THE EVOLUTION OF THE GERM THEORY OF DISEASE.

AN ESSAY

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FOREWORD.

"What does the germ theory hold?
As commonly understood today the germ theory maintains that infectious diseases are due to certain small microscopic plants or animals known collectively as microbes."

"Chemistry in Medicine" (New York 1929).

As I start, with a quotation, so I continue, and end. For this essay appears to be but a series of quotations strung together in chronological sequence. Yet, perhaps, some excuse may be offered. To use the results of other men in Literature constitutes plagiarism: whereas in Science, the highest reward a scientist hopes to get for his work, is to know that it can be of some use to another in his attempt to bring something fresh before the world.

Clifford Dobell took some twenty years to a study of one man - Antony von Leeuwenhoek; I have had to take a minute fraction of that time to study many men. Am I not justified, then, in using the results and opinions of Dobell, and others like him who are obviously more competent to judge than I am?

Others who have already sifted the great mass of literature on the various aspects of the subject, have picked out those parts which have most direct reference to them. I have sifted further, and present my results, not with the aspiration that they may shine with the divine Aesculapian light, but only with the hope that they may form a comprehensive summary of the evolution of the germ theory of disease, from its inception as a theory to its confirmation as a fact.
ANCIENT THEORIES OF THE CAUSES OF DISEASE.

Pestilence, plague and disease are the penalties imposed by an angry God upon a sinful people –

"Behold, the hand of the Lord is upon thy cattle which is in the field, upon the horses, upon the asses, upon the camels, upon the oxen, and upon the sheep: there shall be a very grievous murrain." (Exodus Ch. IX v.3).

Throughout the religious teachings of every creed, a form of punishment from the "Di Superi" appeared to be the obvious cause of disease, and this idea was to last for centuries.

The Children of Israel were not content to leave it at that: though they accepted the cause as divine, they realised that powers of healing – and better still, of prevention – were human attributes, and in their knowledge of treatment of disease, they became possessed of rudimentary theories of how disease could be spread by contagion and infection. Many instances could be cited where provision was made for the infected individual to be isolated, and his clothes and dwelling purified. Leviticus, Ch. XIV, gives a full account of the necessary steps to bring about the disinfection of the patient's clothes and other property, so ensuring that the disease should not be spread through contagion.

Thus principles and dangers of contagion were fully
recognised in those far off days, but the actual agents of the contagion - or, might we say, the mechanism of contagion - was not yet even hinted at.

"This theurgical theory of pestilence lasted for centuries, but was gradually displaced by the idea that epidemic diseases arise from natural, and especially cosmomettelluric causes such as comets, earthquakes, inundations and changes in the air, which was considered to be vitiated by miasms (miasmata = a stain). The modification of the atmosphere as a result of seasons and climate was a favourite theme of Hippocrates" (1).

Not only such violent manifestations were responsible for the sickness and disease of man and animals, but the normal atmospheric conditions of the seasons were assumed, in the Hippocratic writings, to be of prime importance in determining the state of health in the particular district concerned.

"As to the seasons, a consideration of the following points will make it possible to decide whether the year will prove unhealthy or healthy. If the signs prove normal when the stars set and rise, if there be rains in autumn, if the winter be moderate, neither too mild nor unseasonably cold, and if the rains be seasonable in spring and in summer, the year is likely to be very healthy. If, on the other hand, the winter prove dry and northerly, the spring rainy and southerly, the summer cannot fail to be fever-laden, causing ophthalmia and
dysenteries. For whenever the great heat comes on suddenly while the earth is soaked by reason of the spring rains and the south wind, the heat cannot fail to be doubled, coming from the hot, sodden earth and the burning sun: men's bowels not being braced nor their brain dried— for when spring is such, the body and its flesh must necessarily be flabby—the fevers that attack are of the acutest type in all cases, especially among the phlegmatic. If the weather be northerly and dry, with no rain either during the Dog-star or at Arcturus, it is very beneficial to those who have a phlegmatic or humid constitution, and to women, but it is very harmful to the bilious. For these dry up over much, and are attacked by dry ophthalmia, and by acute protracted fevers, in some cases too, by melancholies.

Hippocrates (460-370 B.C.) is justly called the Father of Medicine: he was the first to show that accurate observation and logical inference are the precursors of correct diagnosis. But, in spite of his acumen in observation, it is very strange to note that in his works—or rather in the works referred to as the "Hippocratic Collection"—there is not the slightest reference to contagion.

Hippocrates was not alone in this omission, for throughout the classical literature of Rome and Greece, it is in the lay rather than in the medical writings that the idea of contagion is promulgated. Thus in Thucydides, Chapter LVIII, we find that
the epidemic at the siege of Potidaea (430 B.C.) was considered to have been propagated by contact, and reference to similar contagious epidemics are cited in Livy, Virgil and Lucretius (C.98-55 B.C.): and with Lucretius we come to the first postulation of a germ theory of disease that I have been able to discover, for he not only noted the phenomena and effects of contagion, but establishes a definite germ doctrine to explain them —

"Now of diseases what the law, and whence
The influence of bane upgathering can
Upon the race of man and herds of cattle
Kindle a devastation fraught with death,
I will unfold. And, first, I've taught above
That seeds there be of many things to us,
Life-giving, and that, contrariwise, there must
Fly many round, bringing disease and death."

Lucretius, "De Rerum Natura",
Liber V, Lines 1083 et seq.

Not one of the authorities I have consulted in the preparation of this essay makes specific mention of this passage. I only came upon it myself through chance; I knew vaguely that Lucretius made some observations upon disease somewhere, and on looking through a translation of "De Rerum Natura", I was lucky enough to come upon the above quotation, and this is the earliest suggestion having any resemblance to a germ theory that I have been able to discover. Perhaps those who have read this in search for such references have overlooked it, as from following the context further, we see that Lucretius places as much stress as Hippocrates upon the
state of the atmosphere as the ruling factor in controlling health - continuing the quotation further:

"When these have, haply, chanced to collect And to derange the atmosphere of earth, The air becometh baneful. Thus when an atmosphere, Alien by chance to us, begins to heave, And noxious airs begin to crawl along, They creep and wind like unto mist and cloud, Slowly, and everything upon their way They disarrange and force to change its state. It happens, too, that when they've come at last Into this atmosphere of ours, they taint And make it like themselves and alien. Therefore, as sudden this devastation strange, This pestilence, upon the waters fall. Or settles on the very crops of grain Or other meat of men and feed of flocks. Or it remains a subtle force, suspense In the atmosphere itself; and when therefrom We draw our inhalations of mixed air, Into our body, equally its bane Also we must suck in ............

Nor aught it matters whether journey we To regions adverse to ourselves and change The atmospheric cloak, or whether nature Herself impart a tainted atmosphere To us or something strange to our own use Which can attack us soon as ever it come."

Bullock mentions that reference to contagious epidemics is found in Lucretius and gives "De Rerum Natura" Book VI as his source, but he does not mention that in this same book can also be found a specific attempt to postulate a germ theory of disease.

