATIONS	1877 MALADIES VIRULENTES
1862 GENERATIONS DITES SPONTANEES	1880 VIRUS VACCINS
1863 ETUDES SUR LE VIN	1885 PROPHYLAXIE DE LA RAGE
1865 MALADIES DES VERS A SOIE	

Beyond the sarcophagus is an apsidal chapel containing an altar of white marble, enclosed by a balustrade of the same material. Above the staircase are inscribed the following words, taken from the oration delivered by Pasteur at his reception into the Academy of Science:—"Heureux celui qui porte en soi un dieu, un idéal de beauté, et qui lui obéit—idéal de l'art, idéal de la science, idéal de la patrie, idéal des vertus de l'Evangile."

In the apse is another inscription:—"Ce monument fut élevé en MDCCCXCVI. à la mémoire de Pasteur par la piété de sa veuve et de ses enfants."

The mosaics, executed by A. G. Martin, represent fowls, cattle, sheep, and dogs, indicating Pasteur's researches on chicken cholera, anthrax, and rabies. There are also designs of hops, vines, and mulberry trees, with silkworms and moths, representing his investigations on the diseases of beer and wine and silkworms.

Pasteur was a devout Roman Catholic, and the religious side of his character is indicated in the mosaics by angelic figures of Faith, Hope, Charity, and Science, and, above the altar, by the figure of a dove descending, representing the Holy Spirit, and on either side the Greek letters *A* and *Ω*.

Here rest, then, the mortal remains of that great man of whom Rénan once eloquently said:

"His scientific life is like a luminous trail in the great night of the infinitely little, in those ultimate abysses of being where life is born."

INDEX.

PRINTED BY CASSELL & COMPANY, LIMITED, LA BELLE SAUVAGE, LONDON, E.C.

Illustrated, Fine-Art, and other Volumes.

Adventure, The World of. Fully Illustrated. In Three Vols. 9s. each.
Adventures in Criticism By A. T. QUILLER-COUCH. 6s.
Africa and its Explorers, The Story of. By DR. ROBERT BROWN, F.L.S. Illustrated. Complete in 4 Vols., 7s. 6d. each.
Animals, Popular History of. By HENRY SCHERREN, F.Z.S. With 13 Coloured Plates and other Illustrations. 7s. 6d.
Architectural Drawing. By R. PHENÉ SPIERS. Illustrated. 10s. 6d.
Art, The Magazine of. Half-Yearly Vols. With Exquisite Photogravures, a Series of Full-page Plates, and hundreds of Illustrations. 10s. 6d. Yearly Vol, 21s.
Artistic Anatomy. By Prof. M. DUVAL. *Cheap Edition.* 3s. 6d.
Astronomy, The Dawn of. By Sir NORMAN LOCKYER, K.C.B., F.R.S., &c. Illustrated. 21s.
Ballads and Songs. By WILLIAM MAKEPEACE THACKERAY. With Original Illustrations. 6s.
Barber, Charles Burton, The Works of. With Forty-one Plates and Portraits, and Introduction by HARRY FURNISS. 21s. net.
Battles of the Nineteenth Century. An entirely New and Original Work, with several hundred Illustrations. In 2 Vols., 9s. each.
Beetles, Butterflies, Moths, and Other Insects. By A. W. KAPPEL, F.E.S., and W. EGMONT KIRBY. With 12 Coloured Plates. 3s. 6d.
"Belle Sauvage" Library, The. Cloth, 2s. each. A list of the Volumes post free on application.
Biographical Dictionary, Cassell's New. *Cheap Edition*, 3s. 6d.
Birds' Nests, British: How, Where, and When to Find and Identify Them. By R. KEARTON, F.Z.S. With nearly 130 Illustrations of Nests, Eggs, Young, etc., from Photographs by C. KEARTON. 21s.
Birds' Nests, Eggs, and Egg-Collecting. By R. KEARTON, F.Z.S. Illustrated with 22 Coloured Plates. *Fifth and Enlarged Edition.* 5s.
Black Watch, The. The Record of an Historic Regiment. By ARCHIBALD FORBES, LL.D. 6s.
Britain's Roll of Glory; or, the Victoria Cross, its Heroes, and their Valour. By D. H. PARRY. Illustrated. 7s. 6d.
British Ballads. With 300 Original Illustrations. *Cheap Edition.* Two Vols. in one. Cloth, 7s. 6d.
British Battles on Land and Sea. By JAMES GRANT. With about 800 Illustrations. *Cheap Edition.* In Four Vols., 3s. 6d. each.
Building World. Half-Yearly Volumes, 4s. each.
Butterflies and Moths, European. With 61 Coloured Plates. 35s.
Canaries and Cage-Birds, The Illustrated Book of. With 56 Facsimile Coloured Plates, 35s. Half-morocco, £2 5s.
Cassell's Family Magazine. Half-Yearly Volumes, 5s. each; or Yearly Volumes, 8s. each.
Cathedrals, Abbeys, and Churches of England and Wales. Descriptive, Historical, Pictorial. *Popular Edition.* Two Vols. 25s.
Cats and Kittens. By HENRIETTE RONNER. With Portrait and 13 Full-page Photogravure Plates and numerous Illustrations. £2 2s.
Chums. The Illustrated Paper for Boys. Yearly Volume, 8s.
Cities of the World. Four Vols. Illustrated. 7s. 6d. each.
Civil Service, Guide to Employment in the. Entirely New Edition. Paper, 1s. Cloth, 1s. 6d.
Clinical Manuals for Practitioners and Students of Medicine. A List of Volumes forwarded post free on application to the Publishers.
Colour. By Prof. A. H. CHURCH. With Coloured Plates. 3s. 6d.
Conning Tower, In a; or, How I Took H.M.S. "Majestic" into Action. By H. O. ARNOLD-FORSTER, M.P. *Cheap Edition.* Illd. 6d.

