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ESSAY ON THE

EVOLUTION OF THE GERM ORIGIN OF DISEASE.

BY

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The malice of a demon, the justice of an avenging god, the ill-will of an enemy or the anger of the dead, to these were ascribed the cause of disease in barbaric days, and on account of the conservatism of the priest-physicians Egyptian medicine never advanced far beyond this. Moreover, the body was supposed in some unknown way to be regulated by the planets and this idea prevailed for centuries.

Following the capture of Babylonia in the seventh century B.C. by the Assyrians medical science spread to that part. Disease, to the Assyrians and Babylonians, was the seizure or attack of the patient by some demon or other, such as the demon of consumption, the demon of liver complaint, and the particularly hideous demon that haunted the bedside of lying-in women. They believed, like the Jews, that blood was the vital force, was in some way identical with the soul, and that it was formed and elaborated in the liver. That organ should therefore, said they, be the object of attention in seeking the cause of disease. In Babylonia, as in Egypt, the conservatism of the priests conserved throughout the ages the medical knowledge of an immemorial past, but the very quality that enabled them to perpetuate traditions, prevented them making any marked advance toward a real medical science. Their faith in the virtue of drugs and in the influence of the stars was detrimental to progress; so did the distinction of making the first great contribution to scientific medicine become reserved for another people, among whom medicine was not dominated by the pristinely caste.

Later, the Greek school of philosopher-physicians considered disease the result of an upset in the harmony of the material elements surrounding the body. In view of our present knowledge, it is interesting to notice that Empedocles, one of this school, is said to have freed a town of pestilence by diverting the stream and driving the marshes in its vicinity, and to have improved the climate of his native city by blocking up a cleft in the mountains.

The late part of the fourth century B.C. saw a new era in medical thought, due to the influence of Hippocrates, one of the oldest, and still one of the world's greatest physicians. He it was who first endeavoured to separate theology, philosophy and medicine. In his treatise "On Airs, Water and Localities" which deals with disease in relation to geographical and meteorological conditions, he states that the idea of attributing the premature impotence of some men to a god is quite wrong. It appeared to him that all affection is as divine as another, and that no one disease is either more divine or more human than another, but that all are alike divine, for each has its own nature, and that no one arises without a natural cause. Surely, he says, it is no hommage to the gods to see their manifestation in the symptoms of diseases such as epilepsy. Hippocrates was the first man to insist on the necessity of cleanliness in the handling of wounds and mentioned healing by "first intention". He may have had the idea that evil existed in dirt.

The next conception of the cause of disease we find is about the seventh century A.D., after the Arabs had overrun Mesopotamia and Syria. Now all sickness was supposed to be due to repletion and indigestion. The greatest of all the physicians to write in Arabic was the Persian Rhazes (860-932). With him we find a return to the old idea that disease followed some unknown change in the blood. He considered that small-pox and measles were an inevitable accompaniment of this natural change and said that small-pox arises when the blood putrefies and ferments, so that superficial vapours are thrown out of it and it is changed from the blood of infants, which is like must, into the blood of young wine which is like wine perfectly refined; and the small-pox itself may be compared to the fermentation and effervescence which takes place in must. Rhazes sought to prevent measles by endeavouring to get this unavoidable change in the blood to take place slowly, so preventing ebullition and fermentation. One of great drawbacks to medical advance in the Arab world was the fact that dissection was a forbidden practice. The fear that the absence of any part on examination of the body by the angels after death might endanger the eternal happiness of the deceased, was the insurmountable barrier.
The first attack against the belief that pus should of necessity be generated in wounds was lodged by Hugh of Lucca in 1214, after medical science had spread across to France and Italy. He observed strict cleanliness in the treatment of wounds and employed compresses soaked in wine. He is quite definite in the advances his methods brought about. It was not necessary, he stated, that pus should be generated in wounds, no error could be greater than this. Such a practice was, indeed, only to hinder nature, to prolong disease, and to prevent the agglutination and consolidation of the wound. An Italian worker Lanfranchi was first to state that air favoured the formation of pus in wounds.

From this time to the seventeenth century medical thought was concentrated in acquiring a more definite idea of the structure and functions of the organs of the body, and endeavouring to correlate structure with function. Practically no attempts were made to define the cause of any maladies, the more important factor appearing to be the cure, once the disease had got the patient in its grip. Nevertheless careful clinical observations, and an attempt at differentiation of disease according to symptoms was carried out.

An idea of the views held in the seventeenth century may be had from the sayings of Sydenham, one of the greatest workers of that time. "Aetiology" he writes "is a difficult and perhaps an inexplicable affair and I choose to keep my hands clear of it." In his opinion, it is impossible for the physician to discover the ultimate causes of the majority of diseases. It is, however, interesting to note that he early mentioned that abundant swarms of insects in summer are the pre: cursors of autumnal diseases, and that before the end of his career he believed that a causal relationship existed between a marshy atmosphere and quartan ague. The importance of this statement was only realised two hundred and fifty years after. There is much in Sydenham's views reminiscent of Rhazes, as also in his view that disease may be explained as a fermentation of the blood. There is evidence, despite the above quotation, that he did not avoid adopting hypotheses regarding the nature and causation of disease. He believed that the human frame is adapted to compressions from without, and that maladies are owing in part to mineral effluvia and other occult atmospheric influences - to particles of the atmosphere - and in part to the different fermentation and putrefaction of the humors. At the same time he was aware that not only the delicate are subject to infection. A man might be as strong as a wrestler, but if he went to certain parts of the country where fever was raging he would sicken within a day or two. The conditions that produced plague were, for Sydenham, a special object of curiosity and the study of them brought him to the view that the atmosphere played a part in the dissemination of disease. The disease must be perpetuated in sporadic cases in the intervals between epidemics, or must continue to survive in some forms, or arise from some infected person from a pestilential locality. Otherwise Sydenham was unable to account for the fact that through the sanitary measures of the Grand Duke Ferdinand II there had been arrested in 1650 at the borders of Tuscany, a plague that had devastated nearly all the rest of Italy. When an epidemic rages the exhalations of the sick and from the corpses of the victims of the disease, spreads the contagion through the whole atmosphere of the affected area, so that the air, in itself and of itself, is sufficient to destroy those whose humors are adapted to the receipt of the influence. Thus there is here notable advance in the theories of the aetiology of disease, and one which some two hundred years later became of the utmost importance.

