AMERICANS AND THE GERM THEORY OF DISEASE

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PREFACE

This study was originally begun as a biography of John Kearsley Mitchell, but the background of Mitchell's cryptogamous theory proved to be so interesting and of such significance that a much fuller study of this field was indicated. The subject of American animalcular hypotheses and their relation to the later development of medical bacteriology has been discussed briefly in a number of studies, and acknowledgement of my indebtedness to these will be noted in the citations. No systematic account of the early American interest in the germ theory of disease has hitherto been written; and the present study has been prepared with this end in view.

A considerable amount of the material in chapters two and four was published in two articles in 1947. The first and longer study, "Etiological Theory in America Prior to the Civil War," appeared in the Journal of the History of Medicine and Allied Sciences, Vol. II, No. 4, Autumn, 1947, and parts of it are presented here with the permission of the publisher, Mr. Henry Schuman. An analysis of the American theories of the animalcular type, "Early American Animalcular Hypotheses," appeared in the Bulletin of the History of Medicine, Vol XXI, No. 5, September-October, 1947, and some data in it are presented with the permission of the editor, Dr. Owsei Temkin.

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Chapter 1. Introductory Note

At the opening of the nineteenth century, modern medicine had progressed so steadily that solutions to outstanding problems seemed just around the corner. In the three centuries following the initial work of Vesalius, anatomy had become a science. The human body was explored as effectively as was the terrestrial globe in the same era. In gross anatomy discovery after discovery was made, and many landmarks bear the names of those who first located them: Glisson's capsule, the antrum of Highmore, the circle of Willis, Peyer's glands, and others. No longer did medicine rely upon the antiquated lore of Galen - medical men observed for themselves. Physiology also profited from the development of anatomy, while renewed interest in clinical medicine led to a return to the principles of Hippocrates. By the end of the eighteenth century, there was a much better understanding of the composition and functioning of the human body than had ever existed before.

This understanding was further advanced by progress in the new field of pathologic anatomy. Less than twenty-five years after the publication of Morgagni's classic work on pathologic anatomy in 1761, French physicians took up this work and added to it. The ravages of disease were not only described as they affected the various organs of the body, but the lesions were correlated with clinical symptoms so as to give a clear picture of the disease under observation. Where heretofore diagnosis of a disease had been dependent almost solely upon the ob-

servation of obvious symptoms, now the physicians were able to differentiate among various disorders - with the knowledge that certain symptoms were characteristic of one disease and not of another.

Accurate clinical observation became doubly important. Characteristic signs and syndromes were added to the diagnostician's repertoire. The development and improvement of aids to the senses, and of measuring devices, became extremely important in diagnosis. The stethoscope, percussion, the use of the watch and the thermometer, to name a few, all aided the physician. Clinical statistics, as applied by P.-C.-A. Louis to prove the danger of venesection, also played a part. Mortality statistics had been compiled as early as 1662, but it took some time to put them on a satisfactory basis. Such statistics were an important feature of Jacques René Tenon's exposé of the hospitals of Paris in 1787.

The nosologists of the eighteenth century had worked out an elaborate systemization of disease based on symptoms. Each symptom was considered a disease in itself. Needless to say, this made a tremendous list. Other systematizers such as William Cullen, were more moderate; but their classifications were, of necessity, based largely on classes of symptoms because there was no other satisfactory basis available at the time. After the work of the pathologic anatomists, however, the classification of disease could be based on a correlation of symptoms with the lesions found at autopsies. This resulted in a new concept of specificity and a different set of specific diseases. It involved

the task of breaking down such a concept as "bilious fever" into malaria, typhus, typhoid and yellow fevers. Diseases of the chest were no longer a unity, but, according to the interrelation of symptoms and tissue changes, now became phthisis, pneumonia, pleurisy, and so on. In some instances, three or four entities emerged where only one had been suspected previously.

These developments raised a new problem. If three or four diseases were now recognized where formerly there had been only one, to what must be ascribed the differences between them? Could it be that there were an equal number of factors in the external and internal (body) environments, which were responsible for the differentiation? By the last years of the eighteenth century, physicians had begun to ask these questions seriously. Some writers, in suggesting answers, attempted to make distinctions among the external factors (remote causes such as miasmata), which they believed to be involved in disease, but there was little material evidence available to substantiate their conclusions.

The classification of diseases into more definite entities, and the subsequent attempt to account for differences between them, proved of great interest to Americans. As early as the 1790's there was already considerable discussion of the specific causes of distinct diseases. Although this discussion was made possible, in the long run, by the developments in disease identification mentioned, a more immediate motivation was supplied in America by the old controversy over contagion.

Whatever the ultimate causal factors might be in such epidemic diseases as were already fairly well-recognized (as yellow fever), how could one account for their rapid spread? Were they transmitted by human contacts? Such questions could also be asked about vaguely defined concepts (such as "bilious remittent fevers") even before the diseases now known to have been involved were identified. Later, the sharper differentiations already mentioned would become more specific and meaningful.

Another factor creating interest in etiology was the prevalence of great epidemics, notably plague in the seventeenth century, smallpox in the eighteenth, and cholera in the nineteenth. In order to free mankind from these scourges, an adequate knowledge of their origins or means of transmission was urgently needed. Meanwhile, by the opening of the nineteenth century, knowledge of causal factors (either ultimate or relating to transmission) was rather confused. But hope abounded, and there seemed good reason to believe that in the normal course of events satisfactory solutions could be found.

Such solutions were sought in America as well as in Europe. It is the purpose of this study to show that American interest in the problems of the causation of disease was greater than has been realized, and that American work in the field had some value - although no great contributions to the development of medical bacteriology came from America before 1880. The negative picture in this respect is of significance in suggesting the limitations of the medical sciences in this country

during the major part of the nineteenth century. The details of the story comprise an interesting aspect of American medical history, since the problems raised involve more than the history of science in general. They clearly have their implications for American cultural development as influenced by the social and cultural milieu of the age. In telling the story, one must, of course, trace the major scientific developments in Europe, whence American thought drew its inspiration. But this European narrative will be recalled primarily in order to interpret American participation. The difference in outcome in this country is then to be explained by factors more or less peculiar to the American scene. Science, like literature and the arts, might originate abroad, but it did not necessarily run the same course in the United States as overseas. In this sense, what follows is American history.*

FOOTNOTES TO CHAPTER ONE

* In this study, the term "disease" is usually employed in relation to the specific infectious illnesses (classification of William Osler). "Specific causes" means the specific factors in causation, now usually known to be micro-organisms. The concomitant factors (proximate causes) which determine whether the invaded organism actually develops the disease - matters of immunity, predisposition, mental attitude, and the like - are excluded. A basic distinction between the "atmospheric" and "miasmatic" theories is made in the second chapter, depending on whether the agency of the atmosphere in general or of a special vapor in the air is intended. The term "animalcular hypothesis" relates to theories of both animal and vegetable origins because little differentiation was made between the two before 1850. The term "mid-century" is used freely to denote the period from 1850 to 1880.

Chapter 2 Theories of the Causation of Disease in the Early Nineteenth Century*

One of the ambitions cherished by American science in the nineteenth century was that of securing intellectual equality with Europe. It is true that colonial attitudes persisted on this side of the Atlantic long after the Revolution. Americans followed European leadership to such an extent that the cultural dependence observable in the colonial period was still common in many fields late in the nineteenth century. In the realm of the sciences, Americans first attained some cultural autonomy by branching into fields other than the classical ones of astronomy, physics, chemistry and general biology. They pioneered in the various branches of geology - especially in oceanography, mineralogy and paleontology. Considerable work was done in connection with the new flora and fauna of the Western Hemisphere. Advances were made in geography and navigation, as when the Wilkes scientific expedition to the South Sea produced valuable information about Antarctica.

In medicine, Americans pioneered in major surgery and anesthesia. Outstanding work in these fields was recognized in Europe, sometimes sooner than at home. For a time it also appeared that American studies in the differentiation of diseases would advance as rapidly as those of Europe. William W. Gerhard's differentiation of typhoid and typhus fevers in 1837, and the supporting work done soon thereafter, made it seem as if the French type of research in pathologic

anatomy had gained a strong foothold in America. This research led, in turn, to a wide interest in etiologic theories. From about 1820 to 1850 Americans shared with Europeans a lively curiosity about the possible origins of the various diseases - once the latter had been identified by pathologic investigations. This logical progress from the identification of disease entities to a study of their "causes" was analogous to the manner in which biologists - having identified many new species - proceeded in this same period to a study of the origins of species.

The field of etiology profited from the importation, from France in the 1820's, of pathologic anatomy and improved methods of diagnosis, and the resulting contributions made in the following two decades on this side of the ocean by Gerhard, George Shattuck, Elisha Bartlett, James Jackson, Jr., and others who had been students of Louis in Paris.[1] The resulting picture of several diseases where only one general condition had been suspected before, gave rise to the very real necessity of differentiating between specific causes. Obviously it was difficult to view such diseases as pneumonia and pulmonary tuberculosis as arising from a single cause, and Benjamin Rush's one-disease-one-cure concept now seemed absurd. It would have taken a special kind of magic to produce the Peyer's patches of typhoid in cases of Asiatic cholera. The crying need in the 1840's was to find the factors causing such variations as had been evidenced by autopsy findings. By the time Elisha Bartlett's famous monograph on fevers had been published in

1847,[2] it was obvious that the differentiation of malaria, typhoid, typhus and yellow fevers as separate diseases made it necessary to search for separate causes in the external environment. This search was carried on in all the various areas of etiologic theory then in vogue.

The great American physician, Benjamin Rush, had solved the question of the proximate and remote causes of disease in a simple manner: he had united all disease into one ailment. This revival of the classic theory of disease had one advantage. It meant that henceforth no one need classify diseases into fancy patterns based on symptoms as the eighteenth century nosologists had done. Causation was equally simple. One need no longer worry about noxious miasmata and poisonous effluvia; although with some caution, Rush was not adverse to including these exhalations as contributing remote causes for his one disease. The direct cause was, to him, a proximate and internal one, a derangement of the system. Furthermore, with only one disease, treatment was simplified. One cure would suffice for everything, as Rush so handsomely demonstrated with his bleeding and purging during Philadelphia's yellow fever epidemic of 1793, to the undying opposition of many of his contemporaries and the misfortune of his patients.