Gun and its Development, The. By W. W. GREENER. With 500 Illustrations. *Entirely New Edition.* 10s. 6d.

Heavens, The Story of the. By Sir ROBERT STAWELL BALL, LL.D., F.R.S., F.R.A.S. With Coloured Plates. *Popular Edition.* 10s. 6d.

Heroes of Britain in Peace and War. With 300 Original Illustrations. *Cheap Edition.* Complete in One Vol., 3s. 6d.

History, A Foot-note to. Eight Years of Trouble in Samoa. By ROBERT LOUIS STEVENSON. 6s.

Home Life of the Ancient Greeks, The. Translated by ALICE ZIMMERN. Illustrated. *Cheap Edition.* 5s.

Horse, The Book of the. By SAMUEL SIDNEY. With 17 Full-page Collotype Plates of Celebrated Horses of the Day, and numerous other Illustrations. Cloth, 15s.

Horses and Dogs. By O. EERELMAN. With Descriptive Text. Translated from the Dutch by CLARA BELL. With Author's Portrait and Fifteen Full-page and other Illustrations. 25s. net.

Houghton, Lord: The Life, Letters, and Friendships of Richard Monckton Milnes, First Lord Houghton. By Sir WEMYSS REID. In Two Vols., with Two Portraits. 32s.

Household, Cassell's Book of the. Complete in Four Vols. 5s. each. Four Vols. in Two, half-morocco, 25s.

Hygiene and Public Health. By B. ARTHUR WHITELEGGE, M.D. 7s. 6d.

Iron Pirate, The. By MAX PEMBERTON. Illustrated. 5s.

Khiva, A Ride to. By COL. FRED BURNABY. *New Edition.* With Portrait and Seven Illustrations. 3s. 6d.

Ladies' Physician, The. By A LONDON PHYSICIAN. *Cheap Edition, Revised and Enlarged.* 3s. 6d.

Lady's Dressing-room, The. Translated from the French of BARONESS STAFFE by LADY COLIN CAMPBELL. *Cheap Edition,* 2s. 6d.

Letters, The Highway of, and its Echoes of Famous Footsteps. By THOMAS ARCHER. Illustrated. *Cheap Edition,* 5s.

Letts's Diaries and other Time-saving Publications published exclusively by CASSELL & COMPANY. (*A list free on application.*)

Library Year Book, 1897. A Record of General Library Progress and Work. Edited by THOMAS GREENWOOD. With over 50 Special Engravings. 2s. 6d.

Loftus, Lord Augustus, The Diplomatic Reminiscences of. First and Second Series. Two Vols., each with Portrait, 32s. each Series.

London, Greater. By EDWARD WALFORD. Two Vols. With about 400 Illustrations. 9s. each.

London, Old and New. Six Vols., each containing about 200 Illustrations and Maps. Cloth, 9s. each.

London, The Queen's. With nearly 400 superb Views. 9s.

Manchester, Old and New. By WILLIAM ARTHUR SHAW, M.A. With Original Illustrations. Three Vols., 31s. 6d.

Medicine, Manuals for Students of. (*A List forwarded post free.*)

Mesdag, H. W., the Painter of the North Sea. With Etchings and Descriptive Text. By PH. ZILCKEN. The Text translated from the Dutch by CLARA BELL. 36s.