From this time onwards investigations into pathology and histology led observers to seek the cause of disease in the organs, the tissues and then in the cells of the body.

It was not however until 1856, when Pasteur made his epoch making investigations into the putrefaction of wines and the cause of fermentation, and the meaning of his investigations was understood, that the whole of medical thought was turned to bacteriology as the cause of disease.

Before proceeding further let us consider for a moment the instrument that made bacteriology possible. The microscope derives its name from two Greek words, one meaning small, and the other, to view, that is to see or view such minute objects as would be invisible without its aid. The honour of the invention is claimed by the Italians and the Dutch; the name of the inventor however, is lost.
If we consider the microscope as an instrument consisting of one lens only, it is probable that it was known by the Greeks and Romans. There is an account of two ancient monks, one of whom invented a primitive sort of microscope and showed the other one what could be seen by it in pond water, etc. The second was greatly disturbed and grieved thinking it a sin, as he considered Man was not supposed to see these things, and together they destroyed it for the good of humanity. Here again we have evidence of the retarding of medical thought and progress by religious superstition.

It was about the end of the sixteenth century that the compound microscope began to be generally known, and soon after this the field it presented to observation was cultivated by men of the first rank in science. It is astounding that with a simple microscope, the lenses of which were of exceedingly short focal length, Leeuwenhoek saw and figured bacteria as early as 1683.

From single simple lenses, microscopy advanced to the very complicated and exceedingly delicate instruments which to-day permits us to see the organisms of disease. The height of man's achievement so far is the wonderful microscope of Professor Siedentopf which magnifies twenty-five thousand diameters. It is therefore possible, nay probable, that ere many more years have passed, when our methods of staining and cultivating organisms have been correspondingly advanced the so-called ultra-microscopic organisms will be displayed by the microscope to the human eye.

As we have seen Pasteur was instrumental in the introduction of bacteriology. Before his day no one knew anything about germs. These invisible forms of life were to all intents and purposes non-existent. It was not that Pasteur was the first man to detect the presence of bacteria in the world, as Ozanam, a French historian of epidemic and infectious diseases says, many writers have dealt with the animal nature of infectious materials, several had maintained not only that these developed from animal substances, but that they are themselves organic and living beings. Varo, Columella, Aquelius, Rather Kircher, Lancisi, Beamur, Christ, Long and others had supported this view. Frémont had, moreover, maintained that infectious materials arise and develop in the body through fermentation. As already mentioned Leeuwenhoek had observed bacteria as early as 1680.

In 1701, Nicolas Andry expressed the conviction that air, water, vinegar, fermenting wine, beer, cider and sour milk are full of germs; that germs exist also in blood, urine, and the pustules of small-pox patients; and the mercury cures venereal disease because it kills the invisible organisms. By 1725 the doctrine of the causal relationship between micro-organisms and disease were so notorious as to be made the subject of a French satire, "Système d'un médecin anglais sur la cause de toutes les espèces de maladies", in which the fainter, the belly-nripper, etc. were playfully described.

In 1768, Limaeus, in his "Systema Naturae" expressed the belief that parasites cause measles, dysentery, plague, small-pox, etc., while Otto Friedrich Müller, in 1785, improved slightly on the knowledge of these organisms by furnishing well executed illustrations of those he observed.

In 1745, Neidham, an English priest, reported an experiment which seemed to support the doctrine prevalent at that time, that organisms were generated spontaneously. He had boiled meat juice in bottles which he had then carefully sealed; nevertheless, after some time, animalcules were observed to have developed in great numbers within the closed bottles. Bonnet indicated two lines of attack on the conclusion: livness of this experiment; creatures so minute as micro-organisms, said he, might find their way into even carefully sealed bottles; and it was possible that a few living forms might survive within the bottles even after the contents had been boiled. These purely theoretical criticisms were supported by the experiments of Spallanzani (1729-99) one of the most distinguished investigators of the eighteenth century. In these experiments he made use of flasks which could be hermetically sealed. If it were true, he argued, that living organisms could be found in preparations that had been boiled in vessels from which the outside air was excluded, then they must have arisen from germs or eggs on the sides of the container, in the decoction, or in the air within the container.

He heated his flasks in the fire, poured into them well-boiled meat and seeds and sealed the flasks hermetically. Notwithstanding this proceed: were living organisms were present in the flask after a few days. He now/
now supposed that some germs might have remained alive in the air within the flasks. Therefore he next poured nineteen different infusions into as many different flasks, sealed the flasks and allowed them to stand in boiling water for one hour. Microscopic examination of the contents of these nineteen flasks failed subsequently to reveal the presence of any living organisms. Other experiments showed that if a flask were slightly cracked, the air might penetrate to the contents, bearing with it the living germs. These experiments were reported in 1867. Two objections were raised against them, one that an insufficient quantity of air had been allowed for the support of life in the infusoria; and also that the conditions of the experiment had robbed the air of its life supporting quality. In 1856 Franz Schulze tried to meet these criticisms by filtering the air in a flask containing an infusion through concentrated sulphuric acid. He renewed the air in this way for over two months and the infusion remained free from organisms. When at the end of that time unfiltered air was admitted various living forms developed. He was now open to the criticism of having subjected the air to vitiating influences. In 1864, however, Schroder and Van Dusen showed that a thick layer of cotton wool sufficed to exclude all germs while permitting the free access of air.

These workers all failed to grasp the full meaning of their experiments and were unable by subsequent experiment to show the relation of a disease to a world so small as to be quite invisible to the naked eye. Nevertheless proof was slowly adding itself to proof until now came the establishment of the view that many diseases, especially those of a contagious or infectious nature, originate from the invasion of the body by special organisms, and their multiplication within the body. It has been shown that there had been many previous admissions of this view, and in its final establishment more than one hand may be discerned.