The theory of the Dean of the American medical profession in the eighteenth century did not carry much weight after the death of its author. The medical profession then was engaged in a much more interesting controversy, and one which was to last for more than a

century. This was the problem as to whether the fevers which raged in great epidemics were contagious or not. It should be noted that, for all practical purposes, knowledge of how a disease was transmitted was a special aspect of knowledge of its "cause." Indeed, means of transmission would have been classified by such writers as Rush as a "proximate cause" of a given form of illness; while the causal factors so transmitted would have been viewed as a more ultimate type of "cause". Such matters related, of course, only to those diseases which we would now say had an infectious origin; whereas pathologists had identified various entities - such as the degenerative conditions - which seemed to have no relation with any factors in the external environment. Some deficiency diseases or poisons (scurvy, ergotism) were included with the regular infectious diseases. It was only natural, however, that those concerned about etiology in the early nineteenth century should have focused their attention upon infectious diseases. It was for these alone that the external environment gave some hints about causal factors. And it was this type of disease which was most feared in that day, because of the constant threat of dire epidemics.

The chief disease involved in the contagion controversy was yellow fever, although opinions could also be obtained regarding typhoid, typhus, malaria, dengue and cholera. The contagionists believed that a disease was of imported (usually ship-borne) or transported origin and spread by human contact or by animals. The non-contagionists thought a disease was of indigeneous or spontaneous origin and spread by in-

fected air. One interesting aspect of this controversy was the fact that many of the individuals involved were contagionists with regard to one disease, such as yellow fever, and non-contagionists with regard to another, such as malaria. The fevers relegated to each catagory varied with the individual or group making a pronouncement on the subject. Elisha Bartlett, famous for his work on the "bilious" fevers, was inclined to think that typhoid and typhus fevers were contagious, whereas yellow fever was non-contagious. Henry Clark believed that all fevers were contagious, while the Quarantine and Sanitary Convention of 1859 preferred to view that hardly any fevers except the exanthemata (measles, etc.) were contagious.[3] Divergent schools of thought arose, particularly with regard to the contagiousness of yellow fever; and in 1805, "the College of Physicians of Philadelphia, as a body, gave their opinion in favour of contagion" in the case of this disease - a view which failed to settle the matter.[4] In fact, the argument over the contagiousness of yellow fever lasted throughout the century until finally settled by Walter Reed and his coworkers.

American arguments over contagion reflected those in Europe - especially the English. In this respect they reflected the cultural dependence of America. Confused terminology helped to lengthen the controversy. Some authors, for example, used the terms "infectious" and "contagious" synonymously, while others differentiated between them.[5] On both continents, logic, backed up by statistics from a scatter-

ing of cases, provided the chief method of proof. Since an accurate knowledge of the causes of disease would settle the problem, the adversaries were constantly looking for more information to bolster up their reasoning. This search helped advance the work in etiology.

In the early part of the nineteenth century, etiologic sections in medical works usually presented an epidemiological approach. The writer who was reporting on a yellow fever epidemic in a certain locality would give a description of weather conditions preceding the epidemic, followed by a geographical and, if possible, a geological survey of the immediate neighborhood - paying careful attention to such sources of miasmata as swamps, pools of stagnant water, gutters, rain barrels and so forth. A few authors mentioned the apparent increase in insect life shortly before epidemics,[6] but this type of information was not considered of much importance and no attention was paid to it. As the century progressed, the only refinement in this technique of reporting was the replacement of swamps by sewers, flooded basements, cesspools, rotten timbers, and contaminated wells. Although sewer gas took the place of miasmata as the bane of the epidemiologists' existence, in both cases the agency of the atmosphere was retained and only the type of poison contaminating it varied.

The most popular theory of disease causation was for centuries that which ascribed epidemic fevers to the action of a volatile poison called <u>miasma,</u> which arose at night from the marshes or similar damp places. This noxious effluvium in the air was assigned in different cases

to decaying vegetable matter, to stagnant water, to decomposing bodies on battlefields, or to putrefying animal matter. Serious debates were held as to which of these matters was the actual cause of the mal aria. Heat, moisture and dead organic matter were generally agreed to be the necessary and sufficient causes for the production of the miasma.

The technical aspects of this production were worked out in detail. Some authors even went so far as to determine the exact degree of temperature involved. All sorts of diseases were ascribed to the action of the malaria. John Macculloch, an English writer, included nearly all diseases known to man in his list. Among the Americans, a Kentuckian, Charles Caldwell, believed that miasmata were responsible for plague, yellow fever, cholera, bilious fevers (intermittents, remittents, continued fevers, dengue, dysentery, and lesser disorders), madness and idiotism. He held that "bilious malaria" arose from vegetable and animal matter, especially the former, in a state of dissolution. The English writer, A. P. Wilson Philip, divided his miasmatic fevers into intermittents and continued fevers, the former caused by marsh miasma, as well as continued exposure to dampness, especially at night, and the latter due to cold and contagion by means of direct contact, fomites, and infected air. Benjamin Rush even enumerated in detail just which vegetable and animal matters gave rise to poisonous exhalations. He also noted the importance of stagnant water in hogsheads, gutters, mill ponds, puddles, sinks, and the stagnant air in the hold of a

ship or a close cellar.[7]

There were certain well-known facts about disease presumably produced by miasmata which were not explained by this theory. It was observed, for example, that cases of fever were found in dry uplands, far away from any swamps. Then there was the "fact" that trees seemed to protect residences from the effects of bad air; in addition, the mal aria was stopped by so fine a barrier as a piece of gauze; it could not proceed against the wind; fire and smoke dispersed it, and although it could not travel very far over sea water, sporadic cases often appeared on ship-board. M. L. Knapp's comment illustrates the problem:

> Malarious fevers occur at sea, are produced on ship-board, where there can be no marsh malaria. Also in arid deserts, where no vegetable or animal decomposition is going on. Also in the cool dry mountains of California where never a marsh or lake existed, where no rain falls for six months of the year, and no vegetation, comparatively, is produced, subject to decay. One such example is fatal to the hypothesis of malaria, and a dozen may be cited.[8]

The lack of any satisfactory solution to these questions led to a search for better theories. Unfortunately, none of those suggested satisfied the searchers. Caldwell, in his Boylston Prize Essay for 1830, asked and answered the basic question:

> 1. What is the NATURE of the malaria that produces bilious fever?
>
> To this my answer is brief. I do not know. Nor is anyone better informed about it than myself.[9]

This same answer was to be given for the next fifty years. Charles

J. B. Williams, the English textbook writer, in 1843 foresaw the fact that "the microscope rather than chemical analysis may be expected to discover the nature of malaria." R. S. Holmes of Missouri, in 1848, was convinced that the discovery of "what malaria really is" was just around the corner.[10] None of these writers realized how difficult turning this corner would prove to be. They looked for a sudden illuminating discovery rather than toward the plodding, careful scientific investigations which finally produced results.

Those people who believed in the miasma theory found it necessary to differentiate between the various miasmata, in order to account for the different diseases resulting from them. As pathologists distinguished more and more closely between specific diseases, the obligation arose to distinguish more sharply between their specific causes. The comparatively simple systems of William Cullen and Noah Webster became the complex and exhaustive systems of Edward Miller, Joseph M. Smith and James Copland.[11] Such fine divisions, with their vagueness and overlapping agencies were the products of elaborate reasoning, but the problems of etiology were no nearer solution after the lists had been made than they had been before.

It should be mentioned in connection with the miasmatists that none of them relied solely upon miasma as the <u>one</u> cause of any disease. Rather they considered a number of causative agencies. The English medical encyclopedist James Copland, for example, recognized five types of causes:

1. external or extrinsic
2. internal or intrinsic
3. principal and accessory
4. remote (predisposing, exciting, determining) and proximate
5. specific
   A. miasmata (stagnant water)
   B. putrefying animal and vegetable matter
   C. emanations from animal matter [12]

The "emanations from animal matter" were considered contagion by medical writers of the period. This system of classification, it may be seen, is largely a speculative one.

Alfred Stillé, a well-known Philadelphia physician, had a similar but more elaborate listing:

Causes:	General -	heat, cold, temperature - air, seasons, climate.
	Special -	hereditary predisposition, age, sex, temperament, constitution, idiosyncrasy, habits of life, etc.
	Exciting -	cold, pain, mental emotion, mechanical, chemical, poisons.
	Specific -	infection, contagion [13]

Other systems of this type with slight variations may be found in textbooks of the 1840's. All of them were products of elaborate reasoning based purely on simple observation. Many of the "causes" are found in modern etiology, having been scientifically demonstrated. Others were totally discarded as scientific knowledge increased. Some which were discarded have now been re-introduced (psychosomatic causes). Most of the theories of causation of disease considered hereafter belong in the "remote" or "exciting" catagory, although this has a tendency to become confused with the "specific" catagory when the fermentation and germ theories are considered.

The second most popular theory placed the blame for disease on atmospheric conditions rather than on miasmata. This theory was chosen in times of epidemics when the adherents of the miasma hypothesis were at a loss to explain how the poisonous content of the air suddenly increased without apparent cause. Proponents of the atmospheric theories were able to ascribe this to a variety of cosmic happenings, ranging from comets to altered pressure or oxygen content. The French physician F. A. Mesmer advanced a magnetic theory based on the action of the planets and stars. The anonymous reviewer in the American Quarterly Review for December, 1828, thought that climate determined whether the same disease would be the yellow fever of New Orleans or a mild remittent in Canada. These ideas were not new. Hippocrates and Galen had placed the origin of disease in weather heat, and the sun. Van Helmont added earthquakes and sieges. Sydenham preferred to believe that some occult properties in the air were responsible for epidemics. In the eighteenth century, Henry Clutterbuck used fumigation to prevent disease; not, as today, to kill the wild life, but to purify the air. Noah Webster, American epidemiologist and famous for his dictionary, included cosmic atmosphere among his causes of disease; he had not only miasmata and noxious gas in his air, but an "electric fire" disturbing it. He also noted a possible correlation between epidemics and comets, earthquakes, meteors, storms, water which had been contaminated by subterranean vapors (hot springs?), fog, and the aurora borealis. Webster's most interesting observation

was that "changes in the air" produced myriads of insects before epidemics. He thought that the electrical changes in the atmosphere might be the cause of this sudden enlargement in their numbers.[14]

Many persons viewed the atmosphere as a conductor of the poisons generated by the sick. Contaminated air would pass the disease along in a confined space. Thus the well received the disease from the sick by being present in the sick room. This is what early nineteenth century writers usually meant when they mentioned contagion. Robert Jackson gives this view in the contemporary medical terminology:

> It is perhaps no longer disputed that those derangements of the human frame denominated fevers, whether endemic or contagious, owe their origin to two sources only . . . [the first is marsh exhalation;] the second, deriving from an animal source, more expressly from an altered condition of the human body, is confined in its sphere of action, communicated only by contact, by near approach, or by a medium connected with this source.[15]

The Viennese Dr. Hildenbrand called this contagion by immediate contact - meaning by close, infected hot air. He also mentioned furs, dirty bed clothes, and the like as being part of this catagory of contagion; but he indicated that in such instances contagion would probably take place by "inoculation", rather than by respiration.[16]

There was a general belief that the atmosphere became a conductor of disease when it was in a certain putrid or corrupted state. One of David Hosack's correspondents thought yellow fever required such an atmosphere for its dissemination. The contagion would then "inoculate and assimilate any confined portion of the atmosphere which

has been exposed to the requisite causes of contamination, so that every part of it shall have the power to communicate that poison." Thus epidemics could be explained by atmospheric changes alone. Richard Mead, famous student of John Radcliffe and renowned practitioner in the eighteenth century, had believed that a person ill with plague gave off "contagious atoms," which would be harmless in a healthy state of air, but virulent in a corrupted state. In 1826, W. C. Daniell of Georgia thought that marsh miasma imparted some property to the air, presumably a pressure change, which impaired the "capillary action of the skin, and affect[ed] the equilibrium of the circulation." This in turn upset the internal capillaries and the net result was fever.[17]

The atmospheric theories explain why, in writing of epidemics, most medical authors began by giving the medical geography of the area and the state of the weather during the few weeks preceding the outbreak of the epidemic. Thus Samuel Henry Dickson of Charleston, reflected that the weather had been changeable before an epidemic started there in 1827. James Gayley was sure that there was usually a higher temperature in a place subject to malaria. Daniel Blair of British Guiana considered that in yellow fever "the efficient cause ... is an aerial poison, probably organic, which requires a certain temperature for its generation and existence, and affects certain localities and persons." J. W. Heustis noted that in Alabama "the appearance of certain diseases is connected with particular temperatures of the

atmosphere. We know, for instance, that a long continuance of hot weather is necessary for the generation and prevalence of the bilious or yellow fever."[18]

Finally there was one school of thought, mentioned by both Charles Caldwell and Usher Parsons, which ascribed malaria to atmospheric moisture alone. An unidentified author quoted by Parsons related:

> Emigrants proceeding to Alabama and other southern regions, from the low countries of Carolina, find no injury from sleeping in the open air, as their custom at night is to build a large fire of logs, and lay themselves beside it, on some part of their baggage. The effect of the fires in destroying malaria is plain, if the fact of its existence depends upon the presence of moisture; for the moisture being evaporated by the heat, the poison is either dispersed with the vapor, or, if separated from it, falls innoxious, and probably inert. It is on the same principle that smoking segars on the decks of ships is salutory. The heat and smoke keep a dry atmosphere about the uncovered face and the air respired, thus deprived of miasmata, safe. [19]

One medical writer, M. L. Knapp of Illinois, in 1855, turned violently against "this Italian absurdity of Lancisi" - the hypothesis of mal'aria. He thought that cholera, malaria and most fevers were of scorbutic origin, and he cured them by feeding his patients lemon juice and a proper diet. In view of the fact that malnutrition was a common condition on the frontier, it is possible that many deficiency diseases were being classified as fevers and treated as such. Copland's classification of infectious diseases included pellegra with syphilis, rabies, cow-pox and other "palpable specific contagions," and scurvy with dysentery and ergotism as caused by "unwholesome and poisonous

ingesta."[20] All this added to the confusion in classifying diseases, to say nothing of determining their causes.

Doctors who were satisfied with neither the miasma nor the atmospheric theories, sometimes turned to chemical hypotheses. Macculloch considered malaria to be a compound made up of nitrogen, oxygen, hygrometric vapor, and a basis of deleterious character - miasma. Today this sounds like ordinary air, plus miasma. To him, however, it was a mysterious compound which could attach itself to solid substances, including furniture, trees, the soil, and gauze window netting. Furthermore he reasoned that it could be chemically decomposed by fire and smoke. John Cooke of Kentucky believed a vapor or gas of miasmatic origin was the cause of Fevers. A Missourian, J. B. McCartney, based his theory on changes in the oxygen content of the atmosphere. Other hypotheses, chiefly borrowed from European theorists, blamed "bad air" on the presence of such varied materials as oxidised nitrogen gas (septon), carbonic acid gas, nitrous oxide, sulphuretted hydrogen (hydrogen sulfide gas), carbonated hydrogen (methane gas), phosphuretted hydrogen (phosphine) and sulphurous emanations in general. Some of these chemical theories display a surprising ignorance of basic knowledge of the toxicity of chemical compounds. Hoffman claimed epidemics were due to the lessened elasticity of the air, and Sir James Murray had an electrical theory. Richard Mead in the eighteenth century had suggested that the infectious matter of contagion was "perhaps in the Nature of a Salt, generated chiefly from the Corruption of a

Humane Body..." R. S. Holmes of Missouri explained that "moisture and heat operating on mineral and vegetable products are necessary to the constitution of malaria."[21] It is startling to encounter the idea that mineral exhalations had something to do with inducing disease. None of these chemical theories survived well-founded criticism.

The importance of pure water was known, at least on an empirical basis, even before it was possible to examine it microscopically. Stagnant water was to be avoided because it gave rise to miasma. It was presumed to have deleterious qualities because of its odor. For a considerable time after the work of John Snow, On the Mode of Communication of Cholera (1854), doctors were attributing water-borne diseases to aerial miasmata. Both Rush and Caldwell were aware that wells became contaminated from privies and disease resulted.[22] The actual chain of contamination was not worked out by either of them.

It is amazing in so many instances to find physicians so close to finding the actual specific causes of disease or the agencies whereby diseases are passed along, and yet never quite realizing them. Most appeared content with shrewd guesses or insights, and never attempted the experimental approach. As an example, one might take the putrid water hypothesis, which gained converts when the French physiologist, François Magendie, claimed to have produced yellow fever in dogs by injecting them with putrid water and putrid matter. This series of experiments received some attention in America during the 1840's,[23] but no one seems to have taken the trouble to repeat Magendie's work

here. The almost total neglect of experimental work in connection with etiological theories in this country is one of the striking aspects of the American story. Attempt will be made in a later chapter to account for this neglect.

A common conviction, dating back to the Middle Ages, was that of contagion by fomites. It was believed that infected matter clung to cloth, fur, baskets, bedding and such, and contagious diseases were passed along in this manner. Henry Clark noted that the spread of Ship Fever (typhus) was decreased by the use of hygienic measures, principally keeping the patients and their bedding clean.[24] In this case, as in many diseases, the empirical approach yielded results while the theory behind them might be totally inadequate. It is interesting that the fomite idea should survive for such a long time. Even as late as 1860, it was one of the more acceptable ideas in the collection of the etiologist.

In addition to the theories already discussed there was also the idea that some kind of a catalyst, acting as a ferment, gave rise to fevers. This viewpoint was influenced by the work of Justus von Liebig in chemistry. The Liebig theory of fermentation, of course, denied that yeast was a living, microscopic plant. In this instance the relationship was purely that of a catalyst which aids the reaction, but does not become a part of it. This type of fermentation idea, as might be expected, fits the gaseous theories of etiology better than any other. Later writers who worried about methane gas (carburetted hydrogen) from sewers

and such sources, or hydrogen sulfide gas (sulphuretted hydrogen) from mineral waters, were concerned with a known chemical, not to be confused with the miasmata of dubious composition of the period under consideration. The problem in the later period was to determine whether the symptoms of gas poisoning were synonymous with such intestinal diseases as typhoid, dysentery, cholera, and enteritis.[25] The problem in this earlier period was to determine whether there was a miasma for every disease, and, if so, to discover how to recognize it.

The groping of the theorists has been summarized best by an English physician, Thomas Herbert Barker, in an excerpt from his Fothergill Prize Essay for 1859:

> Some have considered a malarious influence as something unknown and undiscoverable; others that malarious or miasmatic influences spring up as independent poisons, and contaminating an atmosphere, affect large numbers of individuals at the same time; another body of argumentatists have urged that malaria are in themselves simple agents, perhaps always present in the atmosphere, but are brought at various times into greater activity by the condition of the atmosphere or by meteorological influences; others have supposed that malaria are simple and perhaps well-known substances, that they are always present, but that for their actions as poisons certain modifications or predispositions of the body are demanded; some have believed that there are as many specific malarious agents as there are specific diseases; others have disputed this and have supposed that the poisons which produce typhus and ague are really the same, but are modified in their effects, either by climate and season, or by peculiarity of constitution. Another class opine that there may be a few specific poisons, and that modifications of disease may occur from combinations of these, in like manner as a few chemical agents may by combinations play many parts and produce innumerable compounds.[26]

The miasmatic, atmospheric, chemical, electrical and fermentation theories of the causation of disease, put forth primarily in an-

swer to the problem raised by the differentiation among fevers, all proved to be ineffective in solving it. Too many questions were left unanswered by any of the theories. Too many exceptions had to be made to allow any generalization to stand. The correct solution turned out to lie in a theory which to the miasmatists seemed outrageously illogical, and which ultimately called for the highest degree of exacting scientific experimentation for its proof.

FOOTNOTES TO CHAPTER TWO

* A considerable amount of the material in this chapter and at the end of the third chapter originally appeared in my article "Etiological Theory in America Prior to the Civil War," Journal of the History of Medicine and Allied Sciences, II, No. 4, 489-520 (Autumn, 1947).

1. William Osler, An Alabama Student and Other Biographical Essays (Oxford, 1929), chapters on the influence of Louis and the French work in the early 19th century.

2. Elisha Bartlett, The History, Diagnosis and Treatment of the Fevers of the United States (Philadelphia, 1847). This is the second edition and elaboration of his first book: The History, Diagnosis and Treatment of Typhoid and of Typhus Fever; With an Essay on the Diagnosis of Bilious Remittent and of Yellow Fever (Philadelphia, 1842).