Modern Europe, A History of. By C. A. FYFFE, M.A. *Cheap Edition in One Volume,* 10s. 6d. Library Edition. Illustrated. 3 Vols., 7s. 6d. each.

Music, Illustrated History of. By EMIL NAUMANN. Edited by the Rev. Sir F. A. GORE OUSELEY, Bart. Illustrated. Two Vols. 31s. 6d.

National Library, Cassell's. In 214 Volumes. Paper covers, 3d.; cloth, 6d. (*A Complete List of the Volumes post free on application.*)

Natural History, Cassell's Concise. By E. PERCEVAL WRIGHT, M.A., M.D., F.L.S. With several Hundred Illustrations. 7s. 6d.

Natural History, Cassell's New. Edited by Prof. P. MARTIN DUNCAN, M.B., F.R.S., F.G.S. *Cheap Edition.* With about 2,000 Illustrations. In Three Double Vols. 6s. each.

Nature and a Camera, With. Being the Adventures and Observations of a Field Naturalist and an Animal Photographer. By RICHARD KEARTON, F.Z.S. With a Special Frontispiece, and about 150 other Pictures from Photographs by CHERRY KEARTON. 21s.

Nature's Wonder Workers. By KATE R. LOVELL. Illustrated. 2s. 6d.

New Zealand, Pictorial. With Preface by Sir W. B. PERCEVAL, K.C.M.G. Illustrated. 6s.

Novels, Popular. Extra Crown 8vo, 6s. each. Cloth.

- **By a Hair's-Breadth.** By Headon Hill.
- **Cupid's Garden.** By Ellen Thorneycroft Fowler.
- **A Limited Success.** By Sarah Pitt.
- **The Wrothams of Wrotham Court.** By Frances Heath Freshfield.
- **Sentimental Tommy.** By J. M. Barrie. *Illustrated Edition.*
- **The Little Minister.** By J. M. Barrie. *Illustrated Edition.*
- **Treasure Island.** By Robert Louis Stevenson.
- **The Master of Ballantrae.** By Robert Louis Stevenson.
- **The Black Arrow.** By Robert Louis Stevenson.

  } Also a *Popular Edition*, 3s. 6d. each.
- **Kidnapped.** By Robert Louis Stevenson.
- **Catriona: A Sequel to "Kidnapped."** By Robert Louis Stevenson.
- **Island Nights' Entertainments.** By Robert Louis Stevenson.
- **The Wrecker.** By Robert Louis Stevenson and Lloyd Osbourne.
- **Story-Teller's Pack, A.** By Frank Stockton.
- **Mrs. Cliff's Yacht.** By Frank Stockton.
- **The Adventures of Captain Horn.** By Frank Stockton.
- **My Lord Duke.** By E. W. Hornung.
- **Rogue's March, The.** By E. W. Hornung.
- **Tiny Luttrell.** By E. W. Hornung.
- **Ill-gotten Gold: A Story of a Great Wrong and a Great Revenge.** By W. G. Tarbet.
- **Loveday. A Story of a Stirring Time.** By A. E. Wickham.
- **Puritan's Wife, A.** By Max Pemberton.
- **The Impregnable City.** By Max Pemberton.
- **The Sea-Wolves.** By Max Pemberton.
- **What Cheer!** By W. Clark Russell.
- **From the Memoirs of a Minister of France.** By Stanley J. Weyman.
- **The Story of Francis Cludde.** By Stanley J. Weyman.
- **The White Shield.** By Bertram Mitford.
- **Old Maids and Young.** By E. D'Esterre-Keeling.
- **Tuxter's Little Maid.** By G. B. Burgin.
- **The Hispaniola Plate. (1683—1893)** By John Bloundelle-Burton.
- **The Highway of Sorrow.** By Hesba Stretton and * * * * * * * *, a Famous Russian Exile.
- **'Lisbeth.** By Leslie Keith.
- **Wandering Heath.** A Selection of Short Stories. By Q.

Nursing for the Home and for the Hospital, A Handbook of. By CATHERINE J. WOOD. *Cheap Edition.* 1s. 6d.; cloth, 2s.

Nursing of Sick Children. By CATHERINE J. WOOD. 2s. 6d.

Oil Painting, A Manual of. By the Hon. JOHN COLLIER. 2s. 6d.

Our Own Country. Six Vols. With 1,200 Illustrations. 7s. 6d. each.

Painting, The English School of. *Cheap Edition.* 3s. 6d.