Above all others who have worked in this field towers the mighty figure of Louis Pasteur (1822-95). We shall do no grave injustice to any man if we treat the scientific demonstration of the doctrine of the microscopic origin of disease as the product of his superb genius.

The opening of Pasteur's interest in disease can be seen in his work on fermentation. At first he was faced with the opposition of Liebig. According to that eminent physician, fermentation was not the result of vital activity, but was a purely mechanical change. A ferment he regarded as an unstable organic product, the character of which determined the manner of decomposition of the medium in which it is placed. Pasteur demonstrated that, as there is a specific alcoholic ferment, so is there a specific milk souring ferment. Any nitrogenous matter present in a fluid will serve as food for the development of a ferment, but will not of itself induce fermentation. Ferments have, he demonstrated, the power of reproduction. Pasteur rapidly seized on the idea of the specificity of ferments. An albuminous sugar solution can be converted into various products by the addition of various ferments. According as one sows, so will one reap. The milk souring ferment Pasteur concluded is organised and living, and its action is correlated to its development and organisation - no life, no ferment, no ferment, no fermentation.

During the years following, Pasteur applied himself to a study of ferments, notably of those which involved deterioration of wines and beers. This led him to perceive that there is a great multiplicity and variety of these living organisms. Now here was an old and well-known view that fermentation, putrefaction and the infection of disease had much in common. Pasteur was perfectly natural therefore for Pasteur to regard the latter in the light of a vital process. A great difficulty was, however, the demand that any such doctrine made on the germ bearing capacity of the air. Critics were not slow to avail themselves of this weakness, and pointed out that according to Pasteur the air must be one solid mass of germs. In reply, Pasteur boldly asserted that the air was full of germs, though more abundant in some localities than in others, and he proceeded to show his experimental proof of his contention. He filled a large number of flasks with infusion, heated them to boiling point, and then hermetically sealed them. He opened twenty of these flasks, sealing them again immediately, at the foot of the Jural Alps, twenty others at an altitude of eight hundred metres and twenty at two thousand metres. After a few days, eight of the first twenty, five of the second twenty and only one of the third twenty showed the presence of micro-organisms/
micro-organisms. For the opponents of Pasteur the living organisms found in the process of fermentation or decomposition were the result, not the cause, of the process. These organisms were regarded by them as being spontaneously generated in the fermentation process. Thus arose a discussion on the old theme of spontaneous generation. By 1859 - the year of publication of Darwin's "Origin of Species" - Pasteur was involved in a hot controversy as to the origin of life. The discussions specially hinged on what were then regarded as the lowest forms of life, the bacteria. Were they ever spontaneously generated or were they not? If a flask of broth, supposedly sterilised by boiling, went bad and organisms appeared in it, was it certain that they had come from without, or could they have been spontaneously generated by the broth itself? If this view was justifiable ? Pasteur's doctrine of the nature of ferments must fall to the ground. Pasteur had thus before him the task of proving a universal negative - a task admittedly impossible in formal logic, but nevertheless not in science.

In the end he clinched the matter by an exquisitely simple experiment which must at once carry conviction. A flask with a long S-shaped neck is filled with a putrescible fluid and is heated to boiling point to kill all germs, and then left in the still air of the room. Air can enter, but any floating organisms naturally strike the sides of the flask at the S and fall on to the floor of the neck. Months may go by without any change in the liquid, but once the neck is broken so that organisms can enter freely from the air, fermentation sets in within a few hours and the organisms can be detected in the liquid. Only living organisms from the air can have caused the change. Therefore, says Pasteur "there is no circumstance known to-day that permits us to assert that microscopic beings have come into the world without germs, without parents similar to themselves."

The first disease which Pasteur was able to demonstrate as causatively related to a living organism, was a condition that was devastating the silk worm industry of France. In 1866 he proved the contagiousness of the disease, showed that it was due to a living organism and followed the organism through its life history of moth, egg, worm and chrysalis.

In 1870 the Franco-Prussian war broke out. Pasteur now decided to make investigations into the diseases of beer, his object being to improve the French brews. He succeeded in isolating special organisms, mostly yeasts, which produced defects in beer. This work naturally led to an enlargement of his views on the nature and action of micro-organisms.

The first disease affecting man on which Pasteur was able to throw light was Anthrax (1877) in relation to which his work interdigitates with that of Robert Koch. Some other observers had seen a deadly and highly contagious condition which commonly affects cattle and sometimes spread to man. As early as 1838, a German observer, Professor Delafond, had noted microscopic rod-like objects in the blood of beasts dead of the disease. In 1850 another French contemporary of Pasteur, Devaine, had seen them and by 1868 had shown that the bacillus was not merely the inseparable companion of the disease, but its cause, and its only constantly acting cause. At this time the losses of cattle from Anthrax in France were enormous. The character of the outbreaks had been studied and seemed wholly unexplained by what was known of the bacillus. Farmers found that they lost cattle in fields from which infected animals had been excluded for months or even years. How was it to be explained? The explanation was, in fact, advanced in 1876 by the German, Robert Koch (1842-1910), whose work was just beginning. He showed that the Anthrax bacillus under certain conditions formed "spores", that is to say small encysted bodies, exceedingly resistant to heat and to other changes in external conditions, these spores being, in fact, an adaptation against unfavourable conditions. When more favourable conditions returned the less resistant rod-shaped bacillus is reformed. This discovery opened up a new field which was cultivated by Koch, Pasteur and their followers. It was left to Pasteur to show how by burying sheep dead of the disease, the farmers were actually infecting the ground itself. The question was how did the germs reach the surface of the soil when they were buried several feet deep? Wandering about farms where Anthrax was such a terrible scourge, his keen eyes noticed the casts of worms. Was the lowly worm a link in the propagation of Anthrax? He put the soil from the worm casts under his microscope and saw there the bacilli of Anthrax. Taking living worms he dissected them.
them and within the bodies found the same germs. So was the
puzzle solved.