3. Sir Gilbert Blane, Select Dissertations on Several Subjects of Medical Science (London, 1822), Pt. IX, "On the Yellow Fever," 321. See also Robert Jackson, A Sketch (Analytical) of the History and Cure of Contagious Fever (London, 1819), Outline of the History and Cure of Fever, Endemic and Contagious...(Edinburgh, 1798); David Hosack, Essays on Various Subjects of Medical Science (New York, 1824), I; William Currie, A Treatise on the Synochus Icteroides or Yellow Fever as it Lately Appeared in the City of Philadelphia...(Philadelphia, 1794), Observations on the Causes and Cure of Remitting or Bilious Fevers (Philadelphia, 1798); William Cullen, First Lines of the Practice of Physic (1794); Meredith Clymer, Fevers: Their Diagnosis, Patholo y and Treatment (Philadelphia, 1846); Bartlett, History, Diagnosis and Treatment of Typhoid and of Typhus, History Diagnosis and Treatment of the Fevers of the U.S.; Benjamin Rush, Medical Inquiries and Observations (Philadelphia, 1805), IV; Samuel Jackson, An Account of the Yellow or Malignant Fevers as it Occurred in the City of Philadelphia in 1820 (Philadelphia, 1821); Edward Nathaniel Bancroft, Essay on the Yellow Fever (London, 1811), Sequel to an Essay on the Yellow Fever (London, 1817); Noah Webster, Jr., A Collection of Papers on the Subject of Bilious Fevers Prevalent in the United States for a few Years Past (New York, 1796), Brief History of Epidemic and Pestilential Diseases (London, 1800); Edward Miller, Medical Works (New York, 1814); Proceedings and Debates of the Third National Quarantine and Sanitary Conven-

tion held in the City of New York, April 27th, 28th, 29th and 30th 1859 (Document No. 9, New York, 1859). A list of the more prominent adversaries is found in Edward Bascome, A History of Epidemic Pestilences...with Researches into Their Nature, Causes, and Prophylaxis (London, 1851). For a recent account of aspects of the contagion controversy, see E. H. Ackerknecht, "Anticontagionism between 1821 and 1867", Bulletin of the History of Medicine, XXII, No. 5, 562ff (September-October, 1948).

4. Sir Gilbert Blane, Select Dissertations, Pt. IX, "On the Yellow Fever", 321.

5. James Lind, Sir Gilbert Blane and probably Meredith Clymer used the terms synonymously, while David Hosack made a careful differentiation. D. Hosack, Essays, I, 254 (mentions Lind); Blane, Select Essays, "On Infection," 205; Clymer, Fevers, 100-560 passim.

6. James Lind, An Essay on Diseases Incidental to Europeans in Hot Climates, 4th ed. (London, 1788), 68; Benjamin Rush, Medical Inquiries, IV, "An Inquiry into the Various Sources of the Usual Forms of Summer and Autumnal Diseases in the United States," 175; Noah Webster, Brief History, II, 166-67, Collection of Papers, "Letter of Dr. E. H. Smith to William Buel," 76; Valentine Seaman, "An Account of the Epidemic Yellow Fever as it Appeared in the City of New York in the Year 1795," IN Webster, Collection of Papers, 3; Usher Parsons, On the Comparative Influence of Vegetable and Animal Decomposition as a Cause of Fever (Philadelphia, 1830), 12-18; James Copland, A Dictionary of Practical Medicine, ed. Chas. A. Lee (New York, 1845), II, "Epidemics," 777; J. Franklin Reigert, Treatise on the Cause of Cholera (Lancaster, Pa., 1855), 12.

7. John W. Monette, "Observations on the Epidemic Yellow Fever of Natchez and of the South-west," West. Jour. Med. Surg., IV, 172 (Sept. 1841); Parsons, Comparative Influence, 13; Anonymous, "Book Review," Amer. Quart. Rev. IV, 288n (Dec. 1828); Charles Caldwell, Essays on Malaria and Temperament (Lexington, Ky., 1831), 17ff.; A. P. Wilson Philip, A Treatise on Febrile Diseases ... 2nd ed. (Hartford, 1816), 74ff, 149ff; Benjamin Rush, Medical Inquiries, IV, 163ff.

8. M. L. Knapp. Inquiry into the Nature of the Nursing Sore Mouth Affection (n.p., 1856), Ch. III, "Etiological Deductions--Malaria," 261.

9. Caldwell, Essays on Malaria, 35.

10. Charles J. B. Williams, Principles of Medicine, comprising General Pathology and Therapeutics (Philadelphia, 1844), 73-74; R. S. Holmes, "On Malaria in Connection with Medical Topography," St. Louis Med. Surg. Jour., V, No. 6, 532 (May 1848).

11. See, for example, the classification of Dr. Joseph Smith:

Order I. CONTAGION.
- Genus I. Contagion communicable exclusively by contact.
  - Species I. Contagion of itch, syphilis, sivvens of Scotland, laanda of Africa, framboesia or yaws, hydrophobia, vaccina.
- Genus II. Contagion communicable by contact and by atmosphere.
  - Species I. Contagion of smallpox, measles, chicken-pox, scarlet fever, hooping-cough.

Order II. INFECTION
- Genus I. Koino-miasma.
  - Species I. Proto-koino miasma, producing intermittent and remittent fevers.
  - Species II. Per-koino miasma, producing yellow fever, and plague.
- Genus II. Idio-miasma.
  - Species I. Protidio-miasma, producing the mild forms of typhus.
  - Species II. Peridio-miasma, producing the malignant forms of typhus.
- Genus III. Idio-koino miasma.
  - Species I. Protidio-koino miasma, producing the mild forms of compound fevers.
  - Species II. Peridio-koino miasma, producing the malignant forms of compound fevers.

Order III.
- Genus I. Sensible Meteoration, producing croup, pleurisy, and other phlegmasial disorders.
  - Species unidentified.
- Genus II. Epidemic Meteoration, producing influenza, pneumonia typhoides, angina, and various other epidemics.
  - Species unidentified.

- from J. Smith, Medical Works, 196. Reproduced in James Copland, Dict. of Practical Med., III, 1130-31, IV, 404-5n. An even more elaborate system may be found in Copland, Dictionary, IV, "Infection," 402-3. Other schemes in Cullen, First Lines of the Practice of Physic, Part I, "Fevers,", 540ff.; Edward Miller, Works, "Nomenclature," 194ff.; Noah Webster, Brief History, II, 339ff.

12. Copland, Dictionary, II, "Disease,", 556-570.

13. Alfred Stillé, Elements of General Pathology...(Philadelphia, 1848), Pt. I, 5-113.

14. Amer. Quart. Rev., IV, 299; Henry Clutterbuck, Observations on the Prevention and Treatment of Epidemic Fever (London, 1819), 57; Webster, Collection of Papers on the Subject of Bilious Fevers, 233ff.; Webster, Brief History, II, 120-95.

15. Robert Jackson, Outline of the History and Cure of Fever, Endemic and Contagious, I, 102.

16. J. Val. de Hildenbrand, A Treatise on the Nature, Cause and Treatment of Contagious Typhus, trans. S. D. Gross (New York and Philadelphia, 1829), 76, 83. Hildenbrand believed that contagion entered the system through the alimentary canal, lungs, abraded skin, and by means of direct contact - a very modern approach.

17. David Hosack, Essays on Medical Science, I, Appendix, Note I, 359. Letter from Rev. Samuel S. Smith, Princeton, Jul, 24, 1808; Richard Mead, A Short Discourse Concerning Pestilential Contagion, 6th ed. (London, 1720), 13; W. C. Daniell, Observations upon the Autumnal Fevers of Savannah (Savannah, 1826), 47.

18. S. H. Dickson, "Account of the Epidemic which Prevailed in Charleston, S. C. During the Summer of 1827," Amer. Jour. Med. Sci., II, 64ff. (1828); James F. Gayley, "On the Etiology of Intermittent and Remittent Fevers," Amer. Jour. Med. Sci., XVII, No. 33, 53ff. (Jan., 1849); Daniel Blair, Reports on the First Eighteen Months of the Fourth Yellow Fever Epidemic of British Guiana [1853]; J. W. Heustis, "Remarks on the Endemic Diseases of Alabama," Amer. Jour. Med. Sci., II, 27 (1828).

19. Caldwell, Essays on Malaria, 36ff.; Usher Parsons, Boylston Prize Dissertations (Boston, 1839), Ch. 5, 227.

20. M. L. Knapp. Discovery of the Cause, Nature, Cure and Prevention of Epidemic Cholera (Cincinnati, 1855), Inquiry into Nursing Sore

Mouth Affection, 267; Copland, Dictionary, IV, 402-3.

21. Anonymous, Amer. Quart. Rev., IV, 294; John E. Cooke, Essays on the Autumnal and Winter Epidemics (Transylvania Univ., 1829), 7ff.; J. B. McCartney, "Cholera and Periodic Diseases," St. Louis Med. Surg. Jour., XIV, No. 2, 105-119 (Mar., 1865); Caldwell, Essays, 36-49; J. K. Mitchell, On the Cryptogamous Origin of Malarious and Epidemic Fevers (Philadelphia, 1849), Lecture I; Mead, Discourse on Contagion, 17; Holmes, "Malaria and Topography," St. Louis Med. Surg. Jour., V, 520.

22. Rush, Medical Inquiries and Observations, IV, 169-70, 385; Caldwell, Essays, 94.

23. Samuel Forry, "Statistical Researches Elucidating the Climate of the United States and its Relation with the Diseases of Malarial Origin; Based on the Records of the Medical Department and the Adjutant General's Office," Amer. Jour. Med. Sci., July 1841, N.S. II, 46.

24. Henry G. Clark, Ship Fever, so called; Its History, Nature and Best Treatment (Boston, 1850), 21.

25. Thomas Herbert Barker, On Malaria and Miasmata and Their Influence in the Production of Typhus and Typhoid Fevers, Cholera, and the Exanthemata: Founded on the Fothergill Prize Essay for 1859 (London, 1863), Ch. 12 and 13.

26. Ibid., 67-68.

Chapter 3 The Contagium Vivum Theory

There was one ancient hypothesis concerning the causes of disease which received attention from a small minority throughout the ages. This was the theory that disease was caused by minute, self-reproducing forms of life. In the earlier centuries not all proponents of the theory had the same views on the type of life involved. Assuming that everything is living which makes "a self-preservative gesture," to borrow Edgar A. Singer's modification of Aristotle's view, there were two general lines of progress in the development of the contagium vivum theory. One of these involved a virus-like view of contagion and the other an animalcular. The first point of view, coming from the Greek and Roman atomists, held that the seeds of contagion were capable of rapid reproduction within a human body, but did not specify whether a chemical poison or a type of ferment or even some form of organized life was involved. This line, which may be followed through the works of Lucretius, Fracastoro, Mead, Astruc and Tytler, and which culminated in the zymotic or ferment theory of disease, produced the doctrine of specificity in disease. The actions outlined for the "chemical" agent were similar to those of the modern virus.