Lucretius, however. appears to place more importance upon the effect of these "seeds" on the atmosphere, than upon their direct effect on man and animal, and that, maybe, is why no authority quotes Lucretius as being definitely the originator of the germ theory. Another reason may be that the statement
I have just made is not correct, for Lucretius, it is well known, was rather more apt to redress old theories in poetic guise than to formulate new ideas of his own, and thus he may have borrowed the concept of air-borne seeds of disease from some unknown source.

Dobell in "Anthony Van Leeuwenhoek and His Little Animals" draws attention to a suggestion found in the writings of Varro - (116-27 B.C.) and therefore antedating Lucretius or at least contemporary - that malaria is caused by certain minute "animals" which arise from marshy places -

"Attention should also be paid to any marshy places thereabouts: both for the same reasons, and because certain minute animals grow there, which cannot be detected by the eye, and which get inside the body from the air, through the mouth and nostrils, and give rise to stubborn distempers."

cf. Varro, lib. I Cap. XII

This, however, is not a general germ theory of disease - the word "morbos" or "distempers" referring to the different types of malaria; but it is conceivable that Lucretius saw this suggestion and enlarged on it.

As Lucretius' postulation appears to have had no influence at all upon contemporary medicine, and was to remain unnoticed for some 1400 years, it is perhaps hardly worth giving an important place to Lucretius in the history of the evolution of the germ theory of disease. But as he appears to be one of
the originators of the theory, and perhaps the originator, I have thought it worth while expatiating at length upon him.

The thread of our story is lost in the labyrinth of the Dark Ages, following the destruction of the Roman Empire. The suppression of learning among the lay by the Church, and the consequent ignorance of the people led to the complete annihilation of science and culture, and the shadow of superstition and charlatanism fell upon the world. Again it began to be taught that epidemic diseases were brought about through supernatural agencies and were manifestations of divine judgement. No other cause was sought for disease than the supernatural, and no other cure was deemed possible than could be afforded by the clergy with their charms, incantations, and almost negligible knowledge of materia medica and herbalism.

One interesting theory does emerge from the midst of all this groping in darkness, and that is the opinions shared by two medical writers - a Greek and a Persian - that certain diseases are caused by putrefaction and fermentation -

"When the blood having become more melancholic than natural, ferments and fixes in a part, the diseases called carbuncles are formed."

(Paul of Aegina (625-690) On Carbuncle or Anthrax.) (4)

"ON THE CAUSES OF SMALLPOX.

"Every man, from the time of his birth till he arrives at old age, is continually tending to dryness; and for this reason the blood of children and infants is much moister than
the blood of young men, and still more so than that of old men ........

Now the small-pox arises when the blood putrefies and ferments, so that the superfluous vapours are thrown out of it, and it is changed from the blood of infants, which is like must, into the blood of young men, which is like wine perfectly ripened: and the small-pox itself may be compared to the fermentation and the hissing noise which take place in must at that time".

(Rhazes of Persia (860-932)) (5).

The interest in this theory lies in its strange anticipation of the work of Pasteur, who was to show proof positive of the existence of a bacterial cause of disease: his researches on fermentation led him to the belief that the agents responsible for fermentation of organic substances might resemble those responsible for disease: and with his characteristic industry and patience he proved his belief to be justified - that disease is analogous to a process of fermentation and putrefaction.

**The Renaissance - and Theory.**

The Renaissance - "the whole process of transition in Europe from the medieval to the modern order" (Jebb) - commencing about 1350, brings with it a revival not only in literary and intellectual activity, but also in practical science. Medicine was delivered from the hands of the clergy
into the safe-guarding of those whose business it became to look after the health of the body alone, and with that it passed from the realm of the mystic into the realm of the real.

Boccaccio's Decameron (c. 1350) consists of a number of stories, told, to pass the time, by a group of young Florentines who have shut themselves up in a country mansion to escape the ravages of the plague, then playing havoc with human lives in Italy. And the dangers of infection and contagion are further emphasised in the works of Benedetti (1493).

Towards the end of the Renaissance, when Europe had satiated itself with the fruits of classical learning, there arose a man of genius who interested himself in various branches of science, and made important contributions to each. This was Girolamo Fracastoro (1484–1553), a Veronese, who was "at once a physician, poet, physicist, geologist, astronomer, and pathologist ........... His medical fame rests on that most celebrated of medical poems, "Syphilis sive Morbus Gallicus ...." and his treatise, "De Contagione" (1546), in which he states, with wonderful clairvoyance, the modern theory of infection by microorganisms." (7).

"To explain contagion, he postulated the existence of seeds of disease - seminaria prima - which were capable of being propagated from one individual to another. In his opinion, contagion was transmissible (1) by direct contact alone, (2) by contact and fomites, and (3) at a distance. The word "fomes"
was used ... by Fracastoro in a special sense for such things as clothing, furniture and other objects ("fomitem apello vestes, ligua et ejusmodi") which, non-corruptible in themselves, could conserve the seeds of contagion and thus infect. Fracastoro likened contagion by direct contact to the corruption that sets in when grapes or apples come into contact with each other. He supposed that the "seminaria" of disease propagate and generate until the whole mass is affected." (8).

To see exactly what Fracastoro meant, I went to his original treatise, and in the last few lines of Book I, Chapter III of "De Contagione", I found what appears to be his first definition of that expression - "principium autem sunt particulae illae insensibiles, quae evaporant, calidae quidem, et acres, sed humidae commistione, quae deinceps seminaria contagionum dicantur." -- "The source (of contagion) is those imperceptible particles which evaporate when hot and dry, but become moist on commingling: these I shall continue to call the seeds of contagion."

Bulloch suggests (9) and this idea is supported by Garrison (10) that Fracastoro's 'seminaria' of disease are not necessarily to be considered as living organisms.

"Some have supposed that Fracastoro considered that the 'seminaria' of disease were necessarily living, and his writings may be interpreted in this sense. On the other hand, he compared the idea of disease propagation with that of 'halitus' or exhalation, for just as the onion can cause the eyes to water, so
a 'halitus' from a contagious ophthalmia can produce a similar state in another individual at a distance." (9)

But I find that the only interpretation I can put upon 'seminaria' is that they are alive, for Fracastoro believes them to be capable of reproduction in appropriate media — and surely reproduction is one of the criteria which distinguish the living from the non-living. Consider the following two quotations from "De Contagione" —

"Even although the greater number of mortals have contracted this disease by contagion, yet innumerable others have been observed to have become affected without contagion, and per se."

"Consequently its 'seminaria', upon which every spontaneous contagion depends.....we must consider the air from which every contagion has its origin to have contracted a condition of the same character, the seminaria of which are sluggish and analogous to the phlegm, and in their turn are productive of others like the former. Inasmuch as this contagion is erodent, its seminaria must be sharp, although hemmed in and buried in much viscosity." (11)

It seems obvious that he ascribes to his 'seminaria' not only the power of reproduction, but also the capability of spontaneous generation, and that can be applied to living organisms only. Garrison (12) makes a definite statement that Fracastoro nowhere refers to bacteria as living organisms. It appears absurd to me that the power of spontaneous generation should be applied to something which the author meant to be
considered as non-living.

