

Th. Sect.

Wellcome Gold Medal.

THE INFLUENCE OF THE WORK
OF
P A S T E U R
ON
MEDICINE AND SURGERY.

By
J. D. ALLAN GRAY, M.B., Ch.B.,
ASSISTANT, PATHOLOGY DEPARTMENT,
UNIVERSITY OF EDINBURGH.

MAY, 1927.





LOUIS PASTEUR.

INDEX.

	PAGE.
Introduction .	1.
Medicine prior to Pasteur .	2.
Bacteriology prior to Pasteur .	4.
Surgery prior to Pasteur .	9.
The Work of Pasteur .	17.
The Influence of The Work of Pasteur upon Medicine	26.
and upon Surgery .	32.
Conclusion .	42.
Bibliography .	44.

ILLUSTRATIONS.

Pasteur .	Frontispiece .
Lister .	page 31.

The Influence of The Work of Pasteur on Medicine and Surgery.

"L'homme, né dans une ignorance complète des vérités scientifiques doit les conquérir par l'étude attentive de la nature." Despine.

The work of Pasteur has been epoch-making. Its influence on Medicine and Surgery has been enormous. The discoveries in bacteriology inaugurated by Pasteur are amongst the most brilliant of the age. They have revealed the causes of many diseases previously obscure, and have permitted methods of treatment fundamentally different from those formerly employed. "Medicine and Surgery have never been slow to appropriate, and apply the biological facts of pathology," and at no period have they followed more closely in its wake than during the latter half of the nineteenth century.

To assess the influence of the work of Pasteur we must consider the conditions of medical and surgical practice prior to his time.

Medicine prior to Pasteur.

According to Garrison, three factors predominated in the evolution of modern medicine, as of modern science. The first was the intensification of the feeling for intellectual and moral liberty, and the emphasis laid on the importance of all kinds of human labour. The second was that traditional beliefs which had long hampered the advancement of medicine were upset by the appearance of classics such as Helmholtz's "Conservation of Energy" (1847), and Darwin's "Origin of Species" (1859). The third was the study of physics, chemistry and biology along scientific lines instead of by metaphysical speculation. These led to revolutionary changes. The last of these three factors is well illustrated in the work of Pasteur.

In the first half of the nineteenth century, medicine "was, with a few noble exceptions, only part and parcel of the stationary theorising of the preceding age"; but in the second half France, Germany and Britain all shared in the evolution. The part-

played by France was largely due to Pasteur. Undoubtedly, Immanuel Kant, Schelling, and Hegel had hindered progress by "diverting mental activity away from the investigation of concrete facts into the realm of fanciful speculation"; but the work of the statistician, Pierre Charles Alexandre Louis (1787-1872) in phthisis and typhoid fever; of René Théophile Hyacinthe Laënnec (1781-1826) in thoracic diseases aided by the stethoscope which he invented; - supplementary and complementary to Auenbrugger's work, - and of Philippe Pinel (1745-1826) on the humane treatment of the insane, is well known. Many diseases and medical terms have received their names from clinicians of this period e.g. Robert-James Graves, (1796-1853); William Stokes, (1804-1878); Dominic John Corrigan, (1802-1880); Richard Bright, (1789-1858); Thomas Addison, (1793-1860); Thomas Hodgkin, (1798-1866); James Parkinson, (1755-1824); Johann Lucas Schönlein, (1793-1864); Josef Skoda (1805-1881); Ferdinand von Hebra, (1816-1880); Theodor Schwann, (1810-1882); Jacob Henle, (1809-1885); Johannes Evangelista Purkinje, (1787-1869); François Magendie, (1783-1855); the brothers Ernst

Heinrich Weber, (1795-1878); Eduard Friedrich Weber, (1806-1871); and Wilhelm Eduard Weber, (1804-1891); William Sharpey, (1802-1880); Sir William Bowman (1816-1892); Justus von Liebig (1803-1873); Friedrich Wöhler (1800-1882); and Leopold Gmelin (1788-1853).

Bacteriology prior to Pasteur.

Discovery of Micro-organisms. Probably the earliest observations of living micro-organisms, of which we have record, are contained in the "Scrutinium pestis" (1658) of Athanasius Kircher (1601-1680) of Fulda, who with a 32 power microscope demonstrated the presence in putrid materials of "minute living worms". Antonij van Leeuwenhoek (1632-1723) of Delft with the aid of a lens ground by himself described protozoa in 1675, and bacilli and spirilla in 1683, but did not speculate on their significance. While O. F. Müller knew several important forms in 1773, Ehrenberg (1795-1876), in 1830 advanced to the commencement of a scientific classification of these organisms.

The early ideas as to protozoal structure were drawn from analogy, and were that each protozoon, as each metazoon, contained organs and tissues. Motility was due to imaginary muscles, tendons and articulations, and food was absorbed from an imaginary alimentary tract. Many of the structures seen were fancifully interpreted, - for instance the contractile vacuole of the protozoa, discovered in 1754 by Joblot, was regarded in turn as lung, stomach, etc.:. However, Matthias Jacob Schleiden (1804-1881) in 1838, following up the work of Robert Hooke (1665), Malpighi (1675), Nehemiah Grew (1682), Robert Brown (1773-1858) and Gabriel Valentin (1836) showed that the cell was the unit of structure. His work along with that of Dujardin (1801-1860) gradually made for the recognition of micro-organisms as single cells without definite organic structure. In 1842 John Goodsir described sarcinae of the stomach.

Relation of Micro-organisms to Infectious Diseases.

Long before microbes had been discovered, the Venetian physician, Frascatorius (1484-1553) in his "De Contagione" of 1546, spoke of the seeds

Frascatorius

of contagion passing from one person to another, and he first drew a parallel between fermentation of wine and contagion, - a relationship which was to be rediscovered by Lister, three centuries later, with such profound results. It is clear that Robert Boyle (1627-1691) also recognized this parallel, for he wrote that "phenomena of diseases will perhaps be never properly understood without an insight into the doctrine of fermentation". Kircher in his "Scrutinium pestis" (1658), mentioned above, however was undoubtedly the first to state explicitly the doctrine of a "contagium animatum" as the cause of infective disease. In 1762 Marcus Antonius Plenciz (1705-1786) of Vienna added to the idea of a "contagium animatum" a special "seminium verminosum" for each disease by which he tried to explain the difference in symptoms and incubation periods of different infectious ailments. Much of this was largely speculative, but was so plausible as to be accepted by many, and some of it has proved correct. Jacob Henle (1809-1885) in his essay on "miasmas and contagia" (1840) "clearly defined the character and action of

bacteria upon certain phases and symptoms" of infectious diseases.