Painting, Practical Guides to. With Coloured Plates:—

MARINE PAINTING, 5s.; ANIMAL PAINTING, 5s.; CHINA PAINTING, 5s.; ELEMENTARY FLOWER PAINTING, 3s.; WATER-COLOUR PAINTING, 5s.; NEUTRAL TINT, 5s.; SEPIA, in Two Vols., 3s. each, or in One Vol., 5s.; FLOWERS, AND HOW TO PAINT THEM, 5s.

Paris, Old and New. Illustd. In Two Vols., 9s. or 10s. 6d. each.

Peoples of the World, The. In Six Vols. By Dr. ROBERT BROWN. Illustrated. 7s. 6d. each.

Photography for Amateurs. By T. C. HEPWORTH. Illd. **1s. or 1s. 6d.**

Phrase and Fable, Dr. Brewer's Dictionary of. *Entirely New and Greatly Enlarged Edition.* 10s. 6d. Also in half-morocco, Two Vols., 15s.

Picturesque America. Complete in Four Vols., with 48 Exquisite Steel Plates and about 800 Original Wood Engravings. £12 12s. the set. *Popular Edition.* In Four Vols., 18s. each.

Picturesque Australasia, Cassell's. With upwards of 1,000 Illustrations. In Four Vols., 7s. 6d. each. [the Set.

Picturesque Canada. With 600 Original Illustrations. Two Vols. £9 9s.

Picturesque Europe. Complete in Five Vols. Each containing 13 Exquisite Steel Plates, from Original Drawings, and nearly 200 Original Illustrations. Cloth, £21. POPULAR EDITION. In Five Vols., 18s. each

Picturesque Mediterranean, The. With Magnificent Original Illustrations by the leading Artists of the Day. Complete in Two Vols. £2 2s. each.

Pigeon Keeper, The Practical. By LEWIS WRIGHT. Illustrated. 3s. 6d.

Pigeons, Fulton's Book of. Edited by LEWIS WRIGHT. Revised, Enlarged, and Supplemented by the Rev. W. F. LUMLEY. With 50 Full-page Illustrations. *Popular Edition.* 10s. 6d. Original Edition, with 50 Coloured Plates and Numerous Wood-Engravings. 21s.

Planet, The Story of Our. By the Rev. Prof. BONNEY, F.R.S., etc. With Coloured Plates and Maps and about 100 Illustrations. *Cheap Edition.* 10s. 6d.

Pocket Library, Cassell's. Cloth, 1s. 4d. each.
A King's Diary. By PERCY WHITE. A White Baby. By JAMES WELSH. The Little Huguenot. By MAX PEMBERTON. A Whirl Asunder. By GERTRUDE ATHERTON. Lady Bonnie's Experiment. By TIGHE HOPKINS. The Paying Guest. By GEORGE GISSING.

Portrait Gallery, The Cabinet. Complete in Five Series, each containing 36 Cabinet Photographs of Eminent Men and Women. 15s. each.

Portrait Gallery, Cassell's Universal. Containing 240 Portraits of Celebrated Men and Women of the Day. Cloth, 6s.

Poultry Keeper, The Practical. By L. WRIGHT. Illustrated. 3s. 6d.

Poultry, The Book of. By LEWIS WRIGHT *Popular Edition.* 10s. 6d.

Poultry, The Illustrated Book of. By LEWIS WRIGHT. With Fifty Coloured Plates. *New and Revised Edition.* Cloth, gilt edges, 21s. Half-morocco (*Price on application*).

"Punch," The History of. By M. H. SPIELMANN. With nearly 170 Illustrations, Portraits, and Facsimiles. Cloth, 16s.; *Large Paper Edition,* £2 2s. net.

Q's Works, Uniform Edition of. 5s. each.
Dead Man's Rock. The Splendid Spur. The Blue Pavilions. The Astonishing History of Troy Town. "I Saw Three Ships," and other Winter's Tales. Noughts and Crosses. The Delectable Duchy.

Queen Summer; or, The Tourney of the Lily and the Rose. With Forty Pages of Designs in Colours by WALTER CRANE. 6s.

Queen Victoria, The Life and Times of. By ROBERT WILSON. Complete in Two Vols. With numerous Illustrations. 9s. each.

Queen's London, The. Containing nearly 400 Exquisite Views of London and its Environs. Cloth, 9s.

Rabbit-Keeper, The Practical. By CUNICULUS. Illustrated. 3s. 6d.

Railways, Our. Their Origin, Development, Incident, and Romance. By JOHN PENDLETON. Illustrated. 2 Vols., 12s.