Thus I must give to Fracastoro the credit of being the first of the moderns to offer a sound germ-theory of disease, but unfortunately he was not the last to stop only at theorising, though most subsequent workers in this field began to make use of a newly-invented instrument to substantiate their claims - the microscope.

Here may be mentioned the work of two Englishmen who were beginning to treat the cure of disease more scientifically, applying more humane and true medical methods.

The works of Sydenham (1624-89) may reasonably be regarded as the first great commentary on the Hippocratic theme.

He regarded disease as a developmental process, running a regular course with a natural history of its own, and he set well on its way the conception of infectious conditions as specific entities, a conception which has since been illuminated by the germ theory of disease:

"Sydenham's theory of 'epidemic constitutions' or 'genius epidemicus', maintains that contagious diseases are influenced by cosmic or atmospheric influences which may change their type, that they may spring from miasms from the bowels of the earth, that they may have long periods of evolution and seasonal variations, and that some diseases may be mere variants or sub-varieties of others." (Garrison, P.270: and Singer's "Short History of Medicine" P.102).

Sir John Pringle, an army surgeon and Scottish pupil of
Boerhaave (1707-82) was among the first to see the importance of ordinary putrefactive processes in the production of disease, and quite the first to apply these principles in hospitals and camps. (Singer p.169).

Another who followed in the tradition of Fracastoro was Marcus Anton Von Plenciz, sr. (1705-86), who in his tract on scarlatina (1762) advanced the idea of a contagium animatum, with a special "seminium verminosum" for each disease. (Garrison P.378).

The Modern Era.

Antony Van Leeuwenhoek and his "Little Animals".

The modern era is regarded as a typical era of invention, and it might be as well to start the story of the modern era in the evolution of the germ theory of disease with an account of the invention of that instrument, which was to play the essential part in establishing that theory as a theory no longer, but as a proven fact.

I have, therefore, briefly epitomised the detailed history of the microscope recounted by Dobell (13), and offer it as an important link in the chain of events leading up to the final proof.

Simple Lenses.

It is now known, from the profound researches of the French scholar Martin (1871), that the ancients knew nothing
about magnifying glasses.

Our Roger Bacon (c. 1214-1294) had at least a glimmering of the properties and possibilities of lenses, but the first were probably made, and used as spectacles, about 1300 in Italy.

The actual inventor of spectacles is said to be a Florentine - Salvino d'Armato degli'Armati. Friar Bacon and his brethren in Italy were probably the originators of simple lenses.

According to Govi (1888), the word "Microscope" (microscopio) was invented by Giovanni Fabri, who first used it in a letter to Rederigo Cesi dated 13th April, 1625.

The first pictures made with the aid of this instrument are usually supposed to be those of the bee and the weevil interpolated by Francesco Stelluti (1630) in his Italian translation of the poems of Persius.

The first "micrography" is the "Century of Microscopical Observations" by Pierre Borel, published in Latin at The Hague in 1656, but it was soon followed by the similar work of Henry Power (1663-4) and the more celebrated "Micrographia" of Robert Hooke (1665).

**Compound Microscopes.**

"The compound microscope, to which the name is properly applied, was probably devised in Holland in the final decade of the XVII century (not earlier), while immediately afterwards another form was independently discovered in Italy."
The following names are mentioned with regard to the matter of priority in inventing the microscope - Zacharias, Janssen, Lipperbey, Drebbel and Galileo."

The man who used the simple microscope most, and who made fullest records of all his observations, was Anthony Van Leeuwenhoek (1632-1723), a linen-draper of Delft, whose spare-time hobby was to examine all manner of things under lenses of his own manufacture -

"Preceding the year 1673 Leeuwenhoek was evidently engaged - in his spare time - in making lenses, and mounting them to form "microscopes" of simple pattern: and after he had acquired much skill in the manufacture of these curious instruments, and had taught himself how to grind and polish and mount lenses of considerable magnifying power, he began to examine all manner of things with their aid." (14).

He appears to have commenced his microscopic studies in 1668, starting with an investigation on chalk, and this he followed up with observations on such things as the sting and mouth-parts and eye of the bee, on mould, and on the louse.

The famous Dutch physician, Reinier de Graaf, a fellow-townsman and friend of Van Leeuwenhoek, was at this time in regular correspondence with Oldenburg, the first Secretary of The Royal Society. Now, the "Philosophical Transactions" for 1668 of the Royal Society contained an account of a new microscope made by Eustachio Divini in Italy, with which he claimed to see animals smaller than had ever been seen before. It was doubtless
as a counterblast to this sweeping assertion that de Graaf (1673) sent an account of Leeuwenhoek's work to Oldenburg - "A certain most ingenious person here, named Leeuwenhoek, has devised microscopes, which far surpass those which we have hitherto seen, manufactured by Eustachio Divini (Italy 1668) and others." (15) - with a letter from Leeuwenhoek himself containing some original observations.

And a further tribute to Leeuwenhoek's work also reached Oldenburg from Constantijn Huygens (1673) - the celebrated diplomatist and poet: and in it, too, a good description of this microscopist's character is given - "A person both unlearned in sciences and languages, but of his own nature exceedingly curious and industrious." (16).

Thereafter Leeuwenhoek became a regular correspondent to the Royal Society, sending letters containing observations on matters zoological, botanical, chemical, physical, physiological, medical and miscellaneous. (17). These letters were written in old-fashioned Dutch: many of them appeared in the "Philosophical Transactions" translated into English or Latin.

Leeuwenhoek's importance in this essay is that his eighteenth letter to the Royal Society of London contains the first account ever written of what the bacteria really look like, and how they move, (though the actual name "bacteria" is not yet applied to them) -

["Observations on Sea-water"]

The 18th ditto (August 1676) I again discovered a very
few of the foresaid animalcules: and I now saw a few so exceeding small that, even through my microscope, they well nigh escaped the sight." (18)

["First observation on pepper-water]

(April 1676) The fourth sort of little animals .......... were incredibly small: nay, so small, in my sight that I judged that even if 100 of these very wee animals lay stretched out one against another, they could not reach to the length of a grain of coarse sand ............. I discovered yet a fifth sort (probably bacilli – translator’s footnote), which had about the thickness of the last said animalcules, but which were near twice as long." (19).

"Most exceeding thin little tubes", he mentions in another place, and finally I must quote "a remarkably shrewd observation, which proves conclusively that Leeuwenhoek was here dealing with bacteria" (translator’s footnote) – "They moved with bendings, as an eel swims in the water: only with this difference, that whereas an eel always swims with its head in front, and never tail first, yet these animalcules swam as well backwards as forwards, though their motion was very slow." (20).

Antony Van Leeuwenhoek is thus the first man to have given an account of bacteria that he had actually observed, but he himself made no application of his discovery to medical doctrines of contagion.

The existence, however, of such minute organisms was
proved, and future workers no longer had to postulate their existence as a possibility: thus the whole germ theory of disease was being translated from a plane of speculation to a plane of realisation - though the way was still to prove arduous and beset with difficulties.