While making his studies on ferments in 1865 Pasteur had
witnessed spore formation in the organisms concerned with butyric
fermentation, but had failed to grasp the significance of this. In
1869 he had again found spores forming in the organisms of silk-worm
disease and had shown that they also resisted prolonged drying. On
the basis of their resistance he had explained the persistence and
latency of the silk-worm disease. Other observers had had similar
experiences. The investigations of none, however, approached in
brilliance and completeness those of Koch. Koch found that spores
always form in the blood and tissues of animals dead of anthrax
provided that the temperature is suitable and there is sufficient oxygen.
These two conditions, temperature and oxygen, were found to be essential.
Below 18°C, spores are not formed; at 30°C they occur at the end of
thirty hours; at 35°C, in twenty hours. The readiness with which
spores are formed therefore proportional to the rise in temperature.
Oxygen was also found to be indispensable. Anthrax blood, if deprived
of oxygen, ceases to be virulent in twenty four hours without putref-
cation. When the blood is allowed to putrefy the virulence also
disappears, if putrefaction exhausts the oxygen quickly enough to
prevent the spores having time to form. If the spores have already
formed, putrefaction does not kill them, nor does it prevent them from
developing later, if circumstances become favourable. The persistence
of the disease and its return in an infected country were explained.
It was the spore which was the agent of preservation, which persisted
where the conditions of temperature and aeration had permitted it to
form, and which always held itself in readiness to make new victims.

The matter was carried further by Pasteur in 1877. At that time
he did not know of all the work of Koch. He succeeded in obtaining
pure cultures of anthrax. The question was then still being debated
in France as to whether anthrax was caused by a virus, that is to
say a non-living poison, or by a microbe. Pasteur had long been a
believer in the microbic theory, and it seemed to him probable, that
if the blood of an animal infected with anthrax be sown in a suitable
medium, it would stock it solely with anthrax bacilli, which he could
then keep pure for an indefinite time in successive generations of
cultures, as he had done with yeast and other ferments.

Experiment proved this to be the case, and showed that the anthrax
organism multiplied abundantly in urine made neutral or slightly alkaline
From that time the problem was solved. Take a series of cultures of the
organism derived each time on drop from the preceding culture
into 50 c.c. of fresh neutral urine. The first dilution is 1: 1000
and after ten, the dilution is almost the original drop in an ocean.
Everything that it carried with it, to which we might attribute the
production of anthrax - red corpuscles, white corpuscles, granules of
all sorts - is either destroyed by the change of medium or widely
disseminated in this ocean and lost. Only the organism can escape the
dilution, therefore, it must have multiplied in each of the cultures.
A drop from the last culture killed a rabbit or guinea-pig as surely
as a drop of anthrax blood. It was therefore, max to the organism
that the virulence belonged. A conclusion of the first rank was thus
firmly established.

With a pure culture of anthrax in his possession, Pasteur was
able to experiment in a way which none had previously attempted. The
most interesting stage of his work was now entered upon. He perceived
that there are some species of animals which are refractory to anthrax,
for example, birds. Nevertheless, blood when drawn from one of these
is an excellent culture medium for the bacterium. Why does it resist
infection when in the animal itself? Pasteur showed that the anthrax
organism will not live in the bird because the living bird's blood, in
full circulation, is filled with an infinite number of corpuscles, which
in order to live and perform their physiological functions need free
oxygen. When, therefore, the anthrax organism enters normal blood of
living birds it meets competition in the shape of the red blood corpuscle
ready to seize the oxygen for their own use. But the blood of other
animals besides birds contains corpuscles eager for oxygen. Why,
therefore, can anthrax grow in them and not in birds? This question
Pasteur answered by a convincing series of experiments(1878). The
normal
normal temperature of birds is higher than that of mammals and is, moreover, higher than that at which growth of the anthrax organism is most vigorous. Thus the blood corpuscles of the bird have the anthrax bacteria at a disadvantage. But if, by a cold bath, the temperature of the bird be lowered to that of a mammal, and if anthrax organisms be injected into the blood stream, they will grow and flourish at the expense of the bird. The experiments with anthrax on fowls led to experiments, also on fowls, with another disease, the virulence of which was known to vary, namely chicken cholera. Thus naturally arose Pasteur's idea and observations on the subject of immunity.

If Pasteur can be said to have laid the foundations of the knowledge of the nature of infection, it is to Koch we owe the main basis of the technique by which such diseases are now studied. He was the first to place bacteriology in a position as a separate science. Soon after his work on anthrax he published a remarkable paper in which placed our knowledge of wound infection on a firm footing; he is thus among those who helped to create modern surgical technique. Many communications came from his pen but none was of more far reaching importance than his demonstration of the organism of tuberculosis in 1882. All subsequent work in connection with consumption has been rendered possible only by this discovery of Koch's. Other investigations associated with his name are on cholera and sleeping sickness. Koch was unquestionably the greatest technician in bacteriology the world has ever seen. His genius was limited compared to that of Pasteur, but his exquisite technical skill and acumen have never been excelled.

Since the time of Pasteur and Koch, the study of infectious diseases has developed along various special lines. The work of those two men, however, has determined the direction of those lines, and they themselves are the most typical, as well as the greatest, representatives of the most important of all movements in modern science.

So did the hesitant theories of the origin of disease arrive at triumphant proof, through the agency of the genius Pasteur and the scarcely less brilliant Koch. It is of interest now to take a side-step and consider the work which was being done independently by their contemporaries in midwifery and surgery, resulting in the case of the former, in lifting the scourge of puerperal fever, and in the latter, in laying open the path for modern surgery.