The second concept was derived from the Roman agricultural writers, Varro and Columella, and may be followed through the work of Kircher, Lancisi, Marten, Plenciz, Henle and others, leading directly to the germ theory of disease. These writers were certain that contagion

resulted from the actions of living animals or plants. In the earlier centuries there was little distinction made between organisms of an animal or vegetable nature, and for this reason the proponents of theories of this type are generally referred to as animalculists in this thesis.

The two traditions merged temporarily in the work of Plenciz and Henle, as the animalculists took over the doctrine of specificity - holding that different diseases were caused by specific and separate forms of organized life. In spite of this merger, both lines of development continued to flourish in their independent ways. Liebig's work on fermentation was absorbed into the virus-like line, and aided in producing the zymotic theory of disease. This latter hypothesis was highly plausible before microscopic work disclosed the nature and functions of the pathogenic bacteria, and is still worth considering in the light of current views on the nature of a virus.[1] The animalcular line, for its part, led directly to the "germ theory" of disease. It should be emphasized that there were three types of concepts involved in medical thinking in etiology. The causal factors could be developed in and out of the body as in the case of bacteria; they could only reproduce in the living body as in the case of viruses, or they were purely chemical substances incapable of reproduction. The last case has been considered in the previous chapter, and only the first two are considered here.

I

The general theory of a contagium vivum may have had its original roots in the work of the Greek atomists. In the Letter to Herodotus of Epicurus, the point is made: "First of all, that nothing is created out of that which does not exist, for if it were everything would be created out of everything with no need of seeds." This removes the possibility of spontaneous generation, and calls for the necessity of "seeds" in reproduction of all kinds. In another part of the Letter, Epicurus brings in his atomistic doctrine, to the effect that "living things and plants and all the rest of things we see" are composed of kinds of seeds.[2] The "seeds" of Epicurus are both germ cells in the first instance and atoms in the second case. Thus no difference is made between the original "seed" giving rise to an organism and the "seeds" of which it is made, and furthermore, living and non-living matter are not separated in this latter respect. Nevertheless, his atomism was a first step towards the idea that all living things have parents, and that they are composed of small particles of matter.

The atomistic work of Epicurus was carried on by his successors, notably Lucretius in the Roman period (Fl. 99-55 B.C.). In his poem, De Rerum Natura, Lucretius further developed the theory of atoms, and the first line of development of the contagium vivum theory may be considered as beginning with his work. Much has been made of his conclusion that seeds which are of assistance in producing life could also pro-

duce disease and death, but a full reading of the passage in which this view was suggested makes it plain that Lucretius had an atmospheric theory, and not one involving the idea of living contagion:

> First I have shown before that there are seeds of many things which are helpful to our life, and on the other hand it must needs be that many fly about which cause disease and death. And when by chance they have happened to gather and distemper the sky, then the air becomes full of disease. And all that force of disease and pestilence either comes from without the world through the sky above, as do clouds and mists, or else often it gathers and rises up from the earth itself, when, full of moisture, it has gotten muddiness, smitten by immoderate rains or suns....

The latter part of this quotation even suggests a miasmatic theory. Lucretius, however, goes on to explain his ideas further:

> .....And so each place is harmful to the different parts and limbs: the varying air is the cause. Wherefore, when an atmosphere, which chances to be noxious to us, sets itself in motion, and harmful air begins to creep forward, in the form of cloud and mist; crawls on little by little, and distempers all, wherever it advances, and brings about change; it comes to pass also, that when at last it comes to our sky, it corrupts it, and makes it like itself, and noxious to us. And so this strange destruction and pestilence suddenly falls upon the waters or settles even on the crops or other food of men or fodder of the flocks; or else this force remains poised in the air itself, and, when we draw in these mingled airs as we breathe it, it must needs be that we suck in these plagues with them into our body.[3]

Very clearly it may be seen that a poison of a gaseous nature is involved here, - one with sticky molecules possibly, but definitely not composed of animalculae.

The work of Lucretius was carried on by Girolamo Fracastoro in the sixteenth century. In his famous De Contagione et Contagiosis Morbis et Eorum Curatione, published in 1546, Fracastoro gave a clear expression of the nature of contagion. This was believed to take place

by means of three kinds of imperceptible particles, depending on the type of contagion involved. The first kind of particles were hot, moist ones, passing by touching or direct contact; the second type were fomites - sticky, viscous "germs" clinging to porous bodies; the last category consisted of tiny solid particles passing thru the air to produce the same disease in a new body, a case of action at a distance. Though the text of Fracastoro's work shows much Aristotelian influence, some of his ideas were fairly novel. In Chapter Twelve, he discussed the different modes of attack of the various kinds of contagions, and he noted that particles were produced in the living body by putrefaction, and conveyed to other living, warm bodies, but not to dead ones. Air was judged to be the most suitable medium for conveying infections, but water, marshes, and other sources, such as the action of the heavenly bodies (!) were also significant.

Most important of these ideas was the observation that particles procreate progeny similar to themselves, which carried contagion to other living creatures. These "germs" were then activated by the body temperature of the host and generated more contagious atoms like themselves. In his chapter on "Signs of Contagions", Fracastoro revealed a more classical outlook, discussing astrological, astronomical and meteorological signs, such as comets, certain winds and so forth, large numbers of insects just before an epidemic, the instance of mice leaving their homes, and the influence of earthquakes.[4] Some of these now seem bizarre, while others have some basis in epidemiologic ex-

perience.

In regard to his use of the word "seeds" for germs, the work of Fracastoro is said to be an echo, with adaptation, of the ideas of Lucretius,[5] but rather it appears to be an imaginative expansion following hints in Lucretius. There is probably no doubt that Fracastoro borrowed his original idea from Lucretius, but he developed it into something entirely different. Some modern writers have expressed doubt as to whether Fracastoro's particles were meant to be living, organic matter, or whether they were some chemical substance.[6] His "seeds" have the self-preservative quality necessary to be considered as "life", even though they were not thought to be alive outside the human body. (Again one if forceably reminded of the virus). At any rate, Fracastoro's ideas are the closest approximation of a "germ theory" available before the eighteenth century.

The seventeenth century was a period in which, as a rule, the animalcular line of development was more prominent. Robert Boyle, however, thought that the causation of disease bore some relationship to the nature of fermentation, so that the understanding of one would ultimately lead to an understanding of the other.[7] It is interesting that this eventually proved correct. There was a very close relationship between work on fermentation and the developing germ theory, even though there may seem to be little connection in the early stages.

By the time one reaches the eighteenth century, it becomes apparent that the virus-like concept was beginning to advance considerably

beyond the views of Fracastoro. By this time, too, the European work had begun to have some influence in America. The first eighteenth-century book of importance in both respects is Richard Mead's A Short Discourse Concerning Pestilential Contagion (1719). This work contains a hint of the animalcular hypothesis, which is rejected in favor of a chemical theory of fomites:

> It has been thought so difficult to explain the Manner of this [contagion by fomites], that some Authors have imagined Infection to be performed by the means of Insects, the Eggs of which may be conveyed from Place to Place, and make the Disease when they come to be hatched. As this is a supposition grounded on no manner of Observation, so I think there is no need to have Recourse to it. [8]

Mead believed that contagion was propagated by three causes: the air, diseased persons, and goods transported from place to place. This again is a repetition of Fracastoro. Mead's "matter", "atoms" or "seeds" of contagion were thought to be "perhaps in the Nature of a Salt, generated chiefly from the Corruption of a Humane Body." This term in itself seems to support Winslow's views that such theories related not to organized life, but to chemical substances,[9] but Mead's "salt" was capable of rapid reproduction within a human body - again, like a virus.

In 1736 an interesting French theory appeared, which again shows the influence of Fracastoro.[10] Jean Astruc of Montpellier, writing on the nature of venereal poison in De Morbis Veneris, made the point that venereal disease is conveyed from the sick to the sound by means of "certain Seeds of morbifick Matter, which being introduced into a healthy Body in the smallest Quantity, and by insensible Passages, and gradually

increasing in Bulk, Form and Efficacy, sooner or later are able to infect and corrupt the whole Mass of Humours. And the Seeds of the Disease are usually, and not improperly, named the Venereal Ferment, Venom, or Poison."[11] The similarity to the ideas of Fracastoro is striking, especially so since Fracastoro also wrote on syphilis. Astruc, however, went farther than Fracastoro and applied this method of propagation to all contagious diseases. He introduced the idea of a specific contagion for each disease:

> So the Small-Pox may be communicated by taking a small Portion of corrupted Matter out of the Pustules, and applying it to an Incision made in the Skin; the Plaque, by Matter flowing out of the Buboes, and dropt into a wound made in any Animal; the itch or Tetters, by the Ichor discharged from a diseased Skin, and adhering to a sound one; the Hydrophobia, by the admission of the Saliva of a Mad Dog into the Part that is bitten; the Indisposition occasioned by the Tarantula, by the Humour which the Spider conveys by its Bite into the Skin, as by so many Ferments peculiar to each Disease. [11]

There are several interesting points in this statement by Astruc. It is not clear whether by "seeds" he meant animalculae, chemical poisons or something analogous to a virus, but is is possible to interpret him as suggesting a virus-like concept. The inoculation process in all these cases, especially the plague conveyed to animals, suggests that some experimentation has been done. There was a clear knowledge of the relationship between the itch mite and scabies. The identification of the saliva per se as the offending agency in hydrophobia was important. Astruc's doctrine of specificity in disease laid the groundwork for future developments by Plenciz, Tytler and Henle.

James Tytler seems to have picked up the general idea of specificity, though he did not relate it to animalculae any more than to any other cause. In his Treatise on the Plague and Yellow Fever, which was published for Americans at Salem in 1799, Tytler declared that a disease had similar symptoms wherever it was found. Thus smallpox was the same disease in America that it had been in Turkey. Therefore he concluded that each separate disease must have its own specific contagion. His work evidently received some attention in America because Samuel Brown of Boston went out of his way to ridicule it. Brown especially objected to Tytler's summary:

> Thus the matter of the small-pox, whether existing in the matter of a pustule, in the smoke of burning clothes or paper, or in the effluvia of the blood, is invariably the same, and never produces any other disease.[12]

The statement of Tytler was, of course, a complete denial of the unity-of-disease idea then current in America. Tytler was probably more influenced by Astruc than by any other author.

