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MEN AND BOOKS

A Historical Survey of Disease Concepts

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FOR several thousand years man has directed his philosophical and scientific energies towards an understanding of the universe, himself and his diseases. Although he has gained some comprehension of the universe and himself, science has been much more successful in ferreting out the nature and causes of disease. The story of the various concepts of disease which have been developed throughout human history is a fascinating one. Its study provides an insight into the development of the human intellect.

Man's approach to the problem of disease has evolved through five major stages: (1) demoniacal, (2) humoral, (3) astrological, (4) observational and (5) experimental. The demoniacal theories were most prominent in the ancient world, the humoral in Classical Greece and the Middle Ages, the astrological in the 15th and 16th centuries, the observational in the 17th, 18th and 19th centuries, and the experimental in the 20th century. However, there has been considerable overlapping, with the humoral concept of disease persisting into the 19th century and the experimental approach beginning in the 16th century.

DEMONS

The history of disease concepts probably goes back to the beginnings of conscious thought. Primeval man looked about and saw many bewildering phenomena such as the movements of the sun and moon, and the changing of seasons. What could be simpler to the primitive mind than to attribute these activities to beings similar to himself but far more powerful? Primitive man also observed frightening and occasionally harmful phenomena such as comets, storms and floods. Surely these could be caused only by beings who were also powerful but who were obviously much more malevolent. At this stage of human development it was only natural to believe that the terrifying signs and symptoms of disease were caused by angry gods and demons.[1]

As is true today, the treatment of disease is only as good as is the basic understanding of disease. Thus primitive man treated disease by driving demons out of the afflicted body.[2] The patient was often tortured to obtain a cure. Even today some primitive South American Indians apply stinging ants to the skin of patients. Attempts were also made to transfer the disease to other persons or objects. Thus the medicine man would make a model of the patient in clay. This image would then be rubbed against the patient and buried in the road. The first person to step over the effigy would receive the disease, and the original patient would recover. There is one type of demonological treatment which may have been of some use in cases of increased intracranial pressure. Skulls of patients with mental aberrations were trephined, presumably to let out the demons.[3]

One result of the demoniacal concept of disease is the concept of a sick or dead person as a frightening and dangerous individual who should be scrupulously avoided, if not maligned.[4] Primitive man developed many taboos related to the sick and the dead. This attitude has persisted through the centuries and exists even in our own era, although partly overcome by the development of knowledge and humanitarian ideals.

HUMOURS

The first glimmerings of an attempt to explain disease rationally began at the same time as attempts to develop reasonable philosophical and physical concepts.[5] The ancient Greeks believed that the world and universe were composed of four basic forces—earth, fire, water and air. Similarly, Hippocrates proposed that there were four humours or fluids in the body—blood, phlegm, black bile and yellow bile.[1] Depending on the predominating humour, a man's temperament was either sanguine, phlegmatic, melancholic or choleric. This concept of four humours was developed into a system of disease causation by Galen. Abnormal interactions between the humours were responsible for the various signs and symptoms.

Although early physicians such as Hippocrates and Galen had little knowledge of organic disease, they were excellent clinical observers.[6] Accurate accounts of the symptomatology of some diseases such as malaria and cellulitis have come down to us in their writings. Galen was also familiar with cholera, malaria, emphysema and consumption. But only with the advent of human dissection could the underlying disease changes be studied. In ancient Greece and Rome there was definite opposition to dissection of the dead, although the mangling of living prisoners and slaves by soldiers and animals was encouraged.[7]

During this period of time, only in Alexandria were postmortem examinations performed. The most illustrious name in this school is that of

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Erasistratus.[8] Although he believed that disease was due to an excess of blood, the few of his works available to us include some clinical pathological correlations, such as the association of plethora of the liver with dropsy of the abdomen. Erasistratus was so far ahead of his time that his basic approach to disease causation was overwhelmed by what has been called the Empirical School, which taught that "The important question is not what causes disease, but what dispels it. Diseases are not cured by talk, but by drugs." Treatment was based partly on trial and error and partly on the humoral theory. Thus blood letting, to remove excess humours, became the standard treatment for most diseases until the 20th century.

The influence of Galen has been looked upon as detrimental to the advancement of science during the Dark Ages.[9] His influential works, which were based only on theory and animal dissection, were regarded as absolute authority on anything medical until the renaissance of human curiosity. However, his ideas were actually ahead of his own time, and he can hardly be blamed for the preservation of his works by Arabic translators after the fall of Rome and then in Latin during the Middle Ages. It is only unfortunate for medicine that during this period of history human mentality favoured adherence to absolute authorities.