By the nineteenth century obstetrics was well developed from the mechanical point of view. Great progress had been made in the art of assisting the child-bearing women during the three hundred years that had passed since Pare had opened the way for the return of the physician to the lying-in room. But some of the advantages derived from the development of obstetrics, and the extensive participation of physicians in the art were offset by the increasing prevalence of the disease known as "child-bed fever", or puerperal infection. This disease, which struck only at women who bore children, had been known from antiquity as an occasional occurrence. During the seventeenth, eighteenth and nineteenth centuries, however, it became a pestilence. Between the years 1658-1662 there were two hundred epidemics of this disease, which was then attributed largely to the state of the weather. In 1773 a great epidemic of puerperal fever raged for more than three years in Europe and culminated in Lombardy, where it is said that for one year not one woman lived after bearing a child.

From the seventeenth to the middle of the eighteenth century, the lying-in hospitals were the places in which puerperal infection flourished, so that they came to be looked upon by the public as a sure avenue to death. Until a means of controlling the infection was introduced child-birth ranked in mortality with some of the serious infections.

In 1845 Oliver Wendell Holmes, in a paper entitled "The Contagiousness of Puerperal Fever" showed clearly that the disease was an infective disease, and that the infection was carried by the physician or midwife from one patient to another by sheer lack of cleanliness. This paper, setting forth the essentials of the greatest discovery ever made in the care of the child-bearing woman, was received with indifference in Boston, and openly condemned by Dr. Meigs in Philadelphia. Dr. Holmes replied to his attack with a paper "Puerperal fever: private pestilence" in which he stated that the use of antiseptic "Senderlein" had lessened the mortality from the disease by scrubbing his hands with chloride of lime. This "Senderlein" was no other than Semmelweis. Holmes did not push further his discovery which he had tried to share with the obstetricians in America, and so the
the credit for one of the greatest boons given to humanity by medicine goes instead to Semmelweis.

Undoubtedly, though, the greatest champion of the cause of the child-bearing woman is Ludwig Ignaz Philipp Semmelweis, the man who laboured through lifetime of oppression and persecution in the vile wards of the great charity lying-in hospitals of Europe, who discovered the cause of puerperal fever, who controlled it in the hospitals where he worked, who gave a practical method for its eradication and who died of its infection. If he had wielded the pen of Oliver Holmes, his great discovery would have been adopted throughout Europe soon after it was made; instead, he died before the general principles he set forth were put into practice.

A brief account of the conditions in these lying-in hospitals will suffice to allow of an appreciation of the task that Semmelweis had set himself, that of ridding them of child-bed fever. The sheets in the beds were contaminated and improperly laundered, and the same clothes would be used for successive patients. Ventilation was bad, the rooms were filthy and exceedingly dusty, lying-in women who became ill were all transferred to an isolation room regardless of the nature of their illness, and last but not least, the midwifery pupils attended normal lying-in patients and fever cases alike, performing all the necessary manipulations for every class of case, often coming straight from the dissecting room without washing their hands which had just been handling the post-mortem material.

In the hospital where Semmelweis started his work there were two divisions, the first catering for medical students, and the second for women training to become midwives. The average mortality in the first was 99 per 1000, and in the second 33 per 1000. The differences in these figures started Semmelweis puzzling over the reason.

Every conceivable cause was probed into, and Semmelweis went on, step by step, to eliminate ventilation, dirty laundry, and improper diet etc. on the grounds that these were common to the two divisions. Yet, as he eliminated these possible causes, he knew that the real cause lay undiscovered before him in the hospital. This fact was proven by the observation that women who were overtaken with labour on the street while making their way to the hospital were not affected with child-bed fever in the hospital, even though they were taken into the first division.

About this time, Dr. Kolletschka, while performing a post-mortem examination, received a puncture wound in the finger from the knife of one of his pupils, in consequence of which he sickened and died, the symptoms being identical with those characteristic of child-bed fever. Semmelweis recognised the picture and the vision of it was continually with him. He was now on the verge of his great discovery that child-bed fever was wound infection blood poisoning, which was transmitted to women by the unclean hands of physicians and medical students who examined them before or during the birth of their child.

"In the case of Kolletschka" writes Semmelweis "the cause of the disease was cadaveric material carried into the vascular system; I must therefore put this question to myself. Did then the individuals whom I have seen die from an identical disease also have cadaveric material carried into their vascular system? To this question I must answer YES!"

With this discovery made Semmelweis at once required each student to wash his hands in a solution of chloride of lime before making examinations, with the result that the number of deaths in the first division fell to 12 per 1000, and for two months running there were none at all.

The work of Lister, though quite independent, completed what he had started. The question he set himself to answer was "Why should a scratch, a tiny wound, destroy the miracle of life?" Many men had asked the same question before, but none so insistently as Lister. Others contented themselves by guessing at the cause; Lister determined to trace the cause.

Lister operated brilliantly, yet after operation he could only hope for success, he could never be sure of it. Death seemed to follow the knife - why? The question recurred time and again to him. The wound which was clean yesterday and beginning to heal would suddenly take a new turn. It would begin to discharge and in a short time death would supervene. Hospital gangrene, as it was called, became a sentence of death. It was generally believed that the cause was an inward decay of which the gangrene was merely the outward expression, and that death therefore/
therefore came from within the human body itself. The causal, erratic nature of the condition was incomprehensible. A strong man would be taken to hospital for an operation. Everything would be done skillfully and quickly, but yet in a day or two days or three, the dreaded discoloration of the wound would begin to appear and then it was only a question of time until a figure would be still on the bed with a sheet drawn over its face. On the other hand, a sickly girl would undergo an operation at home because she was too ill to be moved, and that girl would recover.

What was it that struck down the strong and sometimes spared the weak? If it was, as supposed, something from within, would it not first strike down the weak? So Lister pondered.

The hospitals as has already been described, were in these days a veritable preparation for death and to be avoided at all costs. Only in the direst necessity would people consent to go into them. It is no exaggeration to say that they knew they would in all likelihood be carried out in their coffins.