The first actual experimental work in support of microbes being the cause of infectious disease was that of Agostino Bassi (1773-1856) who in 1836 showed that pébrine, the fatal infectious disease of silkworms, was due to a parasitic proto-zoon. Hermann Klencke, too in 1846, demonstrated the possibility of the transmission of tuberculosis by cow's milk, and about ten years later Villemin produced tuberculosis in animals by administering human discharges.

Origin of Micro-organisms. Whence came these micro-organisms? Were they reproduced from pre-existing micro-organisms, or were they the result of Spontaneous Generation?

Lazaro Spallazani (1729-1799) showed that organisms were absent and that putrefaction did not occur in organic matter after it had been boiled in hermetically-sealed flasks; but the supporters of the doctrine of Spontaneous Generation maintained that the putrefaction had been avoided simply by the absence of air, or its gaseous constituents, which they believed were the true

cause of fermentation. Max Schultze (1825-1874), Theodor Schwann (1810-1882) and Cagniard de-Latour now showed that vinous, as well as other types of fermentation, were due not to air, or its gaseous constituents, but to the minute thermo-labile particles contained in the air (1836-1838). Their views were supported by the botanist Turpin, but strongly opposed by Liebig and Helmholtz. Later, (1854) Schröder and Busch showed that putrefaction in organic fluids could be prevented, if the air in contact with them had previously been filtered through cotton wool, - instead of being calcined.

Round this question of Spontaneous Generation much argumentative warfare was waged, and it was not finally settled until by Pasteur in 1862.

Surgery prior to Pasteur.

"Surgery is as old as human needs."

Naturally we know little of the art as practised in prehistoric times, yet skulls of the stone-age have been found showing trephine wounds, callus round the wound indicating survival of the patient subsequent to the operation.

In all the older civilisations surgery had a place. "The ancient Hindoos performed almost every major operation except ligation of arteries." In Egypt, however surgery was curiously-poorly-developed perhaps owing to the detestation in which, according to Diodorus Siculus, the "paraschistes" who made the primary incision for the embalming of the dead was held. This may perhaps explain the failure of the Egyptian physician to cure the "dislocated" ankle of Darius of Persia (Herodotus III. 29). Of the Grecian era, the Hippocratic books on fractures and dislocations, considering the limitations under which they were written are remarkable. Grecian operative Surgery, however, seems to have been very limited. "Under the Romans, surgery attained to a degree of perfection which it was not to reach

again before the time of Ambroise Paré" and 200 different surgical instruments have been found among the ruins of Pompeii. Religious convictions caused Arabian physicians to abstain from dissection and leave operative surgery to wandering specialists.

The Science and Art of Surgery rose and fell with the rise and fall of each civilisation; probably a little knowledge remaining from each of the decaying civilisations to form a foundation for that of the next.

The staunching of blood, the bandaging of wounds, the application of splints to broken limbs, the extraction of arrows and the ceremony of circumcision have been practised from earliest times. Yet great advances did not take place until anatomy came to be studied seriously during the seventeenth and eighteenth centuries by men such as the Monros, Charles, and especially Benjamin Bell. Thread ligatures were introduced in 1805 by Jones of Jersey and twenty-four years later Jean Amussat (1796-1856) revived the old method of torsion for arresting hæmorrhage. John Abernethy (1764-1831), Astley Cooper (1768-1841) and Collis (1773-1843) all

performed ligation for aneurysm. In spite of the poor development of abdominal surgery, Goult-huisen of Munich in 1819 removed a urinary calculus and Jean Civiale (1792-1867) in 1826 removed an ovarian cyst causing ascites.

Orthopaedic surgery however, was more advanced. Plaster of Paris bandages were introduced from the East by the English Consul at Basra in 1841. Fractures which had united in bad position were rebroken and reset. Jacques Delpech (1777-1832) and Louis Stromeyer (1804-1876) performed tenotomy in 1831. Many anatomical and surgical terms have attached to them names of surgeons of this period, - such as those of Percival Pott, (1713-1785), Antonio Scarpa, (1747-1832); Benjamin Brodie, (1783-1862); Jacques Lisfranc, (1790-1847); Robert Liston, (1794-1847); James Syme, (1799-1870); August Nélaton, (1807-1873) and Bernard Langenbeck, (1810-1887). Syme, the discoverer of benzine as a solvent for india-rubber (an idea patented later by Charles Mackintosh) recommended excision in place of amputation for joint-disease and Chassaignac's system of drainage for incised wounds.

The agony of the patient demanded rapid surgery and within decent limits of precision, the speediest surgeon was the best. Of this era, in Edinburgh were Lizars (1787-1860) the first in Scotland to perform ovariectomy, and ligation of the innominate artery for aneurysm; Ferguson (1808-1877) of cleft-palate fame and Liston (1794-1847) renowned for his amputation through the thigh and treatment of fractures, aneurysms and diseases of bone.

Then in 1844-1847 came the boon of Anaesthesia. Longer and more serious operations were now rendered possible by the absence of pain, the relaxation and stillness of the patient and the reduction of shock. But what were their results? Sepsis often accompanied by secondary haemorrhage followed even trifling operations, - no matter how much skill and care had been used. The Hippocratic healing by first intention was extremely rare - in large wounds impossible since the ligatures had to be extruded by a process of suppuration. Sepsis indeed was regarded as inevitable. Suppuration was termed "healthy" and pus termed "laudable," since on their appearance, the clinical condition of the patient usually improved. Only the

"excessive action" of the wound was considered undesirable.

The sepsis often however became generalised and septicaemia, pyaemia, erysipelas, tetanus and gangrene were common. Admittedly results varied in different hands and in different sanitary conditions, but whenever the skin was broken the issue was precarious. Hospitals, especially the older and larger ones became the sites of epidemics of sepsis and were denounced by Sir James Young Simpson who called loudly for their repeated destruction and rebuilding and for the replacement of the corridor by the pavilion system. Out of approximately 2100 amputations in hospitals, 855 died, compared with 226 for a corresponding number in private practice. Fortunately Lister's application of Pasteur's discovery came in time to preserve the hospital system from the counsels of despair.

The methods of wound treatment varied hugely in pre-historian days. Antiseptics of course had been used by the Egyptians, but evidently only for embalming the dead and not on living subjects. Henshi de Mandeville (1260-1320) opposed the

salve-surgery of the Galenists and emphasized the value of cleanliness as originally taught by Hippocrates and reintroduced by Hugh and Teodorico Borgognoni (1205-1296). "Wounds," he said "dry much better before suppuration than after it Many more surgeons know how to cause suppuration than to heal a wound."

Paracelsus (1493-1541) too taught that nature - the natural balsam and not officious meddling healed wounds. The faith of Ambroise Paré (1510-1590) in *vis medicatrix naturae* is shown by his words "Je le pansay; Dieu le guarit." Nevertheless he employed a ointment or salve consisting of the "fat of puppy-dogs":

The value of cleanliness in the prevention of puerperal infection was advocated as early as 1773 by Charles White (1728-1813) of Manchester, but his teaching was later displaced by the doctrine that the cause of the disease was "atmospheric," "cosmic" or "telluric" conditions. In Boston in 1843 Oliver Wendell Holmes (1809-1894) advocated the washing of the hands in calcium chloride and the inadvisability of physicians attending midwifery cases after making autopsies.