Railway Guides, Official Illustrated. With Illustrations, Maps, &c. Price 1s. each; or in cloth, 2s. each.
LONDON AND NORTH WESTERN RAILWAY, GREAT WESTERN RAILWAY, MIDLAND RAILWAY, GREAT NORTHERN RAILWAY, GREAT EASTERN RAILWAY, LONDON AND SOUTH WESTERN RAILWAY, LONDON, BRIGHTON AND SOUTH COAST RAILWAY, SOUTH EASTERN RAILWAY.

Railway Guides, Official Illustrated. Abridged and Popular Editions. Paper covers, 3d. each.
GREAT EASTERN RAILWAY, LONDON AND NORTH WESTERN RAILWAY LONDON AND SOUTH WESTERN RAILWAY, GREAT WESTERN RAILWAY, MIDLAND RAILWAY, GREAT NORTHERN RAILWAY, LONDON, BRIGHTON AND SOUTH COAST RAILWAY, SOUTH EASTERN RAILWAY.

Rivers of Great Britain: Descriptive, Historical, Pictorial.
RIVERS OF THE SOUTH AND WEST COASTS. 42s.
THE ROYAL RIVER: The Thames, from Source to Sea. 16s.
RIVERS OF THE EAST COAST. *Popular Edition*, 16s.

Robinson Crusoe, Cassell's New Fine-Art Edition. 7s. 6d. *Cheap Edition*, 3s 6d. or 5s.

"Rogues of the Fiery Cross." By S. WALKEY. With 16 Full page Illustrations. 5s.

Russo-Turkish War, Cassell's History of. With about 500 Illustrations. Two Vols., 9s. each. *New Edition*, Vol. I., 9s.

Saturday Journal, Cassell's. Yearly Volume, cloth, 7s. 6d.

Scarlet and Blue: or Songs for Soldiers and Sailors By JOHN FARMER. 5s. Words only, paper, 6d.; cloth, 9d.

Science Seiies, The Century. Consisting of Biographies of Eminent Scientific Men of the present Century. Edited by Sir HENRY ROSCOE, D.C.L., F.R.S. Crown 8vo, 3s. 6d. each.
John Dalton and the Rise of Modern Chemistry. By Sir HENRY E. ROSCOE, F.R.S.
Major Rennell, F.R.S., and the Rise of English Geography. By SIR CLEMENTS R. MARKHAM, C.B., F.R.S.
Justus Von Liebig: His Life and Work. By W. A. SHENSTONE, F.I.C.
The Herschels and Modern Astronomy. By Miss AGNES M. CLERKE.
Charles Lyell and Modern Geology. By Professor T. G. BONNEY, F.R.S.
J. Clerk Maxwell and Modern Physics. By R. T. GLAZEBROOK, F.R.S.
Humphry Davy, Poet and Philosopher. By T. E. THORPE, F.R.S.
Charles Darwin and the Theory of Natural Selection. By EDWARD B. POULTON, M.A., F.R.S.

Science for All. Edited by Dr. ROBERT BROWN. *Cheap Edition.* In Five Vols. 3s. 6d. each.

Scotland, Picturesque and Traditional. By G. E. EYRE-TODD. 6s.

Sea, The Story of the. Edited by Q. Illd. In Two Vols., 9s. each.

Shaftesbury, The Seventh Earl of, K.G., The Life and Work of. By EDWIN HODDER. *Cheap Edition.* 3s. 6d.

Shakespeare, The Plays of. Edited by Professor HENRY MORLEY. Complete in Thirteen Vols., cloth, 21s.; also 39 Vols., cloth, in box, 21s.; half-morocco, cloth sides, 42s.

Shakespeare, Cassell's Quarto Edition. Containing about 600 Illustrations by H. C. SELOUS. Complete in Three Vols., cloth gilt, £3 3s.

Shakespeare, The England of. *New Edition.* By E. GOADBY. With Full-page Illustrations. 2s. 6d.

Shakspere, The Leopold. With 400 Illustrations. *Cheap Edition.* 3s. 6d. Cloth gilt, gilt edges, 5s.; roxburgh, 7s. 6d.

Shakspere, The Royal. With Steel Plates and Wood Engravings. Three Vols. 15s. each.

Sketches, The Art of Making and Using. From the French of G. FRAIPONT. By CLARA BELL. With 50 Illustrations. 2s. 6d.

Social England. A Record of the Progress of the People. By various Writers. Edited by H. D. TRAILL, D.C.L. (Completion.) Vols. I., II., & III., 15s. each. Vols. IV. & V., 17s. each. Vol. VI., 18s.

Sports and Pastimes, Cassell's Complete Book of. *Cheap Edition.* With more than 900 Illustrations. Medium 8vo, 992 pages, cloth, 3s. 6d.