As with nearly all scientific discoveries, we find that claims of priority in seeing bacteria are advanced also for another microscopist - Athanasius Kircher (1602-80) of Fulda - another typical virtuoso of his time who dabbled in several branches of science and learning, mathematics, optics, physics and medicine among others. These claims rest on certain passages to be found in Kircher's "Scrutinium Pestis" (1653), where he details the causes of plague, and gives alleged experimental verifications of his statements. But Clifford Dobell, seeking to establish the claim of priority in this discovery for Leeuwenhoek, has made an intensive study of all Kircher's more important biological works, and appears to find no evidence that he ever saw - even by chance - a protozoön or bacterium through his microscope.

"The first person to credit Kircher with the discovery of the bacteria was, I believe, Friederich Löffler (1887), who opens his work on the history of bacteriology with a quotation from the "Scrutinium Pestis" wherein Kircher says: "It has hitherto also been known to everybody that worms swarm out of the rotting bodies, but only after the wondrous invention of the microscope
did it become known that all decomposing things swarm with an innumerable brood of worms invisible to the naked eye."

Now this passage contains no obvious reference to any organisms other than worms or insects - yet for reasons unexplained Löffler alleges that it "announces ....... the discovery of a new world of living creatures" - by which he means, presumably, the Bacteria. But does it? Surely not." (21).

Dobell also dismisses the evidence put forward by Singer (1914) in support of Löffler, and states, in short, that to him "the "Scrutinium Pestis" appears as a farrago of nonsensical speculation by a man possessed of neither scientific acumen nor medical instinct. Kircher obviously had no conception of a real experiment - in the Baconian and modern sense. It is easy enough, of course, to tear a line here and there from his voluble writings, and to use it as evidence on his behalf: but if such lines be considered in their context they have a very different complexion." (22).

On consulting a further authority, viz. Garrison, I find it asserted that Kircher "was probably the first to employ the microscope in investigating the causes of disease ......... and he was undoubtedly the first to state in explicit terms the doctrine of a "contagium animatum" as the cause of infectious disease." (23).

The first statement is presumably correct: Leeuwenhoek had not such motive behind his researches. But I cannot agree with the second statement. Whether or not Kircher saw bacteria -
and I am inclined to believe the second alternative - and granted that he makes a sound theoretical proposition of a germ theory, yet it is hardly different from that already stipulated by Fracastoro. Now Garrison, as I have already shown, considers that Fracastoro's "seminaria" are not to be regarded as alive, and that probably is how he justifies his statement that Kircher was the originator of the doctrine of a "contagium animatum". But Fracastoro gives his "seminaria" as many of the properties of life as Kircher; and, further, Kircher's definition of "seminaria" is hardly to be distinguished from that already given of Fracastoro - "Quod ex putredine perpetuo corpuscula quaedam insensibilia in circumsita corpora expirentur, quae effluvia pestis seminaria dicuntur."

(Kircher's "Scrutinium Pestis" (24))

Therefore it would appear that Kircher made hardly any advance towards the realisation of the germ theory, but was merely the last of the theorists, closing the sequence that leads from Lucretius to Fracastoro, without adding anything tangible in the way of material proof.

**Individual Effort.**

Leeuwenhoek himself made no application of his discovery of "bacteria" to medical doctrines of contagion, but he had established a solid background, and this application of his findings was immediately made by others.
One of the most notable of these is Giovanni Maria Lancisi (1655-1720), of Rome, the greatest Italian clinician of the 18th century, and the man who published and edited the copper plates of Eustachius in 1714. Lancisi was above all a keen epidemiologist, and "his great treatise on swamp fevers (1717) while stating the doctrine of miasms, shows a clear insight into the theory of contagion and the possibility of transmission by mosquitoes (Culices), of which he gives a naturalist's account." (25)

He actually refers to Leeuwenhoek's discoveries in order to prove the existence of such extremely minute animalcules as he himself postulated. (26).

Lancisi does not appear to have attempted to prove his theory experimentally, nor did he ever see the germ responsible for malaria, but he made a safe assumption indirectly based on Leeuwenhoek's discovery.

Another whose speculations run parallel to those of Lancisi is Benjamin Marten, concerning whom nothing is known, save that he published a treatise on consumption in 1720.

"In this book, Marten, assuming that tuberculosis is caused by invisible "animalcules" like those discovered by Leeuwenhoek, develops a theory of the pathogenesis of this disease remarkably similar to current conceptions ...... As a prognostication Marten's book is notable, but he himself never saw the tubercle bacillus, and his writings had no influence on the history of bacteriology." (27).
These two men may not have done anything practical to justify their ideas, but I consider that they do represent a little progress in that they substantiate their claims by reference to what was already an established fact. To theorise like Fracastoro on "seminaria" which had never been seen, and whose like had never been seen; then to argue by analogy from Leeuwenhoek's bacteria that it is conceivable that similar minute organisms are responsible for disease - represents some advance by no means insignificant, if only in that the second theory is more credible than the first.

In Italy and England, then, Leeuwenhoek's work had been recognised and, more important, utilised. France does not seem to have heard of it so soon. J. B. Goiffon (1658-1730) a physician of Lyons, published a dissertation on the plague in 1722. In this he suggests that the cause of the plague is an insect-like agent "which floats in the air and penetrates into the blood either through the pores of the skin or else through the mouth or nose." (28). He never attempted to prove his theories either experimentally or even by reference to Leeuwenhoek's work from which to draw analogy, though this was already well known and even had its imitators.

These speculations are on the same level as those of Fracastoro, representing no advance in the evolution of the germ theory, but rather retrogression, seeing that the existence of bacteria was now an accepted fact, and yet was not correlated with his suggestions.
These three men worked alone in the sense that they sought no, or, at least, very little confirmation from others. Very few realised the significance of their papers. Many frankly disagreed with them. In the scientific world one truth must be built up from another by a series of comprehensive steps. Analogy and speculation were not sufficient to convince even the most liberal minded. But in the same way as there was no violent approval, so there was no violent opposition, because it was then as difficult to prove the negative as the positive by experimental methods. Seeing is believing - not necessarily optic vision, but rather mental vision - and as nobody then was capable of building up an argument optically or mentally visible either for or against, the theorists were permitted to continue on their way unrefuted.

The truth behind this can be realised when we come to the work of Pasteur, who had all the experimental proof necessary to prove the theory, as he thought, when he found violent antagonists with experimental evidence to prove the contrary, and the scientific world became divided into pro-Pasteur and anti-Pasteur - men worked together for him, and together against him.

But we anticipate a little.
The first great authority to consider what place in the biological scheme might be held by these "little animalcules" of Leeuwenhoek and his imitators was Linnaeus (1707-78), the famous Swedish botanist. Linnaeus appeared to doubt whether the then known protozoa and bacteria might not really be stages in the development of the fungi, and, moreover, he questioned their relation to diseases. In the 12th edition of his "Systemae Naturae" (1735) - containing a classification of plants, animals and minerals - all the infusoria described in "the books of the micrographers" are gathered together in a single species - "Chaos Infusorium": but as an appendix he adds six doubtful kinds of "living molecules" which he leaves to his followers to elucidate further.

1. The "contagion" of eruptive fevers?
2. The "cause" of paroxysmal fevers?
3. The "moist virus" of syphilis?
4. "Leeuwenhoek's" spermatic animalcules?
5. The aery mist "floating in the month of blossoming?"
6. "Münchhausen's septic agent" of fermentation and putrefaction?