According to Johnstone, much of the honour due to White has been given to the Hungarian physician, Ignatz Philipp Semmelweis (1818-1865). The latter, after the death of his colleague Kalletschka following a post-mortem-room wound, suspected that the higher incidence and mortality of puerperal fever among women attended by students compared with those attended by midwives was due to a cause connected with the post-mortem-room. His insistence on the use by the students of chlorinated lime in the washing of their hands reduced the mortality greatly. The work of Pasteur and Lister was however quite independent of this. Lister indeed, only learned of it in 1882 when Duka sent him a copy of his biography of Semmelweis. It is noteworthy that ignorance of the microbial origin of the fever made the work of White and Semmelweis, in part at least, empirical.

In spite of the good results obtained by scabbing by John Hunter (1728-1793) huge masses of dressings and ointments were often used in the dressing of wounds early in the nineteenth century in attempts to exclude the air, then thought

to be the cause of suppuration. Volkmann, however, prior to his adoption of Lister's method, used his "open method" which was eventually seen to give results no better than those produced by other methods of treatment. The dressing most frequently used consisted of lint soaked in water and covered with oiled silk. Some surgeons - forerunners of Carrel, - irrigated the wound with water. Valette immersed the wound in water containing creosote, ferric salts or tincture of benzoin. These and other substances now known to possess antiseptic properties, though used then, were not employed to their full advantage and gave poor results owing to ignorance as to the cause of sepsis.

The Work of Pasteur.

" Ces trois choses, la volonté, le travail, le succès, se partagent toute l'existence humaine. La volonté ouvre la porte aux carrières brillantes et heureuses; le travail les franchit, et une fois arrivé au terme du voyage, le succès vient couronner l'oeuvre."

Pasteur.

As set forth in the inscription on the arches of his tomb, Pasteur's work took the form of investigations into:—

1. Molecular dyssymmetry (1848).
2. Fermentation. (1857).
3. Spontaneous Generation (1862).
4. Diseases of Wine (1863).
5. Diseases of Silk Worms (1866).
6. Micro-organisms in Bees (1871).
7. Virulent Diseases (Anthrax and Chicken-Cholera) (1877)
8. Preventive Vaccinations (1880) especially hydrophobia. (1885).

Pasteur was essentially a chemist and in the first instance devoted his attention to molecular dyssymmetry. The earliest example of isomerism

was that of the two tartaric acids deposited from wine-lees and was observed but not explained by Kestner in 1820 and later by J. J. Berzelius and Gay Lussac. Subsequently, J. B. Biot and Mitscherlich independently noticed their difference to polarised light, the one turning the plane of the ray to the right and the other possessing no rotatory power. Pasteur found that the inactivity of the latter acid was due to its being a mixture, or more correctly a racemic compound of an equal number of molecules of the ordinary dextro-rotatory acid already known and a new third acid which was laevo-rotatory; the sodium-ammonium salts of the two constituent acids giving enantiomorphous crystals. The racemic acid was thus inactive by "external compensation" in contradistinction to the fourth isomer, - mesotartaric acid, - which is inactive by "internal compensation" and cannot be resolved by any known process into its active components.

Pasteur then attempted to resolve the racemic form by means other than by the manual separation of the enantiomorphous crystals of its salts. Combination of the inactive substance which is to be resolved with an optically active compound was a second method, and a third method was to

cause the solution of the inactive substance to ferment, by introducing certain low vegetable organisms such as yeast, mould or bacteria, one of the optically-active forms being usually more easily assimilated than the other. For instance, the ferment acts on the dextro-rotatory and not the laevo-rotatory forms of tartaric acid.

In this way Pasteur's attentions were directed from the purely physical aspect of molecular dissymmetry to a study of the whole process of fermentation and manufacture of wines.

Between 1856 and 1861, while working to help the Lille manufacturer Bigo, he added to the work of Schröder and Dusch by demonstrating that air, out of which the dust had been allowed to settle, did not cause putrefaction with organic matter. This was due to the presence in the air of the "animalcules" without which the world would become "encombré de cadavres". He drew the neck of the flask containing the boiled infusion out to a fine tube, and turning it downward, left the mouth open. Gravity prevented the suspended "animalcules" from ascending, and there was no current of air to carry them upwards

into the tube.

With regard to brewing he showed that fermentation with the concomitant production of carbon dioxide occurred only when the sugary liquid was in the presence of a definite organism; and that the acting organism was different and characteristic in each kind of fermentation. He too, discovered that the pellicle necessary in the making of vinegar from wine contained the *Mycoderma aceti* and thereby upset Liebig's mechanical theory of the process.

The vexed question of Spontaneous Generation remained unsettled for long, because even after very careful precautions as to the filtration or sedimentation of the air, fermentation occasionally occurred in his flasks. In 1860, he showed that this was due to the resistance of some of the organisms (- by virtue as he found later, of spore-formation, -) to the temperature of boiling-water especially when the solution was alkaline. All the organisms however were killed at a temperature of 110° to 112° C. - obtained by boiling under a pressure of one and a half

atmospheres. His controversy with Pouchet was probably due to the hay-infusion used by the latter being more difficult to sterilise than his own yeast infusion. It was not until 1862 that he gave forth the edict that "la génération spontanée est une chimère".

Pasteur also introduced the concepts of aerobic and anaerobiosis after his discovery of anaerobic organisms in butyric fermentation.

The practical results of all this work was the remedy for the "diseases" of wines, vinegar and beer by obtaining suitable organisms in pure growth for these different fermentative processes. The aging of wine too was prevented by his process of "Pasteurisation" - a system of partial heat-sterilisation at a temperature of 55° to 60° C which occasioned little or no alteration in the taste or bouquet of the vintage. (1863-1865)

Pasteur then turned his attention towards pathological research when he undertook, at the instance of the French Government, an investigation into the diseases of silk-worms which had been crippling the silkworm industry of France. After five years of arduous toil he eventually

managed to conquer the two diseases of pébrine and flâcherie.

"Thus Pasteur was gradually transformed from a chemist into a medicine man, particularly in his mode of attacking the problem of infectious diseases". He next studied anthrax. Pollender (1849) and later Davaine (1863) had already discovered the bacillus and the latter had shown that the virulence of the disease was proportional to the numbers of bacteria present. (1865). Klebs had proved that the etiological agent was stopped by a filter (1871) and Koch had cultivated the bacillus and demonstrated its relationship with the disease (1876-1877). Pasteur confirmed these results and later in 1880-1882 elaborated a method of immunising animals against anthrax.