The humoral concept of disease causation held sway for many centuries, with many adherents even as late as the 19th century. The great Viennese pathologist, Carl von Rokitansky, who performed over 30,000 autopsies, based the first edition of his "Textbook of Pathologic Anatomy", published in 1855, on the humoral theory. Only after incisive criticism by Virchow did he drop the humoral concept in further editions.[10] However, long before this the concept of the four humours was weakened by study of astrology and the dead.

ASTROLOGY

The heavens have long fascinated man, and it is not surprising that during the Middle Ages diseases were attributed to the movements of heavenly bodies. It was widely accepted by physicians that the position of the stars governed health, sickness and death. Epidemics were attributed to such phenomena as comets. The time and type of treatment were governed by the position of the sun and the change of seasons. Physicians of the Middle Ages carried booklets with astrologic data and illustrations of the Zodiac Man, in the same manner that many of us today might carry tables of normal values for laboratory tests.[11] Only after Copernicus demonstrated that heavenly bodies follow definite laws of movement, was the belief that the stars govern our lives dispelled from enlightened minds. However, horoscopes are still with us and published daily in most of our newspapers.

OBSERVATION

A true understanding of disease could come only with the knowledge that symptoms are produced by diseased organs. And this could only follow familiarity with human autopsies. There are very few records of autopsies performed before the 15th century. The earliest is in the form of a fresco on the wall of a Roman catacomb, executed in the 4th century. It is considered to represent teaching by human dissection. There is another early illustration of a dissection scene on record, drawn in the 14th century.[8] At this time autopsies were only resorted to in cases of national calamity or suspected murder. In 1348 Pope Clement VI, during a plague epidemic in Italy, ordered that postmortem examinations be carried out in order to determine the cause. An occasional postmortem examination was performed in cases of suspected poisoning. However, before the 15th century, dissection of the dead was an anomalous occurrence.[12]

During the 15th, 16th and 17th centuries the performance of autopsies on private patients for the purposes of confirming or correcting clinical diagnoses gradually gained acceptance. One of the first records is a book written by Antonio Benivieni, an Italian physician, and published posthumously by his brother in 1504.[13] The prophetic name of this work is "The Hidden Causes of Disease". It is a 100-page book written in Latin and composed of 111 case histories, many of which are accompanied by brief autopsy descriptions. Among other things, he was the first to describe gallstones. The matter-of-fact manner in which these autopsies are presented indicates that dissection of the dead was not uncommon at the end of the 15th century.

We next come to a French physician who is relatively unknown at the present time but is of considerable importance in the history of medicine and of pathology in particular. He is Jean Fernel, who was born in 1497 and died in 1558. Fernel received an extensive education in mathematics, the humanities, philosophy and medicine. At first he was a proponent of the astrological concept of disease, but soon rejected both this and the humoral theory for a system based on diseased organs.[14] He made autopsies a routine practice. Fernel wrote three works of note, a book on physiology, a book on therapeutics and another on pathology.[15] This latter work was simply entitled "Pathology". It is noteworthy for several reasons. Firstly, it marked the first use of the word pathology, Fernel being its originator. Secondly, this book differs from Benivieni's in that it is not a mere compilation of cases but actually the first textbook of pathology in that it discusses disease changes organ by organ, albeit quite briefly. On the basis of this book Fernel has been called the Father of Pathology by many medical historians. He believed that aneurysms were caused by syphilis, and differentiated between true and false aneurysms. Of further interest is Fernel's descrip-

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tion of autopsy findings in a case which was undoubtedly appendicitis, this being recorded 300 years before the classical description by Fitz.

Accurate studies of diseased organs were not possible before the possession of accurate knowledge of the normal structure of the human body. In the Middle Ages, Galen's descriptions of human anatomy, which were based on animal dissection, constituted the only acceptable concepts. It was Andreas Vesalius, a Flemish anatomist of the 16th century, who broke through the barrier of absolute authority.[9] He wrote the first anatomy book which was based on a careful study of human corpses rather than animals. His work, "The Structure of the Human Body", played a major role in the renaissance of scientific enquiry. Vesalius also performed medicolegal autopsies.

Gradually more and more physicians performed autopsies in order to study disease.[16] Nicholas Tulp, a Dutch physician born in 1593, checked his diagnoses by necropsies. His book "Medical Observations" contains descriptions of postmortem examinations. He was the first to describe beriberi and the ileocecal valve. Franciscus Sylvius, another Dutch physician of this time, also resorted to autopsies. He associated lung tubercles with clinical tuberculosis. Sylvius also described the aqueduct of the mid-brain which is now known by his name.