Dobell (29), to whom I am indebted for all the above information, goes on further to suggest that Linnaeus and his pupils were inclined to be too vague and sceptical to furnish any material advance in the science of bacteriology.

A further attempt to classify not only protozoa, but also
bacterial forms appeared in the works of O. F. Müller (1771, 1773-4, 1786) a great protozoologist and, for his time, bacteriologist, but he makes no attempt to apply any of his discoveries towards establishing a germ theory of disease.

The work of Linnaeus and Müller show no actual advance in the evolution of the germ theory, but it does show how far professional biologists and medical men had profited from the labours of the amateur microscopist, Leeuwenhoek, within a century after he had announced his discoveries.

FERMENTATION. (30).

The study of fermentation played a most important part in the evolution of the germ theory of disease: when the intimate mechanism of that process came to be clearly understood, investigators, returning to the old supposition that disease might be likened to fermentation and putrefaction, began to look for the same microscopical agents in diseased putrefactive tissues as in organic ferments.

It was only in the nineteenth century that the process began to be clearly understood, though already in 1659 the work of an English physician, Thomas Willis, had given a conception of fermentation as an internal commotion of the particles of the fermentable substance: and the idea had recurred again and again in the chemical literature of succeeding years. Yeast had been regarded by these chemical investigators as a complex chemical substance of unknown constitution, but as a result chiefly of the work of Baron Charles Cagniard-Latour (1836), Theodor Schwann (1837)
and Friedrich Kützing (1837), it was shown that yeast is a living organism. The first two workers independently recognised it as being of vegetable origin, and Schwann himself, publishing his results in "Mikroskopische Untersuchungen" (1839), gave there his reasons for regarding yeast globules as fungi; and there also he describes full experimental confirmation of the fact that these globules cause fermentation.

This biological theory of fermentation did not meet with the approval of the contemporary chemists, who sought purely chemical explanations for such phenomena.

Berzelius (1779-1848) considered that fermentation was only an example of the catalytic principle, and Mitscherlich, as a result of experiment, came to a similar conclusion.

"Liebig (1803-73) attributed the processes of decomposition, (eremacausis) putrefactions and fermentation to the chemical instability of certain substances which could communicate their instability to other substances in succession. The unstable substances he called ferments, and they were supposed to arise as a result of some change in vegetable solutions exposed to air, and to continue the fermentation, once started, in the absence of air"; and he refused to believe that there was anything living about the yeast globules. (31).

Wöhler (1800-82), after he had shown that urea (1828) - that most typical of organic substances - could be built up in the laboratory out of inorganic substances, also became enamoured of the idea that all so-called vital phenomena could be explained
on a purely chemical basis, and he consequently ridiculed any biological theory of fermentation.

Blondeau (1847), however, followed in the school of Schwann, and advanced the opinion that each type of fermentation is produced by a specific fungus.

LOUIS PASTEUR (1822-95).

"As a result of all these, and many other researches, a great deal of knowledge had accumulated on the subject of fermentation ....... This brings us down to the middle of last century, when fresh advances were made through the genius and industry of Pasteur (1822-95).

He was not the creator of the doctrine that fermentation is due to the activity of living microscopic organisms, but he built on more solid foundations than his predecessors, who in some degree failed to leave their impress on the scientific thought of their day. The time was not ripe for their efforts, and there is much truth in the Franklands' remark 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 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." " (32).

Pasteur was nominally a teacher of science, lecturing in many institutions, but spending his spare time in research. His original interests lay in crystallography, in which he discovered
and explained the phenomenon of stereo-isomerism.

While studying the formation of the two forms of lactic acid crystals, he noticed how lactic acid solutions underwent putrefactive changes on exposure to the atmosphere, and searching into the reason for this led him into the problem of fermentation generally. He investigated the mechanisms and phenomena involved in lactic, acetic, butyric and alcoholic fermentations. These studies covered a period of twenty years (1857-77), interrupted by other work he had to take up in connection with spontaneous generation, and the silkworm disease ravaging France in 1865. The most important conclusions arising from these researches are briefly that fermentation is a biological process involving the development of microscopic organisms (which he called vibrios): that these vibrios are constant in character for each type of fermentation; and that they live without oxygen — for which phenomenon Pasteur invented the term anaerobic.

"His "Études sur la Bière", a work of nearly 400 pages, was published in 1876, and deals with many points which were of fundamental importance in the development of bacteriology as a science. For example, he investigated the question of the presence of bacteria in normal tissues, and the transformation of one species into another. This book is also interesting as containing his mature views on fermentation in general. In his opinion fermentation is essentially the result of life without oxygen, 'C'est la vie sans l'air, c'est la vie sans gaz oxygène libre?' " (33).
The oxygen is obtained by the ferment by breaking off molecules of oxygen from the substrate, and this, in short, is fermentation —

"It seems therefore natural," wrote Pasteur, "to admit that when yeast is a ferment, acting out of the reach of atmospheric air, it takes oxygen from sugar, that being the origin of its fermentative character." " (34).

SPONTANEOUS GENERATION.

The opponents of Pasteur used as their main line of argument, the ancient theory of spontaneous generation — that animals not manifestly produced by the act of reproduction come into existence by the combined action of heat, air, earth and putrefaction: they considered, then, that the micro-organisms found in fermenting substances had developed spontaneously, that Pasteur's vibrios were the result of fermentation, and not, as Pasteur would have it, that the vibrios were the cause of fermentation.

For a long time the theory of spontaneous generation had been accepted without question. Aristotle cites several instances in his "Historia Animalium": in Judges chapter XIV, v.8, there is a description of the spontaneous development of a swarm of bees in an animal's carcase - "And after a time he (Samson) returned to take her, and he turned aside to see the carcase of the lion: and, behold there was a swarm of bees and honey in the carcase of the lion."
and as late as 1652 Van Helmont, the famous chemist, gave a recipe for the spontaneous generation of mice. Francesco Redi (1626-97) the poet-physician of Arezzo, showed (1668) that the maggots of wormy meat come from eggs deposited by flies, but he was still inclined to believe that the insects in the galls on flowers arise spontaneously - an idea to be dispelled later (1700) by Vallisnieri. Leeuwenhoek is said to have imagined that the animalcules which appear in infusions really come from the air, where they are present in the form of seeds or germs, and Louis Joblot (1718) showed that this was actually the case. He endeavoured to disprove the theory that spontaneous generation was the rule with that vast world of the "infinitely small" that had been revealed by the lenses of Leeuwenhoek and others from 1675 onwards. His experiments, however, were not regarded as conclusive.