The vibrio septique was discovered by Pasteur, Joubert and Chamberland in 1877. This anaerobic organism is probably identical with the *B. oedematis maligni* of Koch and Zeffky (1881) and almost certainly with the *Bacillus* of Ghon and Sachs and *Bacillus III* of Van Hibel. This was the first pathogenic anaerobic organism discovered.

In 1878-1879, Pasteur described the staphylo-

cocci^{pyogenes} of boils and the streptococci pyogenes of purpural sepsis under the titles of "microbes en amas de grains" and "microbes en chapelet-de grains" respectively. Some books however, give Ogston the credit of these discoveries.

Pasteur's work on artificial immunisation was initiated by his discovery that quondam-virulent cultures of the organism of chicken-cholera after the lapse of time changed so that on injection, they not only failed to produce the disease but acted as preventive vaccines against a subsequent dose of virulent homologous organisms. Pasteur then applied this to anthrax and found that the virulence of the *B. anthracis* could be attenuated by continued growth at a temperature other than the optimum. A culture grown at 42°C . for 24 days constituted his "premier vaccin" and was found to protect animals against subsequent inoculation with his "deuxième vaccin", - a similar culture except that having been grown at 42°C . for 12 days, it was more virulent than the "premier vaccin". Animals inoculated with these two vaccines and later with an ordinary virulent culture were found to have acquired an immunity.

lasting for varying periods. The technique of course, has been elaborated since Pasteur's time by workers such as Marchoux, Sclavo and Sobersheim, the two latter having evolved a serum suitable for the passive immunisation of human cases of anthrax.

Perhaps the best known of Pasteur's works however, is that on rabies and has revolutionised the old methods of treatment by cauterisation. Pasteur managed to produce three varieties of the virus; one of natural strength by passage through dogs; a second of attenuated virulence by passage through monkeys and a third of exalted virulence by passage through rabbits. The virus in the spinal cords of the rabbits, he found, could be attenuated by drying the cords in air over caustic potash, "the diminution of virulence being proportional to the length of time during which the cords were kept." He therefore obtained a series of vaccines of varying strengths and was able in view of the comparatively long incubation period in man, to vaccinate anyone bitten by a rabid dog before the gravest manifestations of the disease occurred. His technique with certain modifications is used to this day in all cases bitten by dogs

proved to have rabies by the finding of Negri bodies in the cells of the hippocampus.

The Influence of the Work of Pasteur on Medicine.

"There is no greater charm for the investigator than to make new discoveries; but his pleasure is heightened when he sees that they have a direct application to practical life."

These are Pasteur's own words.

"As the prevalence of the conceptions signified and inspired by the word 'phlogiston' kept alive ontological notions of disease, so the dissipation of vitalistic conceptions in the field of physics prepared men's minds in pathology for the new views opened by the discoveries of Pasteur."

The Influence of the Work of Pasteur on Medicine has been two-fold. Firstly the work actually done by him on pyogenic cocci, anthrax, chicken-cholera and especially on rabies has conferred great benefit on mankind and animals. Secondly an indirect but by far more important influence is that which has resulted in the application by other workers of the methods he used in the investigation, prevention and treatment of disease.

Since Pasteur's time bacteriology has made huge advances. In 1877 Weigert and Ehrlich used aniline dyes for staining micro-organisms, and in

1880 Laveran discovered the cause of malaria. In 1881 Koch propounded his postulates and his "plate method" for the isolation of pure cultures and in 1882 announced his discovery of the *B. tuberculosis*. Later Loeffler and Roux investigated *B. diphtheriae* and its toxins and Kitasato, *B. tetani*. In producing active immunity by the attenuated virus, Duguid and J. S. Burdon-Sanderson and W. S. Greenfield in Great Britain and Pasteur, Toussaint and Chauveau in France were pioneers. Their researches stimulated the immunological work of Behring and later Bordet, Ehrlich and Metchnikoff. The production of active artificial immunity by the introduction of heat-killed cultures (i.e. vaccines) in successive and increasing doses is applied, firstly in the prophylaxis of infections such as typhoid and paratyphoid fever; secondly in therapeutic immunisation such as in the treatment of chronic infections and thirdly in the preparation of anti-bacterial sera in animals. Active immunity is also produced artificially by the introduction of toxins in successive and increasing doses as exemplified in the preparation of diphtheria and tetanus antitoxins. (Mackie and McCarty). A temporary passive artificial immunity by intro-

ducing into the body of a non-immune animal the blood serum of an actively-immunised animal is brought about daily in the treatment of diphtheria.

Immunological methods are responsible also for the new aids to diagnosis such as the Widal, Weil-Felix, Wassermann and Sachs-Georgi reactions.

As the fundamental importance of the early discoveries by Pasteur and others has become apparent, the number of research-workers has steadily increased. Besides bacteriologists, these workers include chemists who have devoted attention to the products of bacterial growth and have studied the action of chemicals on micro-organisms.

Bacteriology has "long passed out of that phase in its history when it presented to the world those dramatic discoveries that established the germ-theory of infective disease, and defined the causal agents of many human and animal scourges."

The results obtained by the world war demonstrated strikingly what can be accomplished even in unfavourable conditions, in preventing diseases that previously had been scourges. Small-pox, enteric fever and cholera were practically eliminated by prophylactic vaccination,

and plague by rat extermination. Typhus fever and the new disease trench fever were lessened by destruction of lice, and malaria by drainage and the administration of quinine. Tetanus was controlled by prophylactic administration of antiserum and gas-gangrene lessened by suitable antiseptics and antisera.

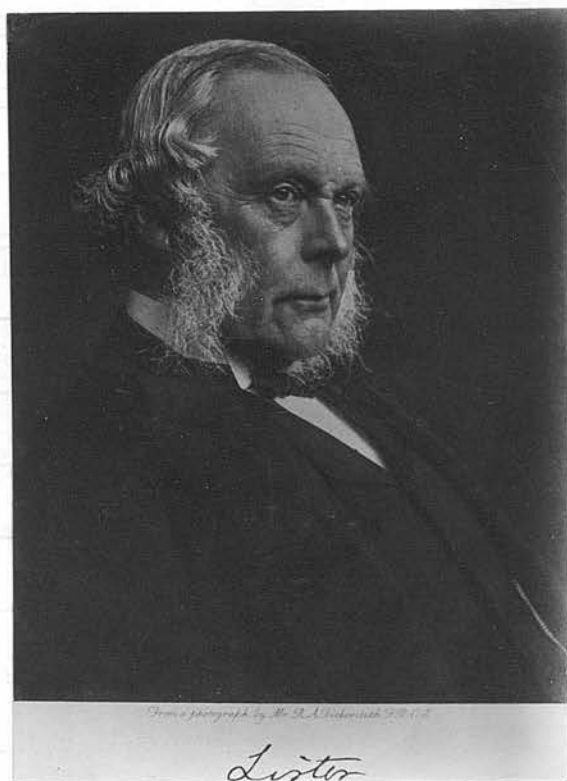
As yet only the frontiers have been passed. Little, for instance, is known of leprosy and the ideas on the etiology of influenza are by no means conclusive.