Star-Land. By Sir R. S. BALL, LL.D., etc. Illustrated. 6s.

Holy Land and the Bible, The. By the Rev. C. GEIKIE, D.D., LL.D. (Edin.). *Cheap Edition*, with 24 Collotype Plates, 12s. 6d.

Life of Christ, The. By the Very Rev. Dean FARRAR, D.D., F.R.S. CHEAP EDITION. With 16 Full-page Plates. Cloth gilt, 3s. 6d. LIBRARY EDITION. Two Vols. Cloth, 24s.; morocco, 42s. ILLUSTRATED EDITION. Cloth, 7s. 6d.; cloth, full gilt, gilt edges, 10s. 6d. POPULAR EDITION. With 16 Full-page Plates. Cloth gilt, gilt edges, 7s. 6d.

Moses and Geology; or, The Harmony of the Bible with Science. By the Rev. SAMUEL KINNS, Ph.D., F.R.A.S. Illustrated. *Library Edition, Revised to Date.* 10s. 6d.

My Life in Christ. Being Extracts from the Diary of the Most Reverend JOHN ILIYTCH SERGIEFF (Father John). Translated by E. E. GOULAEFF, St. Petersburg. 9s.

Commentary for English Readers. Edited by Bishop ELLICOTT. With Contributions by eminent Scholars and Divines:—

> **New Testament.** *Original Edition.* Three Vols., 21s. each; or in half-morocco, £4 14s. 6d. the set. *Popular Edition.* Unabridged. Three Vols., 4s. each
>
> **Old Testament.** *Original Edition.* Five Vols., 21s. each; or in half-morocco, £7 17s. 6d. the set. *Popular Edition.* Unabridged. Five Vols., 4s. each.

*** *The Complete Set of Eight Volumes in the Popular Edition is supplied at 30s.*

New Testament Commentary. Edited by Bishop ELLICOTT. Handy Volume Edition. St. Matthew, 3s. 6d. St. Mark, 3s. St. Luke, 3s. 6d. St. John, 3s. 6d. The Acts of the Apostles, 3s. 6d. Romans, 2s. 6d. Corinthians I. and II., 3s. Galatians, Ephesians, and Philippians, 3s. Colossians, Thessalonians, and Timothy, 3s. Titus, Philemon, Hebrews, and James, 3s. Peter, Jude, and John, 3s. The Revelation, 3s. An Introduction to the New Testament, 3s. 6d.

Old Testament Commentary. Edited by Bishop ELLICOTT. Handy Volume Edition. Genesis, 3s. 6d. Exodus, 3s. Leviticus, 3s. Numbers, 2s. 6d. Deuteronomy, 2s. 6d.

Plain Introductions to the Books of the Old Testament. Edited by Bishop ELLICOTT. 3s. 6d.

Plain Introductions to the Books of the New Testament. Edited by Bishop ELLICOTT. 3s. 6d.

Protestantism, The History of. By the Rev. J. A. WYLIE, LL.D. Containing upwards of 600 Original Illustrations. Three Vols. 9s. each.

Quiver Yearly Volume, The. With about 600 Original Illns. 7s. 6d.

Religion, The Dictionary of. By the Rev. W. BENHAM, B.D. *Cheap Edition.* 10s. 6d.

St. George for England; and other Sermons preached to Children. By the Rev. T. TEIGNMOUTH SHORE, M.A., Canon of Worcester. 5s.

St. Paul, The Life and Work of. By the Very Rev. Dean FARRAR, D.D., F.R.S. CHEAP EDITION. With 16 Full-page Plates, cloth gilt, 3s. 6d.; LIBRARY EDITION. Two Vols., cloth, 24s.; calf, 42s. ILLUSTRATED EDITION, One Vol. £1 1s.; morocco, £2 2s. POPULAR EDITION. One Volume; Persian morocco, 10s. 6d.; tree-calf, 15s.

"Sunday," Its Origin, History, and Present Obligation. By the Ven. Archdeacon HESSEY, D.C.L. *Fifth Edition.* 7s. 6d.

Twilight of Life, The. Words of Counsel and Comfort for the Aged. By the Rev. JOHN ELLERTON, M.A. 1s. 6d.

Educational Works and Students' Manuals.