The supporters of the theory of spontaneous generation or heterogenesis found in Needham and De Buffon (1749) men of sufficient ingenuity to devise a temporarily satisfying explanation of the hypothesis - in every microscopic particle of organic matter there resided a "vegetative force" which permitted the organic matter of the infusion to spring into life. These men in turn found opposition in the work of Spallanzani (1765-76), an Italian naturalist, but his views did not carry enough weight, and the doctrine of spontaneous generation still continued to be held by most of the leading naturalists till well into the nineteenth century. Franz Schulze (1836), Schwann (1837)
schröder (1859, 61), and Van Dusch (1854) among others endeavoured to show that neither the infusion itself nor the air above the infusion was responsible for the appearance of micro-organisms on the surface of the liquid, but that the air contained the germs and seeds of these micro-organisms and could be filtered free of them. Experimental technique, however, had not reached a very high standard of accuracy, and it was easy to draw wrong conclusions from faulty experiments. Pouchet, who in his paper "Hétérogenie" (1859), agreed that the main point at issue was whether germs exist in the air or not, described experiments which appeared to him to prove conclusively that the micro-organisms found in an infusion arose not from seeds in the air, but from the dead organic matter in the infusion; they were the "offspring of death and embodiment of life." The conditions necessary for their birth were - organic matter in mass or solution, water, air, and a suitable temperature. Variations in the relative proportions of these were responsible for producing the different types of micro-organisms. The most persistent supporter of these views in England was Bastian (1872) who fought valiantly for his cause, but in the end was left to fight a losing battle alone.

Pasteur's theories of fermentation were thus being shaken at their very foundation, and so very soon he found himself entering the lists against the Heterogenists. Among the first experiments he undertook was the demonstration that air from a vicinity afar from habitations and vegetation when introduced into
flasks containing fermentable material was incapable of starting fermentation, since that air was clear of dust and germs. For that purpose he went to the Mer de Glace in Chamonix. His results were singularly successful -

"If all the results are compared that I have obtained until now," he wrote, on March 5th 1880, when relating this journey to the Académie, "it seems to me that it can be affirmed that the dusts suspended in atmospheric air are the exclusive origin, the necessary condition of life in infusions."

And in an unnoticed little sentence, pointing already then to the goal he had in view, "what would be most desirable would be to push those studies far enough to prepare the road for a serious research into the origin of various diseases."

"The action of those little beings, agents not only of fermentation but also of disorganisation and putrefaction, already dawned upon him." (36).

His most convincing experiment was perhaps his simplest. He took two similar flasks filled with putrescible material: one of the flasks had an ordinary neck, but the other had a bent S-shaped tube - open to the air - attached to it. In the latter case, air entering the long bent tube deposited its dust and other particles in the bend of the glass, and so the contents of that flask remained unchanged, whereas in the former case, the contents soon fermented. The contents in the flask prepared to admit no dust did not ferment because, said Pasteur. "I have kept it from the only thing man cannot produce, from the germs
which float in the air, from Life, for Life is a germ, and a
germ is Life. Never will the doctrine of spontaneous generation
recover from the mortal blow of this simple experiment ..........

No, there is now no circumstance known in which it can be
affirmed that microscopic beings came into the world without germs,
without parents similar to themselves. Those who affirm it have
been duped by illusions, by ill-conducted experiments, spoilt by
errors that they either did not perceive or did not know how to
avoid." (37). This work was carried on between 1860-64. Some
ten years later it was repeated by Tyndall, who finally clinched
the matter -

"Tyndall's researches gave the final blow to the doctrine
of spontaneous generation as much as, if not more than, Pasteur's.
This was probably due to the fact that his results were diffused
in the form of lectures, demonstrations, papers, books and
correspondence in newspapers and magazines. Whereas the personality
of Pasteur inspired something of the nature of opposition,
Tyndall's magnetic influence, his exact technique, the logic of
his interpretations, and the admirable style of his writings, were
acceptable to a large audience of intelligent people." (38).

Pasteur's work on fermentation and putrefaction thus
inaugurated a new era in bacteriological research, though some
observations had already been made before, but had borne little
fruit. Gaspard had instituted some investigations into the
subject of putrefaction in 1822, and in the following year,
Magenta, by placing animals on a grill above a putrid mass
found that "No ill-effect resulted from the inhalation of the putrid effluvia. This observation rendered improbable the ancient and cherished belief of mankind that the penetration of evil odours into the respiratory system is a frequent cause of disease." (39).

**THE TRUTH IN SIGHT.**

Robert Boyle, the English physicist, had said, two centuries earlier, that he who could probe to the bottom the nature of ferments and fermentation would probably be more capable than anyone of explaining certain morbid phenomena.

Pasteur had hardly begun his work on fermentation, before he saw himself heading towards research into disease. In March 1863 he was presented to Napoleon, the Emperor of France, who took a great interest in what went on in his laboratories. Pasteur gave him an account of his discoveries as far as they had proceeded, and added that "all his ambition was to arrive at the knowledge of the causes of putrid and contagious diseases." (40).

Jacob Henle, the famous German founder of pathology as a separate subject, in his "Pathologische Untersuchungen" (1840) had endeavoured to establish the hypothesis that "the material of contagion is not only organic but living, endowed with individual life and standing to the diseased body in the relation of a parasitic organism." (41).

Pasteur applied this hypothesis first not to living beings, but to a study arising naturally out of his original researches on fermentation - the diseases of wines.
"Might not the diseases of wine," he said at the Académie des Sciences in January, 1864, "be caused by organised ferments, microscopic vegetations, of which the germs would develop when certain circumstances of temperature, of atmospheric variations, of exposure to air, would favour their evolution or their introduction into wines ............ I have indeed reached this result that the alterations of wines are co-existent with the presence and multiplication of microscopic vegetations." (42).

From the midst of these investigations Pasteur was called away to apply his keen powers in saving a great French industry from ruin. An epidemic was destroying in terrible proportions the industry of the cultivation of silk-worms. As a result of long and careful research, he came to the conclusion that the cause of infection was a parasitic micro-organism which persisted through the various stages of development of the silk-worm, and was handed on in the form of seeds, germs or spores to the succeeding generation. Further, he showed how the epidemic could be controlled by isolating and destroying infected worms, and finally his work was rewarded by the re-appearance of a healthy breed of silk-worms and the restoration of the silk industry.

Meanwhile the Vale de Grâce physician, Villemin (1827-92) was independently though unconsciously approaching the ambitious end aimed at by Pasteur. As a result of researches intended to demonstrate the specificity of diseases (1865-9), he "brought the proof that tuberculosis is a disease which reproduces itself,
and cannot be reproduced but by itself; in a word, specific, inoculable, and contagious." (43). He suspected the presence of a virus: the bacillus was found and isolated much later by Koch (1882).

This doctrine of specificity of diseases was strongly opposed, as it appeared to general medical opinion, then, that if different symptoms were manifestations of different specific diseases, and each had its own specific cure, an almost impossible task was allotted to the healers of mankind. Preventive medicine was as yet unthought of.

"A reception somewhat similar to that given to Villemin was reserved for Davaine, who, having meditated on Pasteur's works on butyric ferment and the part played by that ferment, compared it and its action with certain parasites visible with a microscope and observed by him in the blood of animals which had died of charbon disease. By its action and rapid multiplication in the blood, this agent endowed with life probably acted, said Davaine, after the manner of ferment. The blood was modified to that extent that it speedily brought about the death of the infected animal. Davaine called these filaments found in anthrax "bacteria", and added, "They have a place in the classification of living beings." But what was that animated virus to many doctors? They answered experimental proofs by oratorical arguments." (44).