Pasteur's views of Spontaneous Generation are those generally held today for there is no evidence in present conditions of any known organism having originated except from a previous similar body. No one as yet can say when or how life began. It is conceivable that spontaneous generation occurs under unknown conditions but such is mere speculation.

The process called "Pasteurisation" is now applied to many kinds of perishable foods and is of great benefit in the nutrition of infants and in the sterilisation of milk with the least possible change in its chemical constituents.

In the evolution of modern Pharmacology, Pasteur's work on isomerism has played an important

part. According to Garrison his results undoubtedly led to the work of van't Hoff and Le Bell on stereo-chemistry and chemistry in space. Many pharmacological substances are isomeric, - the isomers possessing totally different pharmacological actions. For instance adrenaline is laevo-rotatory to polarised light, the dextro-rotatory isomer having only about a twelfth of the activity of the natural substance. (Cushny). Atropine is racemic hyoscyamine i.e. consisting of equal parts of laevo-hyoscyamine and dextro-hyoscyamine. Since the latter is nearly inactive, the action of atropine is practically that of its laevo-hyoscyamine half. (Cushny). The nearly-related hyoscyne has also two isomers of which, as Moir has shown, the laevo-rotatory form is active and the dextro-rotatory form practically inert. This is of great importance in the production of twilight sleep. Cinchonine and cinchonidine are also isomers and quinine and quinidine further examples. The recent advances in specific chemo-therapy have been rendered possible by discoveries inaugurated by Pasteur's work and are exemplified in Ehrlich's salvarsan and neosalvarsan for the treatment of syphilis, in atoxyl for trypanosomiasis and in trypanamide for trypanosomiasis and neurosyphilis. Silver Salvarsan and sulpharsamol, mercury and bismuth are all used for syphilis. "Bayer 205" is a powerful trypanocide. Antimony salts are beneficial in American leishmaniasis, sleeping-sickness and frambosia. The use of quinine in malaria and emetine in entamoebic dysentery are further examples.



The Influence of the Work of Pasteur on Surgery.

The Influence of the Work of Pasteur on Surgery is mainly due to the application of his results by Lister, and can be appreciated only with difficulty, by those who have not lived in pre-antiseptic days.

As early as 1851 Lister had suspected that sepsis was due to putrefaction of the discharges and not to the action of the air as then generally supposed. He had been impressed with the relative absence of "hospital diseases" in private practice and by the absence of sepsis in spite of the presence of air in a case of generalised surgical emphysema following fractures of the ribs. Nevertheless he could find no clue to the problem until, at the instance of Thomas Anderson, then Professor of Chemistry in Glasgow, he read Pasteur's publications on fermentation.

Pasteur himself does not appear to have recognised the potentialities of his work, although in his "Recherches sur la Putréfaction" published in 1863 he wrote that men had hoped for long to gain a knowledge of diseases from researches into the subject of putrefaction.

François Jules-Lemaire, a pharmaceutical chemist in Paris as early as 1860 used carbolic acid to

inhibit the growth of bacteria in wounds, but evidently did not try to prevent their entrance. Spencer Wells, on the other hand laid stress on the importance of cleanliness. Lister alone, however saw Pasteur's work in the light of a first principle. In Pasteur's own words, "In the fields of observation, chance only favours the mind that is prepared."

If sepsis was simply putrefaction of the discharges due to organisms, thought Lister, could not a search be made for some material to destroy these bacteria in place of the misguided and unsuccessful attempts to exclude the air? The germs must not be allowed to enter the wound, or were they already there, then they must be destroyed or at least their growth arrested with the least possible damage to the tissues. Were these aims attained, the tissues would probably have vitality sufficient to cause healing.

Filtration of the air and heat sterilisation as employed by Pasteur were obviously impracticable for surgical purposes, and recourse was had to antiseptics. German creosote in which the active agent was carbolic acid had been newly introduced for deodourising sewage at Carlisle, and Lister

in 1865 employed it as a dressing for compound fractures - eventually with unprecedentedly good results.

Admittedly carbolic acid had been applied to wounds as a deodorant but until Lister applied Pasteur's results, its use was empirical.

Gradually Lister improved his technique by the use of oiled silk to prevent the skin round the wound being injured by the carbolic acid and by the use of black-tin, paraffin-wax, shellac and gutta-percha to prevent the evaporation of the carbolic acid.

He then applied his method to cases of acute and later of chronic cold abscess - using for these his "anti-septic putty", (a mixture of whiting and carbolic acid in boiled linseed oil).

The technique of operations then received attention and so successful were the results on using the famous "one in twenty carbolic acid" that Lister dared to render simple injuries compound - a procedure requiring in these days great courage but eventually justified by the results. Yet the want of suitable means for the arrest of haemorrhage marred the success of operations. The ligatures which had long replaced Ambroise Paré's method by boiling oil, not being sterile, caused sepsis and often secondary haemorrhage. Indeed their ends were left long to act as a drain

and they were eventually extruded by suppuration.

The introduction by Lister of a strong, sterile, absorbable ligature is one of the greatest triumphs in the application of Pasteur's work.

The irritating, poisonous and volatile properties of carbolic acid stimulated search for a sufficiently potent antiseptic not possessing these drawbacks. Since then innumerable substances have been tested. The great difficulty has always been to obtain a substance with high parasitotrophic and low organotrophic action. The gauze containing the double cyanide of mercury and zinc was introduced by Lister after years of laborious experimentation and to this day remains one of the most perfect of dressings.

Lister realised that micro-organisms could reach wounds firstly by the fingers of the surgeon or his assistants, the instruments or sponges or the skin of the patient and secondly by the air. The copious use of the "one in twenty carbolic solution" minimised the first danger and the different forms of the far-famed "spray" were introduced to combat the possibility of infection from the air or more strictly from the living dust particles in the air. It was eventually found however, that the spray was unnecessary and Lister

himself abandoned its use seven years after Brauns of Tübingen had made the utterance "Fort mit dem Spray!"

As is well known, the new antiseptic method, although supported by surgeons such as James Syme and Timothy Holmes was not by any means universally accepted for many a year after its introduction. The older members of the profession, — those bound by tradition and dogma, — especially opposed it. Simpson in particular obfuscated the minds of many by confusing the introduction of the new system with the introduction of the use of carbolic acid. A large proportion of those who used the method, did so without appreciating the reasons for the details and their results were correspondingly poor. Unfortunately, according to Godlee, others were imbued with the ulterior motive of belittling the new doctrine. That the method made little headway in Britain and especially in London till Lister's own students obtained charge of wards has been freely condemned. Many surgeons ascribed the improvement in their mortality statistics not to the use of antiseptics but to the improvements in the nursing and hospital systems which took

place about this time, overlooking the good results in private practice and in Glasgow and Edinburgh Infirmaries before the changes in the nursing and hospital regime.