John Bell, before Lister's day, was asking himself how he could stop this dreadful disease. He laid the blame on the hospitals, saw that somehow they were the cause of the infection, and wrote strong words of advice for all young surgeons to read: "Let the surgeon bear this in mind that no dressing have ever been found to stop this, that no quantity of wine or bark which a man can bear have ever retarded this gangrene; let him bear in mind that this is a hospital disease, that without the circle of its infected walls, men are safe; let him therefore hurry them out of this house of death, let him change the wards, let him take possession of some empty house and so carry his patients out into good air; let him lay them in a schoolroom, a church or on a dunghill, let him carry them anywhere but to their graves."

John Bell was groping in the dark but he was groping in the right direction. He knew the hospital was infected, he recognised the value of pure air, but the key to the puzzle escaped him.

Lister's first step was to have the hospital scrubbed to get rid of the dirt; his next, to make all doctors and nurses assisting in any way at the operations scrub their hands. The dead, however, still continued to be carried out in a steady stream. Cleanliness seemed to make no difference to gangrene.

His faith undiminished he read steadily through English and German works to try and find a clue, but none was forthcoming until one day he began to read a paper entitled "Researches on Putrefaction," and before he had gone very far he read the words "Putrefaction is caused by living ferment." The full significance of the phrase passed through his mind. Pasteur, whose paper he had just read, had placed the key in his hands. Putrefaction was caused by living organisms, and they were in the air all round him lurking in his hands, his clothes, and in the dust of the room. These organisms caused gangrene, and if he could keep the wounds free of these invisible germs he could overcome the most horrible hospital disease of his age.

Thus to Lister was given the spark of genius which, when he read Pasteur's paper, led him to realise that gangrene was not set up from inside the body but outside; that the germs of disease were planted in the wound from the apparently harmless air.

With this idea firmly in his mind he began to look around for something that would kill the germs and so prevent them from attacking the wounds made by the surgeon. It is a far cry from sewage to surgery, yet sewage is one of the vital links in the chain of knowledge that gave the world antisepsis. In Carlisle the authorities were trying to discover a means of dispelling the disgusting odour that filled the air over a large area round the sewage works. They found that carbolic acid was absolutely effective. To Lister, destroying the smell, was destroy-
ing the germs, and so he employed carbolic acid to prevent hospital gangrene. He made the surgeons and their helpers wash their hands in carbolic to disinfect them before operating, taught them to steep all their instruments in the same fluid and perfected the dressings that kept the bacteria from the wounds.

Thus we see that Lister, and Lister alone, was responsible for the cleansing of the hospitals of the world.

It is interesting to note the tremendous influence Pasteur's words carried with it. At a Medical Congress he attended in London with Lister Easton attacked Lister's theory of antisepsis. In an instant Pasteur swept/
swept the opposition to the winds, "Take an animal's limb, crush it without breaking the skin, and I defy you to find any micro-organisms within that limb so long as the illness will last". These were his words. The Master of Science had spoken.

The value of Lister's work can be seen in the following quotation from the American Ambassador at a banquet given in his honour by the Royal Society: "My Lord, it is not a profession, it is not a nation, it is humanity which with uncovered head salutes you."

Von Bergmann carried Lister's system a step further, and after elaborating the details evolved a system of aseptic surgery which became the model for modern surgery.

After this brief resume of the work done independently on this subject in midwifery and surgery, let us return to the work of Pasteur and Koch.

While the French observer stood above all men for the clearness and steadiness of his vision, and for his persistence and resource in following what he had seen from afar, his German colleague had a genius for visualising particulars and for adapting the chemical devices and scientific discoveries to particular ends. Koch thus vastly improved and elaborated the methods for detecting and examining minute organisms. The significance of his results was at once recognised; but the complexity of the technique involved, and the time and training necessary, demanded the elevation of the subject into the position of a special science. Though but fifty years old the science of bacteriology has itself undergone repeated division.

With Koch's work on anthrax in 1876, and on the bacteria commonly infecting wounds in 1878, and especially with his great discovery of the Tubercle Bacillus in 1882, the study of the infective diseases entered on a new stage. The enemy had been seen and was known now for what he was. The bacteriologist had succeeded in making him a prisoner, had isolated him and made him live in a test-tube. Organisms had been obtained, as bacteriologists say in "Pure Culture", and delicate methods of detecting and differentiating them had been developed. With a pure culture in his hands, the bacteriologist can determine the influences favourable or unfavourable to the growth of the disease, and he can investigate conditions than can exist, destroy, or modify the activity of the causal organism.

An important series of criteria established by Koch have remained the tests, even until to-day, by which the disease-bearing character of these organisms can be established. To prove that an organism is the inseparable cause of the disease, we need to demonstrate the constant presence of the organism in every case of the disease, the preparation of a pure culture, which must be maintained for repeated generations, and the reproduction of the disease in animals by means of a pure culture removed by several generations from the organisms first obtained.

These conditions have been fulfilled for many diseases. Obviously the third test can be applied only in diseases to which animals, other than man, are susceptible. In this matter the organisms than produce disease vary greatly. Some, for instance, those of anthrax, are easily conveyed to a variety of species of animal; others, for instance, those of syphilis, are with difficulty conveyed to a very few species of animal; yet others, for instance human malaria, can be conveyed to no animal save man.

Some light is thrown on the life-history of the second and third classes by recent discoveries. The science of Comparative Pathology, that is, the knowledge of the relations of the diseases of different species of animals, is of very recent growth. It has already demonstrated, however, the existence of organisms bearing some resemblance to each other, for instance, those of human syphilis and human malaria, as the cause of disease in animals. By studying the life-history of these organisms in animals and by studying their effect on animals, valuable side-lighting has often been thrown on the allied diseases in man. More: over, in exceptional cases, and in some special diseases, it has been possible to convey a disease experimentally to man.

A second important factor has gradually come into prominence with the extension of bacteriological knowledge. It is evident that not all micro-organisms are subject to all human diseases. Even in the most destructive epidemic there are some that escape. These lucky ones may be "naturally immune". Again many diseases such measles seldom recur in individuals who have once been infected, so that the fact of an acquired immunity has
has also been established.