During the 17th century, interest in autopsy findings was sufficient to stimulate Théophile Bonet, a Geneva physician, to compile over 3000 human necropsies recorded since the time of Hippocrates.[7] However, modern pathology, in the sense of detailed correlation of clinical signs and symptoms with disease changes in organs, did not begin until the investigations of Giovanni Battista Morgagni, an Italian anatomist and pathologist who was born in 1682 and died in 1771.[17] His massive book, called "On the Seats and Causes of Disease", represents the foundation on which scientific medical concepts have developed. This work is organized along the lines of organ systems, and in each he carefully correlates clinical findings with necropsy changes. For example, Morgagni described the presence of necrotic cavities in the brain on the side opposite to paralyzed limbs in cases of hemiplegia. This monumental work was translated into English in 1769. In 1960, a facsimile reproduction of this English edition was published.[18]

After the publication of Morgagni's classic, numerous additional clinical pathological observations were made. Mention can be made of only a few of the more outstanding ones.[16] Richard Bright, an English clinician born in 1789, was the first to recognize the relationship of edema and proteinuria to diseased kidneys. Jean Cruveilheir, a French pathologist born in 1791, performed thousands of autopsies and described various conditions such as multiple sclerosis, peptic ulcers and congenital cirrhosis. Thomas Addison, an English physician born in 1793, was the first to associate constitutional symptoms with diseased adrenal glands. The simultaneous enlargement of spleen and lymph nodes in some autopsy cases was first recorded by Thomas Hodgkin, an English pathologist and physician born in 1798. Guido Banti, an Italian pathologist born in 1853, described the association of splenomegaly with cirrhosis. The first recorded instance of the correlation of clinical with necropsy findings in coronary thrombosis is credited to George Dock, an American pathologist and clinician born in 1860.[6]

These are but a few of the innumerable investigators of the 18th and 19th centuries who established organs as the seats of disease. However, Morgagni's concept of organ pathology gradually became refined to a concept of tissue pathology. Marie François Xavier Bichat, a French anatomist and pathologist born in 1771, recognized the fact that some diseases are not confined to specific organs but involve the same tissue in different organs.[19] He performed over 600 extremely detailed autopsies.

The next major figure on the scene of disease concepts is Rudolf Virchow, an outstanding German pathologist who lived from 1821 to 1902.[20] He established three significant precepts: (1) Cells arise only from other cells. (2) The cell is the true unit of all living organisms. (3) The cell is the basic unit involved in disease.[21] Others before him had recognized that cells were involved by disease, but it was Virchow who recognized the cell as a basic unit of life and disease and so gained medical immortality.

We have seen the keenness of man's observations advance from the organ to the tissue to the cell. The next stage was the discovery of bacteria in relation to disease. Although bacteriology as such did not begin until Pasteur, several individuals of the preceding three centuries had laid the groundwork which was necessary before any appreciation of bacterial infection was possible. Hieronymus Fracastorius, an Italian physician born in 1483, recognized that certain diseases were spread by contact and by fomites.[6] Antony van Leeuwenhoek, a Dutch naturalist born in 1632, constructed the first practical microscope and used it to study anything in sight.[22] Although he saw blood cells, sperm and protozoa, he did not recognize bacteria as such. Athanasius Kircher, a German scholar and naturalist of the same time, is credited with being the first to use the microscope in the study of disease.[6] He described bacterial bodies in putrefied meat, and believed that contagion was due to these invisible animals. Ignaz Philipp Semmelweis, a Hungarian physician born in 1818, recognized the contagious nature of puerperal fever.[9] However, he died a broken man because of the complete rejection of his concepts by the medical world.

It remained for Louis Pasteur to establish without doubt the bacterial causation of many diseases. Pasteur was born in France in 1822. He was trained as a chemist, and his first research project was con-

cerned with the isometric structure of certain crystals.[23] Although his work provided a great stimulus to crystallography, he soon turned to the study of wine fermentation. Within a remarkably short time he recognized the fact that fermentation depends upon the presence of bacteria. This remarkable man then turned his genius to the study of animal and human disease because he was impressed by the analogies between fermentation and infectious disorders.[24] It was but a short step for Pasteur to the discovery of the bacterial cause of certain diseases of silkworms. He next studied anthrax in sheep. Although the bacillus had been seen before in the blood of infected animals, Pasteur enlarged these studies and succeeded in convincing even the most virulent of his opponents. He further established the germ theory by studies on chicken cholera, yellow fever and swine plague. Even more important was his discovery that inoculation of a weakened germ would protect the animal from further exposures to the infection. The story of his development of a vaccine for rabies is too well known to bear repeating.