Probably even more directly influenced by the work of Astruc was the French authority L.-B. Guyton-Morveau, famous in the field of chemistry. Guyton-Morveau thought that each contagious disease had its own specific agent or virus. This material was a kind of ferment, capable of reproducing itself under proper conditions.[13]

A less distinct solution as to the nature of the contagious agent was made by the Englishman Robert Jackson in 1819. He believed that typhus was contagious by some means which propagated

> its kind through the mechanism of animal organism, and thus, propagated, it attaches itself to foreign substances, and is conveyed to distant places and different persons in a state of more or less activity..... It is evident that a cause which generates its kind and manifests that kind by an external product, cannot act otherwise than on an organ of exretion. The product is invisible; it must, therefore, be supposed to be manufactured by and to proceed from the minutest of secreting vessels, viz., those which give out invisible exhalation from the external skin or lining of interior canals.[14]

Jackson's views had considerable currency in America, although they seem rather vague. The "cause which generates its kind" is not sufficiently defined to make it clear whether he was referring to a chemical or organic substance, but the fomite approach suggests a chemical material similar to the fomites of Fracastoro.

Another European who had considerable influence in America was J. V. de Hildenbrand, a Viennese professor whose book on typhus fever was translated for American readers in 1829. Hildenbrand's theory of disease is interesting because it comes close to the animalcular hypothesis, while retaining an atmospheric approach. He said:

> Every contagious miasm possesses the properties, 1, of producing a similar virus in the disease which it has occasioned; and 2, of spreading and extending itself ad infinitum, by virtue of this secondary development, that is so long as there exists a matter capable of receiving the miasm, and of producing a new one. Both these properties are similar, by their power of reproduction, to the germs of animals and of plants; but the last property is analogous to the matter of fire, since a single atom of contagious virus, like a spark, is capable of spreading itself ad infinitum, and of traversing, when unobstructed in its progress, all bodies capable of receiving it.[15]

The difficulty of expressing scientific ideas with an inadequate terminology is nowhere better seen than in this paragraph. Hildenbrand uses

"miasm", "virus", "germ", "atom", all to convey the same basic idea. He does not consider his virus as a living contagion, but it possesses the properties of a live organism. This could easily fit into the virus-like concept. Hildenbrand also wrote that contagious matters had different degrees of volatility, some like the virus of rabies having none at all, and others like scarletina having a high volatility when suspended in an animal atmosphere. This seems to be a sort of specificity, with each contagion considered as a distinct gas.

The works of Tytler, and of Guyton-Morveau were not very popular in America. Tytler's specificity doctrine may have influenced the miasmaticists who were dividing up their miasmata among the known diseases; and the ferment idea of Guyton-Morveau and Liebig was mentioned in up-to-date texts after 1845, such as those of Wood and Stillé.[16] The writings of Jackson and Hildenbrand, with their ambiguous terminology, were capable of more liberal interpretation and therefore were less apt to arouse controversy. Jackson was frequently quoted by contagionists in their controversy with the non-contagionists.

The virus-like line of development of the contagium vivum concept has been traced from Lucretius to the early nineteenth century. It did not involve the idea of an organized living creature of minute size, but rather the notion of a chemical substance or specific ferment endowed with the properties of life - similar to the modern virus. The next stage, which took place in the mid-century, was that of determing the exact nature of the ferment, and assigning a special "zyme" or ferment-poison

to each disease. In the meantime, the animalcular line of development had also progressed, and this theory must be examined in both its European and American aspects.

II

The animalcular version of the doctrine of contagium vivum originated in the work of the Romans, Varro and Columella. Varro attributed the adverse affects of marsh air to the presence of tiny insects, too small to be seen by the eye. These were breathed in and caused disease.[17] Though similar ideas are supposed to be found in Ovid's Fasti and Metamorphoses and Pliny's Natural History, I have not been able to find anything tangible in any of these works. In Columella's book on agriculture, however, there is a passage very much like that in Varro. Speaking of the location of farm buildings, he says:

> And neither should there be any marsh lands near the buildings... for the former throws off a baneful stench in hot weather and breeds insects [animalia] armed with annoying stings, which attack us in dense swarms; then too it sends forth plagues of swimming and crawling things deprived of their winter moisture and infected with poison by the mud and decaying filth, from which are often contracted mysterious diseases whose causes are even beyond the understanding of physicians.[18]

The hypotheses of Varro and Columella definitely attribute disease to the action of living organisms, in both cases to little animalia - "insects" or animalculae.

This concept of the Roman agriculturalists was apparently ignored during the Middle Ages, but it was revived during the sixteenth century.

Jerome Cardan thought the "seeds" of disease were themselves alive; and others of his century, Gabriele Falloppio, Paracelsus and Victor de Bonagens (Bonagentibus), held similar views. In the seventeenth century, the idea of a living contagion was employed in the work of Athanasius Kircher (and his supporters Christian Lange, Marchmont Needham and others), possibly in that of Pierre Borel; and it also appeared, with regard to the parasitic nature of scabies, in the writings of August Hauptmann, Michael Ettmüller, and Cosimo Bonomo.

There is considerable difference of opinion as to whether or not Kircher deserves recognition as a full-fledged animalculist. Some authors, such as Winslow, rank him very highly, while others, such as Torrey, believe he merely copied his predecessors and added nothing to existing ideas.[19] His scientific reputation suffers from the fact that his microscopic "worms" could not possibly have been bacteria because his microscope was not strong enough to see them, and these "vermes" were probably rouleaux of red blood corpuscles. The conclusion to which he jumped is his great redeeming feature and this definitely places him in the ranks of those who believed in a contagium animatum. Similar disagreement exists regarding Borel. Not much work has been done on the less famous figures of the sixteenth and seventeenth centuries. It is entirely possible that other animalculists have yet to be discovered.

Several able animalculists were active during the eighteenth century, though none of these except Plenciz based their work on observation as Kircher had done. One of the clearest animalcular hypotheses was that

of Giovanni Maria Lancisi, published in his De Noxiis Paludium Effluviis in 1717. Lancisi believed that the marshes gave rise to some extremely minute insects which escaped into the atmosphere and were scattered in all directions. He suggested that the eggs of such tiny insects caused disease when swallowed with food or water, when entering the body with the saliva of such a biting insect as the mosquito. These eggs developed into minute worms in the blood stream, and he thought that the blood of patients with typhus and plague should be examined microscopically to see if there were any such animalculae in it.[20] This was an effective explanation in the case of malaria, and the choice of plague and typhus as insect-derived diseases was a rather fortunate coincidence. The views of Lancisi were made available to American readers, one hundred years after their publication, through Samuel Latham Mitchill's translation of his work, which appeared in the Medical Repository for 1818.[21]

A few years after Lancisi published his theory, three English writers, of which two were physicians and one a layman, employed the animalcular view in accounting for contagion in plague and phthisis. One of the physicians was Sir Richard Blackmore, who, in 1721, considered the possibility that microscopic "worms" might cause plague, but he dismissed this notion in favor of the conclusion that these "worms" were the effect and not the cause of "pestilential putrefaction." The other physician was Benjamin Marten, who suggested in the following year that animalculae, reproducing by means of ova or eggs, were the cause of phthisis, and these differed from those causing smallpox.[22] This is the

first known suggestion of a differentiation among animalculae to account for different types of diseases. Probably the influence of Fracastoro accounts for this, since the work of Astruc had not yet appeared.

The layman was the author, Daniel Defoe, who had picked up the animalcular hypothesis, and a rather effective expression of it was put to scorn in A Journal of the Plague Year (1721):

> [I look with contempt] likewise upon the Opinion of others who talk of Infection being carried on by the Air only, by carrying with it vast Numbers of Insects and Invisible Creatures, who enter the Body with the Breath, or even at the Pores with the Air, and there generate or emit most acute Poisons, or poisonous Ovae or Eggs, which mingle themselves with the Blood, and so infect the Body.[23]

A suggestion of the work of Leeuwenhoek is also brought in by Defoe:

> I have heard, it was the opinion of others, that it [plague] might be distinguish'd by the Party's breathing upon a piece of Glass, where the Breath condensing, there might living Creatures be seen by a Microscope of strange monstrous and frightful Shapes, as Dragons, Snakes, Serpents, and Devils, horrible to behold: but this I very much question the Truth of, and we had no Microscopes at the Time [1665], to make the Experiment with.[23]

As Leeuwenhoek's first communication to the Royal Society was not sent until 1763, this accounts for Defoe's "no microscope" statement. The explanation of contagion accepted by Defoe is Richard Mead's air-fomite-direct contact one.[23]

Other important contributions were made by Linnaeus, who supported the idea of a parasitic origin of disease to some extent, and who classified the odd creatures discovered by Leeuwenhoek with the infusoria - a fortunate choice foretelling the relationship between the infusoria and microbes. J. C. Nyander, whose work was published in 1757, adopted the

opinion of Kircher in connecting animalcular causes with contagious diseases. He declared that the existence of animalculae was already demonstrated in the case of scabies, dysentery, syphilis, smallpox, plague, and some skin diseases, but this claim was slightly premature.[24]

The most important work of the eighteenth century was probably that of Marcus Antonius Plenciz, who adapted the specificity concept of Jean Astruc to the animalcular hypothesis. Plenciz, in 1762, wrote that disease was spread by numbers of minute animalculae, which were admitted to the human body by the pores or other openings (including abraded skin - inoculation, or by inhalation, or by being taken in with bits of sputum - a clear case of contagion). He linked the animalculae found in putrefying material with those producing disease, and he gave each disease its own specific, living, organic cause. This agent, when introduced into the body, underwent rapid reproduction and resulted in a particular disease.[25] Plenciz produced much supporting evidence for his argument, some of which may have been obtained by experimentation. His views and those of Nyander were essentially correct, but incapable of demonstration at the time because the microscopes and techniques were not sufficiently developed.

The influence of Plenciz, or possibly Nyander, appears unexpectedly about 1788 in the lectures of John Walker, Regius Professor of Natural History at the University of Edinburgh. Walker told his classes that it was highly probable that "the Itch, the Pox, the Plague, are the effects of Animalculae of different species."[26] If any Americans then studying in

Edinburgh absorbed this notion at Walker's lectures, they do not appear to have retained it long.