Godlee has shown that the common belief that the continent accepted the new doctrine more readily than Britain did is only partially true. Admittedly its value was appreciated at an early date in Germany, Switzerland and Scandinavia and undoubtedly these countries influenced the rest of the world. That the new theory appealed more to the German than to the British mind was probably due to the scientific education obtained at German Universities in place of the British system of apprenticeship and "walking the hospitals." Thiersch of Leipzig and Richard von Volkmann were early devotees of the new principle - the latter earning the appellation of Lister's "travestier Jünger," and Stromeyer of Hanover, von Müssbaum of Munich, von Bardeleben, A. W. Schultze and Ernst von Bergmann, the last three of Berlin all adopted it. Thamayn translated Lister's papers into German in 1874 and Lucas-Championnière made, - in French, - the first complete account of antiseptic surgery.

Modern Surgery dates from the introduction of antiseptics. The avoidance of sepsis has rendered possible methods of treatment undreamt of before the discovery and to this day further advances are continually being made. Many patients too, are now operated upon simply for aesthetic purposes. No longer is Surgery a desperate remedy for a desperate disease.

Orthopaedic surgery has been revolutionised. In cases of compound fracture, conservative surgery is the general rule in place of amputation. Deformities, - whether the result of injury, paralysis, rickets or congenital defects, - which previously would have been left alone are now constantly dealt with. Recent, malunited or ununited fractures are boldly cut down on; joints are freely opened, and bones, muscles and even nerves are transplanted often with wonderful results in the way of increased beauty and usefulness. "Since we are as yet entirely without any key to the control of congenital deformities such as club-foot, or the prevention or cure of the infection which produces infantile paralysis, and since we shall always have accidents with us, it is evident that orthopaedic surgery has an assured future."

The scope and safety of modern surgery and the vitality of the body to repair injury provided it is not asked to fight infection as well are all illustrated in present-day abdominal operations such as those on the abdominal wall, the alimentary tract, the gall-bladder and bile-ducts, the spleen and the uro-genital organs. Today the abdomen may be opened without the dread of causing peritonitis. When the latter does occur, it is nearly always due to organisms introduced not from without, but from within as in perforation of a part of the alimentary tract, and in such cases, the surgeon intervenes to arrest, not to cause the infection. So great is the safety, that it was probably at first abused by the performance of an excessive number of "exploratory laparotomies". Operative gynaecology in which Thomas Keith was a pioneer, and the modern operation of Caesarean section practically owe their existence to antisepsis. It is difficult to explain why sepsis has not been as greatly reduced in midwifery as in general surgery.

In the thorax, thoracoplasty (collapse-therapy or "Entspannung"); operations for empyema and pneumotomy for pulmonary gangrene and abscess

are now recognised procedures. Operations on the heart are occasionally performed, such as suture of the heart, the removal of foreign bodies, the relief of mitral stenosis and cardiomyopathy.

The freedom enjoyed by the surgeon thanks to antiseptics is also illustrated well in the modern operations on the skull and brain, such as trephining, decompression, Wagner's operation, operations for the arrest of intracranial haemorrhage, for mastoid disease and intracranial suppuration, for hydrocephalus, for lesions of the pituitary body and for division of the sensory root of the Gasserian ganglion and in the surgery of the jaws, tongue, oesophagus, of the ear, nose and throat; and of the thyroid gland, and modern dentistry and skin-grafting. Neoplasms upon which no surgeon in pre-antiseptic times would have dared to operate are now removed. We can only hope that this need for surgery will ere long be obviated by a means of prevention of cancer.

The mortality from major operations in hospitals was found by Sir James Young Simpson to be 41%. Now, thanks to antiseptic surgery as the outcome of Pasteur's work, it is, according to Sir William Watson Cheyne, between 3 and 4%; and in comparing these figures, it must be

remembered that the surgeon of today performs operations more dangerous by far to life than his predecessor of fifty years ago would have dared to attempt.

In the treatment of war wounds, the antiseptic system has saved innumerable lives. In the Franco-German, the Boer, the Russo-Japanese and the World Wars, the value of attention to wounds has been emphasized by results. In the early stages of the Great War few surgeons were familiar with the grossly septic wounds, for which to find a parallel it would have been necessary to go back more than half a century. The orthodox antiseptic and aseptic methods were found sadly wanting. Sir Almonroth Wright's "Hyper-tonic Treatment" was replaced by the Irrigation Method of Carrel and Dehelly and the Edinburgh School is justly proud of the Eupad and Eusol introduced by the Dean and his collaborators.

Some have attempted to draw a distinction between the "antiseptic" and the more recent "aseptic" surgery, but Miles has pointed out that this distinction is "specious but fallacious" for the disciples of the "aseptic" school attain their aims only by the use of "antiseptic" measures.

Conclusion.

The application by Pasteur of the exact methods of chemical and physical research to the elucidation of the complex problems of disease enabled him to bring under scientific laws phenomena which had so far baffled human endeavour.

He had the good fortune and just reward of living to see his results applied to the everlasting benefit of men and animals. The application of his methods has already worked wonders in both Medicine and Surgery and "bids fair to render possible the preventive treatment of all infectious diseases." The work on immunisation against diphtheria facilitated by the Schick reaction and the researches of the Dicks and Dochez on scarlet fever give indications of what the future may bring in the way of bacteriological development.

Although Pasteur was not a medical man, his name will descend to posterity as that of one of the greatest figures in the annals of medical science and indeed of science in general. Not since the discovery of the

law of gravity has the scientific world been impressed so profoundly as by the revelation of the part played by micro-organisms in nature and probably never has any discovery been fraught with such momentous issues in so many spheres as that made by Pasteur.

Bibliography.

1. Adams, W. A Sketch of the Principles and Practice of Subcutaneous Surgery. London, 1857.
2. Allbutt, J. C. "Medicine - Modern Progress," in the Encyclopaedia Britannica, 12 ed. New York, 1925.
3. Allbutt, J. C. "Lister," in the Encyclopaedia Britannica, 12 ed. New York, 1925.
4. Allbutt, J. C. "Semmelweis" in the Encyclopaedia Britannica, 12 ed. New York, 1925.
5. Bennet, J. Hughes. The Atmospheric Germ Theory. Edin. Med. Journ. 1868. vol. xiii.
6. Bowlby, A. The Bradshaw Lecture - On Wounds in War. Brit. Med. Journ. 1915. vol. ii. p 913.
7. Broca, A. The After-Effects of Wounds of the Bones and Joints. Trans. by J. F. White. & ed. by R. C. Elmshie. London 1918.
8. v. Brauns, P. Wound Treatment in War. Beiträge z. Klin. Chirurg., Bd. xcvi. Heft. 2. 6^{te} War Surgery Nummer. (Synopsis in Edin. Med. Journ. March 1916. p. 231).
9. Cameron, H. C. Reminiscences of Lister and of his Work in the Wards of the Glasgow Royal Infirmary, 1860-1869. Glasgow. 1927.
10. Cameron, H. C. On the Evolution of Wound Treatment during the last forty years. Glasgow. 1907.