On the nature of immunity much might be written; we may direct attention, however, only to the more important points here.

Immunity may be relative or absolute; and it may, moreover, vary according to the circumstances of the individual. Thus for instance a well-fed, well-housed person of temperate habits, living an open-air life, is unlikely to develop tuberculosis. Restrict his diet, confine him in an office, lower his standard of living, and he may well fall a victim to it. The investigations of facts such as these on a large scale has demonstrated that the soil in which disease grows, is of no less import than the seed from which it grows.

In the production of disease by living organisms two main factors are involved. There is, firstly, the multiplication of the organisms themselves, and secondly, the production by the organism of poisonous substances or toxins. The first toxins to be investigated were those isolated from putrefying material and named "ptomaines" (1876 by false formation from the Greek ptoma a corpse). These are in fact definite chemical substances, of the group known to chemists as "alkaloids". Later, toxins were prepared from actual disease organisms such as those of typhoid and tetanus. The method was introduced of filtering the bacteria away from their fluid cultures, and thus obtaining a liquid containing the poisonous bacterial products alone. The use of these toxins has been essential for the scientific study of immunity. Immunity means a relative or absolute exemption from the incidence of a disease. There are various types of immunity but only "artificial immunity" can be dealt with here.

Artificial immunity is itself of two kinds, active and passive. The former is obtained by injection of living organisms or their products and the latter by the injection of the serum of an individual who has already been treated to produce the active type.

The first man to produce immunity was a farmer Simon Jesty in 1774. His knowledge arose from observation of the fact that in some way a person who had cowpox, did not take small-pox. This, a common observation, was so deeply engrained in his mind that he decided to give cowpox to his wife and sons. Taking some of the matter from the pustules of a cow he introduced it into the arms of his family in order to prevent them from taking small-pox. What Jesty did in 1774 was true vaccination, and it was thus that a farmer anticipated one of the greatest discoveries ever made.

Jenner, knowing nothing of Jesty's experiment, but also noting that people who had suffered from cowpox did not fall victims to the dreaded small-pox, was convinced beyond all doubt that cowpox rendered a person immune. A touching testimony to his faith in his discovery is that the first person on whom he tried his vaccination was his own little son.

Pasteur found by accident that when organisms are cultivated outside the body they lose their virulence to a greater or less degree. While working on chicken cholera, he accidentally laid aside a test-tube which sometime later he discovered. On injection of some of the contents of that tube into a hen he found no cholera developed, and moreover the subsequent injection of a virulent strain produced no effects. Such are the results of chance! Thus by the use of such "attenuated" cultures he was able to establish a state of active immunity against chicken cholera. Jenner's noble work in sweeping away small-pox by vaccination leapt to the mind of Pasteur. Could he prevent chicken cholera in the same way as vaccine prevented small-pox? A long series of experiments solved the question. He learned how the oxygen in the air weakened the virus; how by keeping the virus in various periods he was able to induce the disease in all its symptoms, from the mildest of forms to the fatal form; how birds vaccinated with this weakened virus obtained immunity against the disease.

From chickens his mind turned back to anthrax in sheep. If it was possible to give immunity to chickens, would it not be possible to deal in a similar manner with the germs or virus of anthrax, and thus by vaccination, render sheep immune from that disease? When he announced that he could, he was met with keen opposition, and only after demoralizing the immunity produced by his vaccine on fifty sheep, before the Agricultural Society of Melin, were his opponents routed.

Pasteur also showed that there are many other ways of attenuating virulence, and also that for the production of active immunity, the bodies of the organisms are not always necessary; in these cases the toxins/
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toxins obtained from them being sufficient. Thus he produced in
animals, and later in man, immunity to hydrophobia, a very common disease
at that time, and produced by the bite of a wild dog, though he failed
to discover the germ which, indeed, still remains undiscovered, though
the disease itself has been conquered.

"The germ" preached Pasteur, for he firmly believed that each
disease had its germ, and he dreamed of the day when every disease
would have its vaccine that would bring immunity.

These studies in immunity have resulted in the greatest mechanism
we have at the present day for the success of preventive medicine.

Before drawing to a conclusion I must first mention the work
which has been done on the germs of Tropical diseases, which has result-
ed in converting the so-called "White Man's Grave" into a more habitable
land; and then the very recent work on the ultra-microscopic organisms.
Malaria, Yellow Fever, Sleeping Sickness, Plague, Cholera, Elephant:
tiasis, these are some of the diseases which made certain zones of the
tropics little more than death-traps to the white man. The natives
have developed a certain degree of immunity against them, just as the
white man has against tuberculosis. This immunity of the natives is
nothing more than a natural form of vaccination, but in place of the
needle of the doctor, we have the stilletto of the mosquito.

Strange as it seems, it is nevertheless true, that the deadliness of
the tropics is due to insects that buzz round us and which we allow
to alight on our face or garments. These are the creatures that spread
the disease there acting as carriers of the causal organisms, and it
is only by fighting these, that the tropics can be made safe for the
white man. It seems only yesterday since we learned this, and we owe
our knowledge to the genius of a noble Scotsman, Sir Patrick Manson,
who is rightly called "The Father of Tropical Medicine." He it was
who, in 1877, made the great discovery that the mosquito was the carrier
of the filaria parasite, which is responsible for the disease elephant:
tiasis. This discovery of Manson's may be said to rank with that of
Pasteur's, that fermentation was caused by living organisms, for it
marks an epoch in tropical medicine, and on it, our modern knowledge
of the transmission of the majority of tropical diseases, has been found:
ded. Pasteur proved that diseases are caused by living organisms, and
Manson revealed that many of these are carried from one human being to
another by the insects that creep and fly.

Subsequently the part played by the mosquito in the transmission
of malaria and yellow fever was discovered, though, as is so often the
case in medicine, the organism responsible had been seen and reported
by observers, long before it was accepted by the medical world, and
isolated and cultured by Noguchi. The heroes who have worked in this
field are too many to mention, but their self-sacrifice will be a lasting
testimony to the zeal, courage and devotion of the workers in the
greatest of all sciences.