Before considering the animalculists of the nineteenth century, a word should be said concerning the discoveries made in connection with skin diseases. The "worms" of Lancisi and Blackmore, and the earlier "vermes" of Kircher had some basis in fact. It had long been known that intestinal worms caused illness. Moreover, the parasitic origin of scabies had been demonstrated in the Middle Ages by the Mohammedan physician, Avenzoar the Cordovan (died 1162). The actual itch acarus was discovered in the seventeenth century by August Hauptmann (1657), Michael Ettmüller (1682), and C. G. Bonomo (1687). It was rediscovered in the eighteenth century by J. E. Wichmann, who, in 1786, clearly described it. Other skin diseases were known in the early nineteenth century to be of parasitic origin. For example, Johann Lukas Schönlein picked up Agostino Bassi's work on the silkworm disease, muscardine, and decided to search for human diseases of similar parasitic origin. He soon discovered the cause of favus. Other parasitic skin diseases yielded up their secrets to contemporaries of Schönlein. The several discoveries of the trichina spiralis in this same period created something of a sensation, since this painful muscle disease was then shown to be of parasitic origin. It seems odd that there was not more carry-over from the known causation in these parasitic afflictions to the idea of microscopic parasites as specific causes of the infectious diseases, particularly of fevers.

The discovery of parasitic ailments in the early nineteenth century

coincided with an increasing interest in the animalcular hypothesis. The contagium vivum idea had developed slowly until the nineteenth century. Then followed a period of rapid advancement, involving three types of theory: First, the living organisms were seriously thought to be "little animals". In Ehrenberg's classification, protozoa such as the amoeba and paramecium were placed in the same catagory as types of bacteria.[27] By 1850, the animalcular hypothesis was related largely to the protozoa. Secondly, there was a theory that these living particles were vegetable germs or spores of plants or fungi. The cryptogamous theories followed this pattern. Thirdly, both catagories were accepted, but the living organisms were considered to be a ferment or catalyst and not in themselves the exciting cause of the disease. This aspect of the animalcular theory should not be confused with the zymotic theory, in which the ferment involved was a specific chemical poison, with properties of life, but not itself organized life. Ultimately a combination of the first and second views into a new concept of living contagion proved to be the correct solution. The third is retained in the concept of a bacterial toxin.

A glimpse into the future may be caught from the speculations of J. G. Millingen, an English writer whose work appeared in an American edition in 1838. In an essay on "Generative Animalcules", Millingen mentioned that an experiment had been performed by "Gale", who had taken animalculae from a case of the itch, kept them alive in a watch-glass culture, and infected himself with them - producing a similar case of the itch.

From this Millingen came to the conclusion that animalculae were the cause and not the consequence of disease, and he added:

> I repeat it, the subject is replete with interest; and microscopic experiments may some time or other throw a material light on the practice of medicine. Those substances that are known to destroy the insect that produces the itch, cures the malady. May not this analogy lead to singular results?[28]

No attempt appears to have been made to follow up this foresight by experimentation. The postulates of Henle and Koch are carried out in the experiment cited, and the author had a clear insight into the possibilities of the method. Yet more than thirty years were to pass before scientific demonstration of the method took place.

One theorist who received a considerable amount of attention in America was the English physician, Sir Henry Holland. He declared in 1839, that it was entirely possible that minute insect life, invisible to the naked eye, might be the cause of disease. Furthermore, he considered that perhaps epidemic cholera was occasioned by swarms of insects going from one place to another, and that the cycles of virulence in this disease might be due to the incubation periods in the reproductive life of the insects involved. He then logically proceeded to the idea that the insects provided a constant reservoir of infection, ready to expand if opportunity presented itself.[29] Holland also advanced the thought that man himself might be the agent of transmission. His combination of man and "insect" or vibrio as the agents in producing cholera might have led to the final solution, if he had also been able to add John Snow's pump and complete the cycle by showing it to be a water-transmitted disease. This

compound type of reasoning was to evade the theorists for another thirty years.

Jacob Henle, who published his essay, On Contagions and Miasms in 1840, was in advance of his time. Though he lacked exact terminology, which made it difficult for him to express his theories precisely, he realized the real nature of contagion. He clearly stated the criteria necessary in order to prove the germ theory of disease - the famous Henle postulates, which his pupil, Robert Koch, clarified and put into practice.[30] Henle noted that a broken skin was essential in the inoculation type of contagion. Writers like the Americans Hodge and Meigs, who fulminated against Oliver Wendell Holmes' work on contagion in puerperal fever, missed this point altogether.

Henle believed that disease was caused by seeds or germs, which were living organisms. These entered the system through mucous membranes, the alimentary canal, and broken skin. Inside the body they increased rapidly, a fact verified by the period of incubation after exposure to the disease. Henle thought the germs were probably plant parasites or fungi, of which different varieties produced different diseases. This was Astruc's doctrine of specificity in combination with the animalcular hypothesis. Fever, in Henle's scheme, was caused by local inflammation in inoculation cases, and by changes in the blood caused by parasites in the miasmatic types of disease. He reversed the usual thinking of the day by stating that putrefaction was caused by infusoria or fungi. The nearby air was filled with their germs. From this it followed that

effluvia must be infusoria, hence alive and capable of reproducing. He considered endemic disease the result of localized germs which infected the air near active infusoria or fungi. The human factor was thus eliminated for diseases in this catagory. The result is the old combination of Varro and Columella: bad air containing a contagium vivum which makes it deleterious.

One of Henle's views has since come into vogue in connection with pathogenic microorganisms. He thought that a strain could be gradually transformed from a mild form to a more virulent one. The example he used, however, shows that he had not yet absorbed the work of Gerhard and others who were differentiating specific disease entities: he thought it entirely possible that an intermittent fever could be gradually transformed by stages into a contagious typhoid or yellow fever. This idea seems in conflict with his previous conclusion that different parasites cause different diseases, and it rather confuses his doctrine of specificity. Evidently the influence of the older, accepted theories was still strong.[31] The work of Henle seems to have had little influence in America, though mention of his Pathologische Untersuchungen found its way into the British and Foreign Medical Review for 1840 and could have been noted by interested Americans.

There were many minor figures who held to the animalcular hypothesis, such as the Italians Mojon, Rasori, Grassi, the Frenchmen Grognier and Paulet, and the German, Boehm.[32] These men received little attention in America. In addition, there were others who were

quietly at work on parasites, infusoria and fermentation: Agostino Bassi, C. G. Ehrenberg, Baron Charles Cagniard de Latour, Theodor Schwann, and J. L. Schönlein. Their work was destined to lead directly to that of Pasteur and Koch and to modern bacteriology. Thus the groundwork was being laid for the experimentation that would eventually prove or disprove the hypotheses of the theorists.

Two textbooks of European origin which presented the animalcular hypothesis were used in America. The first was Charles J. B. Williams' Principles of Medicine, the American edition of which appeared in Philadelphia in 1844. On etiology, Williams wrote:

> Does the matter of contagion consist of animal ova or vegetable seeds? Are infectious diseases the results of invasions and operations of living parasites disturbing in sundry ways the functions and structures of the body, each after its own kind until the vital powers either fail, or succeed in expelling the invading tribes from the system? Such an opinion has been many times proposed, and is, in a degree, implied in the term incubation (sitting on eggs to hatch them), commonly applied to the period between the reception of the infection and the first appearance of the symptoms... The microscope should solve this problem, by detecting the germs and growths of these infecting agents, if such exist. Until this be accomplished, the nature of contagion must remain a matter of speculation.[33]

This is as open-minded a textbook view of the animalcular hypothesis as can be found. Williams agreed with Holland and Henle that "epidemic diseases are caused by animalcule tribes", giving the following reasons:

1. Epidemic diseases [occur in varying, uncertain periods] like blights or tribes of insects...

2. Proofs are accumulating of the occasional existence of parasitic animals and plants in living animals and in some cases as causes of disease...

3. [Epidemic diseases of some sorts - cholera, influenza— show disease may appear when animalcules suddenly develop from ova in the blood.][34]

There seems to have been little doubt in Williams' mind that epidemic diseases resulted from the presence of some kind of parasites. Any American student using this text must at least have been made aware that there were in existence other promising theories besides the common ones involving miasmata.

The second textbook, The Pathological Anatomy of the Human Body, was written by Julius Vogel and translated from the German by George E. Day for English readers in 1847. Vogel paid considerable attention to parasitic animals, particularly the infusoria. On this he wrote:

> The occurrence in the living body of the infusoria which have been thus described, and of other species which probably will yet be occasionally observed, need occasion no surprise, if we consider that infusoria generally, and especially the specified forms belong to the most abundant of all the lower animals, which make their appearance by the millions whenever conditions favourable for their development are afforded. They have little or no pathological importance, and at most serve but to show that, where they appear, there exists a putrid decomposition of the elements of the body to a greater or less extent, not otherwise demonstrable by exact means. Donné maintains that the vibriones of chancres... constitute the true contagion of syphilis, an opinion which is directly controverted by the fact, that these animalculae do not exist in the pus of syphilitic buboes, which, nevertheless, according to Ricord's experiments, by inoculation also produce actual chancres... Klenke states that he has observed in human blood the appearance of animalcules resembling infusoria, and traces their connection with the occurrence of periodical attacks of vertigo... How these animals gain access to the vascular system, is a point upon which at present we can only entertain conjectures, although I have no doubt that they penetrate from without, and are not engendered by equivocal generation.[35]

Vogel wavers between acceptance of a parasitic theory and a strong

skepticism about it. He is sure the infusoria are pathogenically unimportant, and yet he includes statements which support the opposite contention. He flatly confutes Donné, but mentions the work of Ricord which would sustain Donné's views! One is forced to the conclusion that Vogel thought the animalcular hypothesis worth mentioning, but was too cautious to accept it wholeheartedly. His text, like that of Williams, made it available to American readers, leaving them to form their own opinions on the matter.