11. Carrel, A. et Dehelly, G. Le traitement des plaies infectées. Trans. by Capt. H. Child. London, 1917.
12. Cheyne, W. Watson, Lister and his Achievement. London, 1925.
13. Cheyne, W. Watson, Antiseptic Surgery; its Principles, Practice, History and Results. London, 1882.
14. Cheyne, W. Watson, Report on a study of certain of the conditions of infection. Brit. Med. Journ. 1886. vol. ii. p. 197.
15. Cheyne, W. Watson, Suppuration and Septic Diseases. Edin. 1889.
16. Cheyne, W. Watson. Manual of the Antiseptic Treatment of Wounds. London. 1885.
17. Chick H. and Martin, C. J. The Principles involved in the Standardisation of Disinfectants and the Influence of organic Matter upon Germicidal Value. Journ. of Hygiene. vol. 8. 1908. p. 654.
18. Comrie, J. D. "Medical School to 1870" in Edinburgh's place in Scientific Progress. (Brit. Assoc. Edin. Meeting. 1921). Edin. 1921.
19. Creighton, C. "Surgery, (History)." in Encyclopaedia Britannica. 12th. ed. New York, 1925.
20. Cumston, C. G. An Introduction to the History of Medicine, from the time of the Pharaohs to the end of the XVIIIth. century. London, 1926.
21. Dakin, H. D. On the Use of Certain Antiseptic

- Substances in the Treatment of Infected Wounds.
 Brit. Med. Journ. 1915. vol. ii. p. 318.
22. Dakin, H. D.; Cohen, J. B., Daufresne, M. and Kenyon, J.
 The Antiseptic Action of Substances of the
 Chloramine Group. (Report to Med. Research Committee)
 Proc. Roy. Soc. (1916). B. vol. 89. p. 232.
23. Descours, L. Pasteur and his Work. Trans. fr. French
 by A. F. and B. H. Wed. London, 1922.
24. Dunham, E. K. and Dakin, H. D. Observations on
 Chloramines as Nasal Antiseptics. (Report to Med.
 Research Committee). Brit. Med. Journ. 1917. vol. i. p. 865.
25. Erichsen, J. E. On Hospitalism and the Causes of Death
 after Operations. London. 1874.
26. Erichsen, J. E. The Science and Art of Surgery. 15th ed.
 London, 1853.
27. Erichsen, J. E. The Science and Art of Surgery, 10th ed.
 rev. and ed. by M. Beck and R. Johnson. 2 vols. London. 1895.
28. Frankland, P. and M^{rs} G. C. Pasteur. London 1898.
29. Frankland, P. and M^{rs} G. C. Micro-organisms in water -
 their significance, identification and removal etc. London, 1894.
30. Fraser, J. The Value of Hypochlorous acid in the Treatment
 of Cases of Gas Gangrene. (Report to Med. Research
 Committee). Brit. Med. Journ. - 1915 vol. ii. p. 525.
31. Fraser, J. and Bates H. J. The Treatment of Acute Toxicemia

- secondary to Gas Gangrene by the Intravenous Injection of a Solution of Hypochlorous Acid. (Report to Med. Research Committee). Brit. Med. Journ. 1916. vol. i. p. 83.
32. Fraser, J. and Bates, H. J. The Surgical and Antiseptic Values of Hypochlorous Acid (Eusol). Edin. Med. Journ. March 1916. new Series. vol. xvi p. 172.
33. Garrison, F. H. Introduction to the History of Medicine. 3rd. ed. Philadelphia, 1921.
34. Godlee, R. J. Lord Lister. London. 3rd. ed. 1924.
35. Gorton, D. A. The History of Medicine. 2 vols. New York, 1910.
36. Hamilton, D. J. and Muir, Rhd. "Pathology." in the Encyclopaedia Britannica, 12th. ed. New York, 1925.
37. Holmes, J. and Hultke, J. W. A System of Surgery. 3 vols. 3rd. ed. London. 1883.
38. Hunter, J. The Works of, ed. by J. F. Palmer. 4 vols London 1835-1837.
39. Johnstone, R. W. "Puerperal Infection,"— Chap. xxxv in Text-Book of Midwifery. 4th. ed. London. 1923.
40. Keith, A. Menders of the Married. London. 1919.
41. Keith, J. Ovariectomy before and after Antiseptics. Brit. Med. Journ. 1878. vol. ii.
42. Keogh, A. General Introduction to Surgical Series of the Military Med. Manuals, ed. by Director General Sir A. Keogh and Lt. Gen. J. H. J. C. Goodwin. London, 1917.
43. Koch, R. Investigations into the Etiology of Traumatic

Infective Diseases. Trans. by W.W. Cheyne. New
Sydenham Soc. London, 1880.

44. Lemair, J. De l'acide phénique, de son action sur
les végétaux, les animaux, les ferments, les
venins, les virus, les miasmes et de ses applic-
-ations à l'industrie, à l'hygiène, aux sciences
anatomiques et à la thérapeutique. 2^{me} édit. Paris, 1865.
45. Lister, J. Collected Papers. — Collected by Sir Hector
Cameron, Sir W. Watson Cheyne, Sir Rickman J.
Godlee, Dr C. J. Martin and Dr Dawson Williams. 2 vols.
Oxford, 1909.
46. Lister, R. Practical Surgery. 4th ed. London 1846.
47. Lucas, C.E. On the Principles of Inflammation and Fever.
London, 1822.
48. Mac Cormac, H. The Nature, Treatment and Prevention
of Continued Fever. London. 1835.
49. Miles, A. Edinburgh School of Surgery before Lister. Edin. 1918.
50. Miles, A. "Surgery", in Edinburgh's place in Scientific
Progress. (Brit. Assoc. Edin. Meeting, 1921). Edin. 1921.
51. Miles, A. Case of Lacerated Wound of the Thigh treated by
Eusol. Edin. Med. Journ. Feb. 1916. new Series. vol XVI. p. 128.
52. Miles, A. Some Observations on the Use of Hypochlorous
Acid (Eusol) in Gunshot Wounds. Edin. Med.
Journ. Feb. 1916. new Series. vol XVI. p. 100.