Here we might stop, since it has been experimentally shown that bacteria cause disease. But the world was not yet
inclined to accept this upheaval of traditional belief. Only in a few isolated cases did the propounders of the germ theory find support, and in these cases the new supporters became convinced of its truth by applying additional experimental verification. Those who opposed used conclusions drawn from antiquated notions and faulty, misleading experiments, which they were prepared to accept without further inquiry.

Full significance of Pasteur's work was grasped early by Lister, a Glasgow surgeon. He immediately realised that putrefaction in surgical wounds should not be considered as a normal unavoidable event, as was then the case, but that it was a type of fermentation caused by germs entering the wound from the air and from dirty instruments and bandages. His antiseptic system was established in 1865, and after two years he published results showing its unquestionable success. Thus a new system was built up on the basis of the germ theory, and its success did much to make the germ theory acceptable to the medical profession.

"The MICROBE alone is true, and PASTEUR is its Prophet".

The Franco-Prussian War (1870-71) was a great blow to Pasteur. During its course he went about as in a dream, unable to do much of fundamental importance. But his results and Lister's were being applied in the hospitals of those wounded on either side. The questions of septicaemia and pyaemia were gone into with a thoroughness characteristic of Pasteur himself. The work of Davaine, confirmed by Vulpian (1872) and others, proved that septicaemia was due to bacterial infection. On the German
side, Klebs (1872), the pathologist to the Karlsbad military hospitals, made microscopic observations after autopsies when he found death due to pyaemia or septicaemia, and he discovered bacteria in almost every instance, but he regarded the different microbic forms as belonging to one organism called "Microscoporon Septicum." (45).

Towards the end of the war, a French surgeon, Alphonse Guérin, drawing inspiration from Pasteur's work on fermentation, in the same way as Lister had done in Scotland, introduced a sort of aseptic modification to the antiseptic precautions already then in common vogue. He believed, as Lister, that the germs from the air, on entering the wounds caused gangrene. To filter them, therefore, he applied layers of cotton wool to the wound already washed with carbolic solution or camphorated alcohol, and the bandages were not removed for periods of a fortnight and longer. His success was greeted with amazement by his fellow-surgeons, one of whom remarked - "We had grown to look upon purulent infection as upon an inevitable and necessary disease, an almost Divinely instituted consequence of any important operation." (46). - thus showing the deplorable condition of surgery - an expedient undertaken to save life which had hitherto proved itself almost as dangerous as no remedy at all.

Guérin invited his acknowledged teacher to inspect his wards, so that he could see the benefits that had been conferred upon humanity as a direct result of his researches. Pasteur thereafter became a regular frequenter of the hospitals, taking a
keen interest in those cases which were being treated by methods directly or indirectly due to his discoveries. The wards became a part of his laboratory where he could watch results and take notes.

A letter from Lister sent in the following year, 1874, invited Pasteur to visit Edinburgh Royal Infirmary, and expressed the writer's gratitude to him for leading him in the direction of making surgery no longer fraught with mortal danger to the patient. -

"Allow me to take this opportunity to tender you my most cordial thanks for having, by your brilliant researches, demonstrated to me the truth of the germ theory of putrefaction, and thus furnished me with the principle upon which alone the antiseptic system can be carried out. Should you at any time visit Edinburgh, it would, I believe, give you sincere gratification to see at our hospital how largely mankind is being benefitted by your labours." (47).

Any Tyndall recognised that the full benefits of Pasteur's work were soon to be realised in the establishment of a new interpretation of medical method - "For the first time in the history of science", he wrote to Pasteur. "We have the right to cherish the sure and certain hope that, as regards epidemic diseases, medicine will soon be delivered from quackery and placed on a real scientific basis. When that day arrives, Humanity, in my opinion, will know how to recognise that it is to you that will be due the largest share of her gratitude." (48).
The struggle had so far been confined to France and Britain: other countries had added nothing or little by way of conclusive evidence. Then Germany entered the field, and by Teutonic methods of calculated precision and accuracy in experimental work, a further advance was made. In 1876, Robert Koch, while practising as medical officer at Wollstein, became interested in a disease that was creating havoc among livestock - anthrax, known also as splenic fever or charbon. He accepted from previous workers, Davaine and others, that a bacillus was the cause of the disease. Now it occurred to him to seek a culture medium for the bacteridium: this he found in aqueous humour collected in the eyes of oxen or of rabbits.

Having settled, then, to his own satisfaction, the bacterial nature of anthrax infection, he applied himself to confirmatory studies in sepsis. His results were published in 1878 as "The Aetiology of Traumatic Infective Diseases".

His object was to determine whether infective diseases of wounds are of parasitic origin or not, admitting that the results of previous investigators had rendered the parasitic nature of disease probable.

Koch set out with the idea that conclusive evidence could only be obtained "by finding the parasitic micro-organisms in all cases of the disease in question; when we can further demonstrate their presence in such numbers and distribution that all the symptoms of the disease may thus find their explanation, and finally when we have established for every individual traumatic
infective disease the existence of a micro-organism with well defined morphological characters."

Using new experimental methods on animals, he was able to induce six different infective diseases in animals, showed that they vary in symptoms and pathology, and that they were invariably accompanied by bacteria which differed in form and distribution.

Koch was unable through force of circumstances to determine whether the infective diseases of wounds in man are of parasitic origin or not. (49).

By the improved methods of bacteriological investigation he was able to elaborate, he thus transformed the science of the study of infection. In 1882 he isolated the bacillus of tuberculosis, and, in the following year, having been sent on an official mission to Egypt and India to study the aetiology of Asiatic Cholera, he identified the comma bacillus as the specific organism of that malady.

Koch's work on sepsis was carried on from where he had left it by Alexander Ogston (1880,81,83) at that time surgeon to the Aberdeen Royal Infirmary. He concluded that inflammation and suppuration are produced by micrococci.

Rosenbach and Passet (1804–5) grouped Ogston's micrococci into differentiated species in the classification table, and further investigations merely modified Ogston's conclusions, showing that abscess formations in the ordinary suppurative processes of man and animals are mainly coccal in their aetiology,
though suppuration is not necessarily caused by micro-organisms. (50).

Now we must return to Pasteur, to show how he consolidated these discoveries, and by his vigorous efforts made them no longer objects of doubt, but the foundations of a new branch of medical science—bacteriology. He went into the subject of anthrax, revised Koch’s work, showed again that it was a bacterial infection and, further, instituted new systems of prevention and cure based on these researches.

In March, 1878, Dr. Sédillot, and army surgeon, read a paper to the Académie des Sciences, entitled “On the Influence of M. Pasteur’s Work on Medicine and Surgery.”

“In that treatise, Sédillot invented a new word to characterize all that body of organisms and infinitely small vibriones, bacteria, bacteridia, etc: he proposed to designate them all under the generic term of “microbe”. This word had in Sédillot’s eyes, the advantage of being short and of having a general signification.” (51).