Agricultural Text-Books, Cassell's. Edited by JOHN WRIGHTSON, Professor of Agriculture. Illd., 2s. 6d. each.—**Farm Crops.** By Prof. WRIGHTSON.—**Soils and Manures.** By J. M. H. MUNRO, D.Sc. (London), F.I.C., F.C.S.—**Live Stock.** By Prof. WRIGHTSON.
Alphabet, Cassell's Pictorial. 2s. and 2s. 6d.
Arithmetics, Cassell's "Belle Sauvage." By GEORGE RICKS, B.Sc. Lond. With Test Cards. (*List on application.*)
Atlas, Cassell's Popular. Containing 24 Coloured Maps. 1s. 6d.
Book-Keeping. By THEODORE JONES. For Schools, 2s.; cloth, 3s. For the Million, 2s.; cloth, 3s. Books for Jones's System, 2s.
British Empire Map of the World. New Map for Schools and Institutes. By G. R. PARKIN and J. G. BARTHOLOMEW, F.R.G.S. 25s.
Chemistry, The Public School. By J. H. ANDERSON, M.A. 2s. 6d.
Cookery for Schools. By LIZZIE HERITAGE. 6d.
Dulce Domum. Rhymes and Songs for Children. Edited by JOHN FARMER, Editor of "Gaudeamus," &c. Old Notation and Words, 5s.
N.B.—The words of the Songs in "Dulce Domum" (with the Airs both in Tonic Sol-fa and Old Notation) can be had in Two Parts, 6d. each.
Euclid, Cassell's. Edited by Prof. WALLACE, M.A. 1s.
Experimental Geometry. By PAUL BERT. Illustrated. 1s. 6d.
French, Cassell's Lessons in. *New and Revised Edition.* Parts I. and II., each 1s. 6d.; complete 2s. 6d. Key, 1s. 6d.
French-English and English-French Dictionary. 3s. 6d. or 5s.
French Reader, Cassell's Public School. By G. S. CONRAD. 2s. 6d.
Gaudeamus. Songs for Colleges and Schools. Edited by JOHN FARMER. 5s. Words only, paper covers, 6d.; cloth, 9d.
German Dictionary, Cassell's. (German-English, English-German). *Cheap Edition.* Cloth, 3s. 6d.; half-morocco, 5s.
Hand and Eye Training. By G. RICKS, B.Sc. 2 Vols., with 16 Coloured Plates in each Vol. Cr. 4to, 6s. each. Cards for Class Use, 5 sets, 1s. each.
Hand and Eye Training. By GEORGE RICKS, B.Sc., and JOSEPH VAUGHAN. Illustrated. Vol. I. **Designing with Coloured Papers**; Vol. II. **Cardboard Work**, 2s. each. Vol. III. **Colour Work and Design**, 3s.
Historical Cartoons, Cassell's Coloured. Size 45 in. × 35 in., 2s. each. Mounted on canvas and varnished, with rollers, 5s. each.
Italian Lessons, with Exercises, Cassell's. Cloth, 2s.
Latin Dictionary, Cassell's. (Latin-English and English-Latin.) Cloth, 3s. 6d.; half-morocco, 5s.
Latin Primer, The First. By Prof. POSTGATE. 1s.
Latin Primer, The New. By Prof. J. P. POSTGATE. Crown 8vo, 2s. 6d.
Latin Prose for Lower Forms. By M. A. BAYFIELD, M.A. 2s. 6d.
Laws of Every-day Life. By H. O. ARNOLD-FORSTER, M.P. 1s. 6d. *Special Edition* on Green Paper for Persons with Weak Eyesight. 2s.
Lessons in Our Laws; or, Talks at Broadacre Farm. By H. F. LESTER, B.A. Parts I. and II., 1s. 6d. each.
Little Folks' History of England. Illustrated. 1s. 6d.
Making of the Home, The. By Mrs. SAMUEL A. BARNETT. 1s. 6d.
Marlborough Books:—Arithmetic Examples, 3s. French Exercises, 3s. 6d. French Grammar, 2s. 6d. German Grammar, 3s. 6d.
Mechanics and Machine Design, Numerical Examples in Practical. By R. G. BLAINE, M.E. *New Edition, Revised and Enlarged.* With 79 Illustrations. Cloth, 2s. 6d.
Mechanics for Young Beginners. By the Rev. J. G. EASTON, M.A. *Cheap Edition.* 2s. 6d.
Mechanics, Applied. By JOHN PERRY, M.E., D.Sc., &c. Illustd. 7s. 6d.
Models and Common Objects, How to Draw from. By W. E. SPARKES. Illustrated. 3s.

Models, Common Objects, and Casts of Ornament, How to Shade from. By W. E. SPARKES. With 25 Plates by the Author. **3s.**

Natural History Coloured Wall Sheets, Cassell's New. 16 Subjects. Size 39 by 31 in. Mounted on rollers and varnished. **3s.** each.