53. Moynihan, B. Hunter's Ideal and Lister's Practice.
Hunterian Oration 1927. Brit. Med. Journ. 1927. vol. i. p. 313.
54. Muir, Robt. "Bacteriology. II Pathological Importance" in
the Encyclopaedia Britannica. 12th ed. New York. 1925.
55. Muir, Robt. and Ritchie, J. Manual of Bacteriology. 7th ed.
London. 1921.
56. Owen, E. "Surgery, (Modern Practice)." in the Encyclopaedia
Britannica, 12th ed. New York. 1925.
57. Paget, J. Clinical Lecture on the Treatment of Fractures
of the Leg. Lancet. 1869. vol. i. p. 317.
58. Paget, J. Clinical Lectures and Essays ed. by H. Marsh, London, 1875.
59. Paget, S. Memoirs and Letters of Sir J. Paget. London. 1901.
60. Paget, S. Pasteur and after Pasteur. London. 1914.
61. Park, W.H.; Williams, A.W. and Krumwiede, C. Pathogenic
Micro-organisms. 8th ed. London. 1925.
62. Parker, G. The Early History of Surgery in Great Britain,
its organisation and development. London. 1925.
63. Pasteur, L. Études sur la bière, ses maladies, causes
qui les provoquent, procédé pour la rendre
inaltérable, avec une théorie nouvelle de la
fermentation. Paris. 1876. Trans. with notes by
F. Faulkner and D. C. Robb, as Studies on Ferment-
ation, - the Diseases of Beer, their Causes and means of
preventing them. London, 1879.

64. Paterson, R. Memorials of the life of James Syne. Edin. 1874.
65. Payne, J. F. "Medicine - History." in the Encyclopaedia Britannica, 12th ed. New York, 1925.
66. Rettie, J. Antiseptics. Journ. of Soc. of Chem. Indust. 1918. vol. xxxvii. p. 23. 6.
67. Roscoe, H. E. "Pasteur." in the Encyclopaedia Britannica, 12th ed. New York, 1925.
68. Salisbury, C. W. Modern Surgery and its Making, - A Tribute to Listerism. London. 1917.
69. Schäfer, E. Presidential Address to Brit. Assoc.: Dundee. 1912.
70. Sherman, The Value of Hypochlorite Solutions for the Treatment of Wounds. (Roy. Soc. Med.). Brit. Med. Journ. 1916. vol. ii. p. 621.
71. Semmelweis, J. P. Die Aetiologie, der Begriff und die Prophylaxis des Kindbettfiebers. Pest, etc: 1861.
72. Semmelweis, J. P. Semmelweis' gesammelte Werke: horg. und zum Theil aus dem ungarischen übersetzt von Tiborius von Györy, Jena, 1905.
73. Simpson, J. G. The Works of Sir. J. G. Simpson, Bart., 3 vols. ed. by J. W. Black, W. G. Simpson and A. R. Simpson. Edin. 1871-1872.
74. Smith, J. L.; Ritchie, J.; and Rettie, J. On a Case of Septic-æmia treated by Intravenous Injection of Eusol. Brit. Med. Journ. 1915. vol. ii. p. 716.

75. Smith, J. L.; Drennan, A. M.; Rettie, J. and Campbell, W.
Experimental Observations on the Antiseptic Action
of Hypochlorous Acid and its Application to
Wound Treatment. Brit. Med. Journ. 1915. vol. ii. p. 129.
76. Smith, J. L.; Ritchie, J. and Rettie, J. On a Convenient
Method of Preparing Eusol. Brit. Med. Journ. 1917. vol. ii.
77. Smith, J. L.; Ritchie, J. and Rettie, J. On the Treatment of
Common Infections in Children by Intravenous
Injection of Eusol. (Report to Med. Research Committee).
Edin. Med. Journ. Sept. 1917. p. 143.
78. Tait, R. Lawson. The Antiseptic Theory tested by the
Statistics of one hundred Cases of Successful
Ovariectomy. Medico-Chirg. Trans. 1880. vol. Lxiii. p. 161.
79. Tait, R. Lawson. Recent Advances in Abdominal
Surgery. Internat. Med. Congress. London, 1881. vol. ii. p. 228.
80. Syndall, J. Essays on the Floating Matter in the Air in
relation to Putrefaction and Infection. London - 1881.
81. Vallery-Radot, R. Oeuvres de Pasteur. Trans. as life
of Pasteur by M^r R. L. Deonskire. 2 vols. 1901. (reprint
1 vol. 1920). London.
82. Vallery-Radot, R. Louis Pasteur, his life and labours,
by his son-in-law (R. V-R). Trans. by Lady Claud
Hamilton - London, 1885.
83. Volkmann, R. Beiträge zur Chirurgie, anschliessend



an einen Bericht über die Thätigkeit der
Chirurgischen Universitäts-Klinik zu Halle, im
Jahre 1873. Leipzig, 1875.

84. Ward, H. M. and Blackman, V. H. "Bacteriology I The
Study of Bacteria" in Encyclopaedia Britannica,
12th ed. New York. 1925.
85. Waterhouse, H. F.; Harmer, W. D. and Marshall, C. J. Notes
from the Anglo-Russian Hospitals. Brit. Med.
Journ. 1917. vol. ii. p. 441.
86. Wells, J. Spencer. Some Causes of Excessive Mortality
after Surgical Operations. Brit. Med. Journ. 1864.
vol. ii. p. 384.
87. Wise, J. A. A Review of the History of Medicine. 2 vols.
London, 1867.
88. Wrench, G. J. Lord Lister - his life and Work. London, 1913.
89. Wright, A. An Address on Wound Infections. Brit. Med.
Journ. 1915. vol. i. p. 721.

Also: -

90. Obituary Notice of Lord Lister. Brit. Med. Journ. 1912. vol. i. p. 397.
91. Obituary Notice of Lord Lister. Lancet. 1912. vol. i. p. 465.
92. Lister and the Lister Ward in the Royal Infirmary of
Glasgow - a Centenary Contribution. Glasgow. 1927.
93. Lister Centenary Number of Brit. Med. Journ. 1927. vol. i. p. 653.
94. Clinical Report on the Applications of Eusol. (Report to

Med. Research (nttee). *Lancet*, 1916. vol. i. p. 300 and p. 356.

and.

95. Cushny, A. R. *A Text-Book of Pharmacology and Therapeutics*. 7th Ed. London, 1918.
96. Mackie, J. J. *The Present-Position of Medical Bacteriology*. *Brit. Med. Journ.* 1923. vol. ii. p. 1241.
97. Mackie, J. J. and McCartney, J. E. *An Introduction to Practical Bacteriology*. Edin. 1925.
98. Moir, J. C. *An Investigation of the Clinical Effects of Laevo-Rotatory and Dextro-Rotatory Hyoscine*. Edin. *Med. Journ.* Feb. & March, 1925. New Series. Vol. XXXII, Nos. 2 & 3.
-