The ultra-microscopic organisms are so small that the most powerful
microscopes in existence fail to reveal them. They are minute
enough to pass through the finest filters known, and appear to be able
to pass wherever liquid can. Professors Froesch and Dahmen, using
specially prepared media, have been able to isolate them in culture.
It remained for them to test whether the isolated culture produced a
specific disease in animals. After numerous experiments, they found
that when a culture grown on a certain medium and prepared in a certain
way, was injected, the animal always contracted a particular disease.

Definite as were these results, these experimenters were not satisfied:
field, and wished to see the organisms for themselves. By means of a
special camera constructed by Kohler of Jena, which produces an image
twice as large as that which is actually visible to the human eye, actually:
photo: graphing things they cannot see even with the microscope. The draw-
back in the use of this apparatus generally is, that the manipulation
requires extreme care, the least tremor upsetting the whole thing;
thus work with it is best carried out in the stillness between midnight
and dawn. By this means Professors Froesch and Dahmen have placed
in the hands of the scientific world the photographs of the organism—a
filter-passers—they maintain is responsible for foot-and-mouth disease.

An English Commission sent to Berlin has not been able to satisfy
itself that a little of their culture, when injected into guineas, pigs
sets up, in most cases, symptoms of foot-and-mouth disease.

If the germ is indeed disclosed, it should be possible in due


course to vaccinate animals and make them immune from the disease.

When a little more is known of these filter-passers, a new world may be lit up populated by creatures so small, that even now we cannot hazard the guess at what they may, or may not, exist.

As a result of all this work, we pride ourselves on the advance in knowledge of infectious disease, which the germ theory has brought us, and yet we are utterly and completely ignorant of the two things about infectious diseases which are perhaps the two things most worth knowing. No man has conceived the way in which the parasites of disease first fastened themselves on the animal body, a specific parasite to a specific animal. In other words, we have no idea of how diseases first began.

It may be that if these tiny organisms existed before Man, as they undoubtedly did, they must have undergone considerable modifications before they were able to invade him, and live and multiply within him. For ought we know, the first vegetation that clothed the earth may have given rise to the first disease germs. Mammals eating the vegetation, would unconsciously take these germs of disease into their systems. Whereas most of these germs would be digested and cast out, the day might dawn when a single germ might survive the digestive process of the mammals, suit itself to the new conditions, and breed new races of germs which eventually invaded Man. On the otherhand, the first mobile forms of life may have given rise to their own germs of decay, which waited until the cycle of life was finished before they operated as nature's scavengers and reduced the body to its natural elements, so that it could be again absorbed by earth and air. As the forms of life became higher, the germs of decay probably changed to suit the new environment. Instead of waiting until the cycle of life was finished and then acting on the dead body, they may have advanced that comparatively tremendous step which them attacking life itself, in order to obtain food. The original germs of decay may have given rise to the more highly developed germs of disease, which strive to provide food for themselves, instead of waiting for it to be provided.

Secondly, no man has conceived why diseases, distributed over a wide area and in many bodies, should vary in virulence from time to time, why, for instance, a relatively mild infection such as influenza should suddenly devastate the whole world. It is easy to say that human resistance varies, but that is only to restate the problem in terms of which we know nothing. On these high topics of medicine we know as much, and as little, as Hippocrates.

Moreover, if we turn to definite diseases, there are many conditions, and those among the most important, of which our ignorance is almost complete. Thus, of the very common and painful diseases, muscular rheumatism and rheumatoid arthritis, we hardly know anything and our remedies are little more effective than those used in olden times. The common cold - economically the most important disease, not excluding cancer and tuberculosis - has a vast literature, but the physician is almost helpless in its presence and can but let it run its course. Measles, influenza and whooping-cough have become more deadly of late years, and we have still no clear line of treatment for them. Nor have we any real insight into the nature of cancer. Those who reach advanced age have no better chance of life than they had two hundred years ago, though it is true that now there are many more people who reach advanced age. Above all it must be remembered that the great majority of deaths are caused by diseases theoretically preventible. There is a natural term of life to which it is desireable all should attain. Yet, most of us will surely die a violent death, as truly as though struck down by a felon's hand. Death from disease is an unnatural and a violent death.

Thus life is ever a struggle. On all sides Man is menaced by myriads of foes, visible and invisible. The unseen foes are recognised and feared, but the unseen foes are little known to the multitude, and barely understood by the scientist.

The greatest protection of these microbes is their invisibility to the human eye, and their great danger to mankind lies in the power of some species, for each individual to reproduce its own, the rapidity with which they multiply and the fact that they are indirect feeders, and can obtain sustenance direct from the oxygen, nitrogen and other elements of the soil.

Up to within comparatively recent times, Man carried on his battle against the deadly germs unconsciously. So the germ armies have gone!
gone on massacring humanity, fighting under a cloak of invisibility which we are only now tearing aside. The great European War, with its appalling slaughter, bulks large in the history of the world. It has created a tremendous impression on mankind. Yet the great war, and all other wars, are mere affrays compared with that greater war which mankind has been fighting for ages. This greater war is the battle between germs and Man. It is never-ending, but goes on day and night, and the people who have been slain by the germs, innocent men, women and children, total thousands of millions.

For untold ages Man has fought against Nature and battled with the foes that are seen. He has become the most highly developed of living creatures, wielding powers both wonderful and terrible. From afar he can launch death and kill his fellow-man. He can strike the creatures of the world dead in their tracks. Yet Man himself, for all his powers, eventually dies. While he lives, he has to fight for his existence against the foes that are visible, and the invisible foes generally drag him down at last. Man, who has vanquished the greatest of living creatures, generally succumbs in the end to the tiniest of living organisms, the microbes of disease. So may the importance of the discovery of the Germ Origin of Disease be appreciated.

Men live and learn; and slowly, through the patience and heroism of the pioneers of medicine, the infectious and other diseases of mankind are being vanquished one by one.

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