Object Lessons from Nature. By Prof. L. C. MIALL, F.L.S. Fully Illustrated. *New and Enlarged Edition.* Two Vols., **1s. 6d.** each.

Physiology for Schools. By A. T. SCHOFIELD, M.D., M.R.C.S., &c. Illustrated. Cloth, **1s. 9d.**; Three Parts, paper covers, **5d.** each; or cloth limp, **6d.** each.

Poetry Readers, Cassell's New. Illustrated. 12 Books, **1d.** each; or complete in one Vol., cloth, **1s. 6d.**

Popular Educator, Cassell's. With Revised Text, New Maps, New Coloured Plates, New Type, &c. In 8 Vols., **5s.** each; or in Four Vols., half-morocco, **50s.** the set.

Readers, Cassell's "Belle Sauvage." An entirely New Series. Fully Illustrated. Strongly bound in cloth. (*List on application.*)

Readers, Cassell's "Higher Class." (*List on application.*)

Readers, Cassell's Readable. Illustrated. (*List on application.*)

Readers for Infant Schools, Coloured. Three Books. **4d.** each.

Reader, The Citizen. By H. O. ARNOLD-FORSTER, M.P. Illustrated. **1s. 6d.** Also a *Scottish Edition*, cloth, **1s. 6d.**

Reader, The Temperance. By J. DENNIS HIRD. **1s.** or **1s. 6d.**

Readers, Geographical, Cassell's New. Illd. (*List on application.*)

Readers, The "Modern School" Geographical. (*List on application.*)

Readers, The "Modern School." Illustrated. (*List on application.*)

Reckoning, Howard's Art of. By C. FRUSHER HOWARD. Paper covers, **1s.**; cloth, **2s.** *New Edition*, **5s.**

Rolit. A Means of Learning French. By J. J. TYLOR. **3s.**

Round the Empire. By G. R. PARKIN. Fully Illustrated. **1s. 6d.**

Science Applied to Work. By J. A. BOWER. **1s.**

Science of Every-day Life. By J. A. BOWER. Illustrated. **1s.**

Shakspere's Plays for School Use. 9 Books. Illustrated. **6d.** each.

Spelling, A Complete Manual of. By J. D. MORELL, LL.D. **1s.**

Technical Manuals, Cassell's. Illustrated throughout:—
Handrailing and Staircasing, **3s. 6d.**—Bricklayers, Drawing for, **3s.**—Building Construction, **2s.** — Cabinet-Makers, Drawing for, **3s.** — Carpenters and Joiners, Drawing for, **3s. 6d.**—Gothic Stonework, **3s.**—Linear Drawing and Practical Geometry, **2s.**—Linear Drawing and Projection. The Two Vols. in One, **3s. 6d.**—Machinists and Engineers, Drawing for, **4s. 6d.**—Model Drawing, **3s.**—Orthographical and Isometrical Projection, **2s.**—Practical Perspective, **3s.**—Stonemasons, Drawing for, **3s.**—Applied Mechanics, by Sir R. S. Ball, LL.D., **2s.**—Systematic Drawing and Shading, **2s.**

Technical Educator, Cassell's. With Coloured Plates and Engravings. Complete in Six Volumes, **3s. 6d.** each.

Technology, Manuals of. Edited by Prof. AYRTON, F.R.S., and RICHARD WORMELL, D.Sc., M.A. Illustrated throughout:—
The Dyeing of Textile Fabrics, by Prof. Hummel, **5s.**—Watch and Clock Making, by D. Glasgow, Vice-President of the British Horological Institute, **4s. 6d.**—Steel and Iron, by Prof. W. H. Greenwood, F.C.S., M.I.C.E., &c., **5s.**—Spinning Woollen and Worsted, by W. S. B. McLaren, **4s. 6d.**—Design in Textile Fabrics, by T. R. Ashenhurst, **4s. 6d.**—Practical Mechanics, by Prof. Perry, M.E., **3s. 6d.**—Cutting Tools Worked by Hand and Machine, by Prof. Smith, **3s. 6d.**

Things New and Old; or, Stories from English History. By H. O. ARNOLD-FORSTER, M.P. Fully Illustrated, and strongly bound in Cloth. Standards I. & II., **9d.** each; Standard III., **1s.**; Standard IV., **1s. 3d.**; Standards V. & VI., **1s. 6d.** each; Standard VII., **1s. 8d.**

This World of Ours. By H. O. ARNOLD-FORSTER, M.P. Illustrated. *Cheap Edition*, **2s. 6d.**