Between the enthusiasm of his supporters and the violent unreasoned antagonism of his opponents was a great group of biological thinkers, watching for Pasteur’s results with open minds, and ultimately accepting them with applause. But Pasteur was not satisfied with that: he wanted to convince even his most active opponents. To this end he read a celebrated lecture on the germ theory to the Academy in 1878, in his own name and that of two pupils and collaborators, Messrs. Joubert and Chamberland. It began by a proud exordium: - (52)
"All Sciences gain by mutual support. When, subsequently to my early communications on fermentations, in 1857-8, it was admitted that ferments, properly so called, are living beings: that germs of microscopical organisms abound on the surface of all objects in the atmosphere and in water; that the hypothesis of spontaneous generation is a chimera: that wines, beer, vinegar, blood, urine and all the liquids of the economy are preserved from their common changes when in contact with pure air — Medicine and Surgery cast their eyes towards these new lights. A French physician, M. Davaine, made a first successful application of those principles to medicine in 1863."

Showing by his own example — how he had started as a crystallographer and had passed on to studies in the chemistry of fermentation and thence to research in disease — he proved that science was indeed one and all-embracing. His present studies on septicaemia were not unrelated to his past researches on the aetiology of charbon. Then he went on to give a succinct explanation of how anaerobic microbes can multiply and thrive in a culture open to the air. The vibriones on the surface die and protect their brothers below from the action of oxygen: these reproduce normally at first, but later give rise to germs and spores. "Here then is the septic dust, living the latent life of germs, no longer feeling the destructive action of oxygen, and we are now prepared to understand what seemed at first so obscure: the sowing of septic dust into putrescible liquids by the surrounding atmosphere, and the permanence of putrid
diseases on the surface of the earth."

And, elsewhere, "If it is terrifying to think that life may be at the mercy of the multiplication of those infinitesimally small creatures, it is also consoling to hope that science will not always remain powerless before such enemies."

Pasteur went on from this to a dissertation on diseases "transmissible, contagious and infectious, of which the cause resides essentially and solely in the presence of microscopic organisms", and as a protection against these organisms in surgical theatres he advocated asepsis.

Yet in spite of this and similar discussions and arguments, he found himself and his few supporters attempting to convince an incredulous world. As the bacterial natures of such diseases as diphtheria were individually discovered, more and more were won over to the acceptance of the germ theory, but the lack of general approval must be regarded as amazing in these days of rapid progress in matters scientific, when we show no reluctance to overthrow a theory based on tradition for one grounded on experimental proof, and fitting the facts better.

Puerperal fever had been studied chiefly by Oliver Wendell Holmes (1809-94), the American physician-philosopher, and Semmelweis (1818-65) of Hungary: both demonstrated its contagiousness and showed how antisepsis in midwifery cases considerably decreased risk of that condition. When Pasteur (1879) pointed out the presence of bacteria in the blood of a woman who had died of puerperal fever, and insisted that these
were the cause of the disease he was greeted with an outburst of opposition, the chief argument of the opponents being the spontaneous generation of these bacteria — and this after spontaneous generation had been described before the Académie des Sciences as a "Chimera"!

Yet Pasteur was bent on surmounting all obstacles, for he foresaw the triumph of the germ theory arising from the ruin of the old doctrines — at the price, it is true, of many efforts, many struggles, but those were of little consequence to him. So famous was he — a non-medical man — in the world of medicine, as a result of work that had brought new vigour and hope into that world, that he was invited to attend the International Medical Congress in London in 1881. His convincing arguments based on the simplest of experiments soon converted nearly all the other delegates into accepting the germ theory.

"As Pasteur, coming to this Congress, was not only curious to see what was the place held in medicine and surgery by the germ theory, but also desirous to learn as much as possible, he never missed a discussion and attended every meeting. It was in a simple sectional meeting that Bastian attempted to refute Lister. After his speech, the President suddenly said, "I call on M. Pasteur," though Pasteur had not risen. There was great applause: Pasteur did not know English; he turned to Lister and asked him what Bastian had said.

"He said," whispered Lister. "that microscopic organizations in disease were formed by the tissues themselves."
"That is enough for me," said Pasteur. And he then invited Bastian to try the following experiment:

"Take an animal's limb, crush it, allow blood and other normal or abnormal liquids to spread around the bones, only taking care that the skin should neither be torn nor opened in any way, and I defy you to see any micro-organism formed within that limb as long as the illness will last." (53).

The straightforwardness of Pasteur's character, his patience in refuting opposition step by step, slowly but surely, and his modesty in his hour of triumph, all endeared him alike to his listeners. It is no wonder that he was reported to have been the greatest success of the Congress.

One can hardly omit making mention of Pasteur's work on hydrophobia. Here again he suspected a bacterial source of infection, but he himself was unable to discover the microbe. His methods of preventive inoculation in that terrible disease indeed proved a blessing to humanity, and the world rewarded him by coming forward with funds to endow the famous Pasteur Institute. In the experimental stages of finding the cause and cure for hydrophobia he was ably assisted by two French physicians, Dr. Grancher and Dr. Straus. These novel studies fascinated them so much that they made similar research their life-work, and may claim to be the first French bacteriologists proper.
CONCLUSION.

It is indeed unfortunate that we cannot say that now at a certain definite date was the germ theory accepted by the world. Many more diseases were shown to be caused by microbes before that took place. Tetanus and diphtheria were studied by many medical men, each of them discovering the bacterial origin of the disease. A great advance was made when Dr. Roux, as a result of research in chicken cholera and diphtheria, pointed out to the London Royal Society in 1889 that "Microbes are chiefly dangerous on account of the toxic matters which they produce." (54).

When Bacteriology became no longer a subject for research workers, but began to be taught in medical schools as an important subject in the curriculum, then can it be said that the germ theory was vindicated.

But the great name we must associate with the founding of Bacteriology as a separate sphere of science is that of Louis Pasteur. "In what obscurity were fermentation and infection enveloped before his time, and with what light he had penetrated them! When he had discovered the all powerful rôle of the infinitely small, he had actually mastered some of those living germs, causes of disease; he had transformed them from destructive to preservative agents. Not only had he renovated medicine and surgery, but hygiene, misunderstood and neglected until then, was benefiting by the experimental method. (55).
"You have," said Lister to Pasteur, "raised the veil which for centuries had covered infectious diseases: you have discovered and demonstrated their microbian nature." (56)

And in the "Veterinary Press", the editor, M. Rossignol, expressed himself as follows: "Will you have some microbe? There is some everywhere. Microbiolatry is the fashion, it reigns undisputed; it is a doctrine which must not even be discussed, especially when its Pontiff, the learned M. Pasteur, has pronounced the sacramental words, "I have spoken." The microbe alone is and shall be the characteristic of a disease; that is understood and settled: henceforth the germ theory must have precedence of pure clinics: the Microbe alone is true, and Pasteur is its Prophet." (57).
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(7). Garrison, Pp.227-8
(8). Bulloch, P.16
(9). " "
(10). Garrison, P.228
(11). Long, Pp.54-5-6
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(13). Dobell Pp.363-5
(14). " P.40
(15). " P.41
(16). " P.43
(17). " P.44
(18). " P.131
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(21). " P.366
(22). " P.367
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(52). Radot, p.271 et seq.

(53). " p.331

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