Pasteur, although not a doctor, is obviously one of the giants of biology and medicine. His ingenious experiments, which helped to discredit the concepts of spontaneous generation, played a major role in the development of modern biological thought. There have been others who have made as important discoveries as Pasteur, but few who have had the persistence and tenacity which enabled him to overcome the violent opposition which his studies and his concepts first met. Of interest is the fact that Virchow is credited by many to have opposed the germ theory of infective diseases. However, what he actually did was to caution that discovery of bacteria in disease states should not be accepted as etiologically significant without intensive study. The wisdom of his views is borne out by the numerous rash claims at the turn of this century as to the bacterial causation of many diseases.

Next to Pasteur in stature as an originator of medical bacteriology is Robert Koch.[24] Koch, born in 1843, was at first a medical practitioner in rural Germany, and it was there that he began his bacteriological studies. He was one of the first to see the anthrax bacillus, and he developed methods for its isolation and culture. Koch invented methods for the staining and culturing of many bacteria. Of more importance are his discoveries of the Vibrio comma of dysentery, of the tubercle bacillus, and of tuberculin. He is best known at present for the so-called Koch postulates for the acceptance of a bacterium as the causative agent in any given disease.

In a remarkably short space of time the germ theory received practical applications. Joseph Lister, an English surgeon born in 1827, was stimulated by Pasteur's work to introduce antiseptic techniques into the operating room.[25] Even though his results showed a fantastic reduction in postoperative morbidity and mortality, it was many years before the brilliance of his work overcame bitter opposition. John Collins Warren, an American surgeon, was the first to introduce Lister's antiseptic technique in North America.

On the heels of Pasteur's revolutionary findings were studies that linked many infective agents to diseases.[6] Bacteria were first described as the cause of endocarditis by a Norwegian pathologist, Emanuel Fredrik Hagbarth Winge, who was born in 1827 and had been a pupil of Virchow. Walter Reed, an American pathologist and bacteriologist born in 1851, proved that yellow fever was transmitted by mosquito bites. The life cycles of parasites such as filaria and hookworm were delineated by Allen John Smith, an American pathologist born in 1863. Many pages could be filled with the names of other workers.

EXPERIMENTATION

So far we have been dealing mostly with the results of observation, whether with the naked eye or with the microscope. At first man attempted to get answers from nature by watching it closely, and only later did he begin to manipulate nature to achieve these ends. Although the majority of advances in the understanding of disease processes were of a static and morbid nature until the 19th century, there were a few individuals who laid the ground-work for experimental medical investigation long before this. William Harvey, the English physiologist born in 1578, was far ahead of his time when he performed the vital experiments which led him to the discovery of circulation.[26] The story of his fortitude and persistence in the face of considerable disbelief and derision is a remarkable one. John Hunter, a Scottish surgeon born in 1728, is often regarded as the Father of Experimental Pathology because of his animal experiments on inflammation, aneurysms and collateral circulation, among many others.[27] He was also an avid naturalist and organized a great pathology museum, some of which is still in existence today.

With the 19th century, experimental medicine and pathology began in earnest.[9] Julius Friedrich Cohnheim, a German pathologist born in 1839, gave us the first modern description and understanding of inflammation. He was a pupil of Virchow. Elie Metchnikoff, a Russian biologist who was born in 1845 and worked in France, studied phagocytosis and delineated its role in the cellular defences of the body. Experimental cancer research began with Johannes Fibiger, a Danish pathologist born in 1860. He was the first to produce cancer in the experimental animal. Fibiger induced carcinoma in the rat stomach by infestation with the parasite Spiroptera. The first chemical induction of cancer was achieved by Katsusaburo Yamagiwa, a Japanese pathologist who was born in 1863. We are all familiar with the story of his prolonged application of tar to the skin of mice. He was also a pupil of Virchow.

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THE FUTURE

This takes us to the present century and the end of the journey. However, it is certain that the disease concepts held by our generation do not represent the final truth. Already we have seen within our lifetime the elaboration of psychosomatic, biochemical and immunological concepts of disease, and within the last decade the first glimmerings of a molecular concept. Future generations may well contain giants such as Morgagni, Virchow and Pasteur whose discoveries could make our present theories seem as primitive as does the humoral theory today. Let us pay heed to the lessons of history by not greeting new disease concepts with the blind and obstinate opposition which met those of Harvey, Semmelweis, Pasteur and Lister. Let us also not forget the fact that men of many different nations were responsible for our present knowledge, so that we will not evaluate future contributions on the basis of an individual's race or creed.

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