A rather interesting incident occurred in England in 1849, concerning the contagiousness of cholera. A quotation in the Southern Quarterly Review reads:

> Dr. Brittain, of Bristol, appears to have been a diligent observer of the phenomena which usually accompany this disease (cholera). He found in the fluids ejected by cholera patients organic cells, which, upon being placed under the microscope, exhibit characters such as naturalists attribute to plants belonging to the order of fungi. He also succeeded in finding these cells in the fluids of cesspools and drains, as well as in the atmosphere of rooms where persons have died of, or were labouring under, cholera. Putting these facts together, Dr. Brittain comes to the conclusion that it is the existence of these cells in the body that produced cholera. These observations had been previously advocated by scientific men, and at the last meeting of the British Association at Birmingham, Dr. Alison, a very high medical authority, expressed the conviction that its propagation depended upon this cause.[36]

In a footnote to this statement, the reviewer added more information, remarking that since the above had been written, the Cholera Committee of the College of Physicians of London had investigated this fungoid origin of cholera and came to the conclusion that

> the bodies found by Messrs. Brittain and Swayne are not the

> cause of cholera, and have no exclusive connection with that disease. In other words, that the whole theory of disease which has recently been expounded is erroneous, so far as it is based on the existence of the bodies in question.[37]

The reviewer righteously added that this was a case of hasty inference from uncertain data. One wonders if Brittan and Swayne ever attempted to push their idea by means of further experimental verification, in spite of the weight of this authority against them. Americans do not appear to have paid more than passing attention to this work. Considering how easy it is now to go back and discover men whose work foreshadowed the coming bacteriology, such as Donné, Brittan, Swayne, Klencke, Valentin, Ricord and others, it is remarkable how little attention any of them received in America.

The animalcular line of development of the theory of contagium vivum has been traced from the Romans through to the textbook writers of the nineteenth century. The work of Lancisi, Plenciz and Henle advanced it to a point where all that was needed was application of a rigid scientific method and an improved laboratory technique. Some hints of things to come were obtained from the writings of Millingen and Williams. The doctrine of specificity had been taken over from the chemical line of development, and, reinforced by the findings of pathological anatomy and the discoveries of the microscopists, it had taken a permanent place in medical thinking.

The writers who have been mentioned in this chapter were by no means the only Europeans who were interested in the theory of contagium

vivum in its various forms. They include, however, the ones whose work most influenced Americans, and for this reason, they have been given special attention.[38] In the early nineteenth century, the Americans themselves were not merely following the course of European argument. Several of them made original contributions to it. These American animalcular hypotheses inspired a period of optimism and intellectual activity in the history of American medicine.

FOOTNOTES TO CHAPTER III

1. The zymotic theory will be discussed in more detail when the period of its hey-day (1860-1875) is taken up. (Chapter 5).

2. Epicurus, Epicurus: The Extant Remains, trans. and ed. Cyril Bailey (Oxford, 1926), 21, 47.

3. Lucretius, Titi Lucreti Cari De Rerum Natura Libri Sex, ed. Cyril Bailey (Oxford, 1947), I, Liber VI, lines 1092-1102 (pp. 570-71):

> .....primum multarum semina rerum\esse supra docui quae sint vitalia nobis,\et contra quae sint morbo mortique necessest\multa volare. ea cum casu sunt forte coorta\et perturbarunt caelum, fit morbidus aer.\atque ea vis omnis morborum pestilitasque\aut extrinsecus ut nubes nebulaeque superne\per caelum veniunt, aut ipsa saepa coorta\de terra surgunt, ubi putorem umida nactast\intempestivis pluviisque et solibus icta.

and Liber VI, lines 1117-1130, pp. 572-73. Commentaries in Vol. III.

4. Girolamo Fracastoro, Hieronymi Fracastorii De Contagione et Contagiosis Morbis et Eorum Curatione, Libri III, trans. W. C. Wright (New York, 1930), Book I, Ch. 1-13.

5. Ibid., Note 5, 302.

6. Charles-Edward Amory Winslow, The Conquest of Epidemic Disease (Princeton, 1944), 131-143.

7. Wade W. Oliver, Stalkers of Pestilence: The Story of Man's Ideas of Infection (New York, 1930), 131. Boyle's statement was in his "Essay on the Pathological Part of Physic."

8. Richard Mead, A Short Discourse Concerning Pestilential Contagion, 2nd ed. (London, 1720), 16.

9. Ibid., 17.

10. Writings in French in the eighteenth century are apt to be confusing as far as the germ theory is concerned because the words "germe" or "germes contagieux" are used in a manner similar to the use of the word "virus" in English at the same time. One author men-

tions "ces foyers pestilentials qui exhalent le germe de toutes les maladies" (Anon., Un malade de l'Hôtel-Dieu (Paris, 1787), advertissement, v), while Tenon, referring to discharged patients, says, "Les personnes guéries reçoivent, en sortant, leur vêtemens chargés de germes contagieux." (Jacques René Tenon, Mémoires sur les hôpitaux de Paris (Paris, 1788), 3rd mémoire, 199). In the first case an atmospheric poison seems intended, while the second refers to fomites.

11. Jean Astruc, De Morbis Veneris Libri Sex in E. R. Long, Selected Readings in Pathology from Hippocrates to Virchow (Baltimore, 1929), 97. Originally published in 1736; English translation 1754.

12. James Tytler, A Treatise on the Plague and Yellow Fever (Salem, 1799), 190; Samuel Brown, A Treatise on the Nature, Origin and Progress of the Yellow Fever (Boston, 1800), 93-95.

13. Louis B. Guyton-Morveau, Traité des moyens de désinfecter l'air, de prévenir la contagion, et d'en arrêter le progrès, (Paris, 1801), 232-34, paragraphs 145-46.

14. Robert Jackson, A Sketch (Analytical) of the History and Cure of Contagious Fever (London, 1819), 159-60.

15. J. V. de Hildenbrand, A Treatise on the Nature, Cause and Treatment of Contagious Typhus, trans. S. D. Gross (New York and Philadelphia, 1829), 73, 75. In point of time, Pierre Bretonneau, famous French clinician, comes between Jackson and Hildenbrand. His doctrine of specificity, however, was not printed until 1922 and had little influence among his contemporaries in France and in America. It belongs to the chemical line of development. Cf. P. Bretonneau, Traités de la dothinentérie et de la specificité publiés pour la première fois d'après les manuscrits originaux avec un avant-propos et des notes de L. Dubreuil-Chambardel (Paris, 1922).

16. George B. Wood, A Treatise on the Practice of Medicine (Philadelphia, 1847), I, 306; Alfred Stillé, Elements of General Pathology: a Practical Treatise on the Causes, Forms, Symptoms, and Results of Disease (Philadelphia, 1848), 104.

17. Varro, Marci Terentii Varronis Libri Tres De Re Rustica (Halle im Magdeburgischen, 1730), Lib. I, Ch. XII, 58-59. "Ubi ponenda sit villa." "...Advertendum etiam, si qua erunt loca palustria & propter easdem causas, & quod arescunt, & quod in iis crescunt [?] animalia in quaedam minuta, quae non possunt occuli consequi & per aëra intus in corpus, per os ac nares perveniunt, atque efficiunt difficiles morbos." (Notes referring to German translation have been omitted in this quotation.)

18. Lucius Junius Moderatus Columella, On Agriculture [Res Rustica], trans. H. B. Ash (Cambridge, Mass. and London, 1941), Bk. I, Ch. V, 62-63." ...quod illa caloribus noxium virus eructat et infestis aculeis armata gignet animalia, quae in nos densismes examinibus involant, tum etiam nantium serpentiumque pestes hiberna destitutas uligine, caeno et fermentata colluvie venenatas emittit, ex quibus saepe contrahunter caeci morbi, quorum causas ne medici quidem perspicere quent;"

19. Winslow, Conquest of Epid. Disease, 145-152; Harry Beal Torrey, MS "Athanasius Kircher and the Progress of Medicine", Stanford University; Hans Zinsser and Stanhope Bayne-Jones, Textbook of Bacteriology, 8th ed. (New York, 1939), 5. Kircher did not see real microscopic life as he thought, yet he connected his observations with disease. Leeuwenhoek, on the other hand, actually saw bacteria, but did not make any definite connection between them and disease.

20. Samuel Latham Mitchill, "A Translation from the Latin of the Celebrated J. Mar. Lancisi's Work, de Noxiis Paludum Effluviis," Medical Repository, N. S., VI, 1818, Appendix, Bk. I, Ch. 16-19.

21. Book I, in which the animalcular hypothesis is found, is printed in installments in the Medical Repository, N. S., VI, 1818, Appendix, 201-12, 322-32, 442-67.

22. Sir Richard Blackmore, A Discourse upon the Plague (London, 1721), 35; Benjamin Marten, A New Theory of Consumptions, 2nd ed. (London, 1722), 40-47.

23. Daniel Defoe A Journal of the Plague Year: Being Observations or Memorials of the most Remarkable OCCURRENCES, as well PUBLICK as PRIVATE, which Happened in LONDON during the last Great Visitation in 1665 (Oxford, 1928), 92, 247, 237. Originally published in 1721. Cf. also Walter Nicholson, The Historical Sources of Defoe's Journal of the Plague Year (Boston, 1919).

24. F. H. Garrison, Introduction to the History of Medicine, 4th ed. 311; Charles Louis Chevalier, Des microscopes et de leur usage... Manuel complet de micrographie. (Paris, 1839), 224. Linnaeus put this work of Nyander in his Amaenitates academicae.

25. Marcus Antonius Plenciz, Opera Medico (sic) Physica, in quatuor tractatus digesta, quorum primus contagii morborum ideam novam una cum additamento de lue bovina, anno 1761, epidemice grassante, sistit. Secundus de variolis, tertius de scarlatina, quartus de terrae motu sed praecipue illo horribili agit (atione) qui prima Novembris

anno 1755. Europam Africam, et Americam conquassabat (Vienna, John Thomas Trattner, 1762), Tractate I, Section I, Chap. 46-57, pp. 32-44, Section II, Chap. 72-94, pp. 55-79. Dr. William C. McDermott of the Department of Classical Studies of the University of Pennsylvania has kindly assisted the author in interpreting the work of Plenciz. A particularly significant passage in this book is found in Section II, Chap. 93: "Hoc ipsum, quod dictum est de communicatione, et propatione contagii variolosi per insitionem, intelligi et dici debet de communicatione et propagatione eiusdem quaecunque alia ratione humoribus nostris mixti sive enim materia contagiosa per vasa absorbentia periphaeriae corporis, sive per inspirationem, sive una cum saliva deglutita aut quaecunque alia ratione corpori communicetur, idem semper exinde exurgit effectus, et affectus."

26. William Smallwood and Mabel S. C. Smallwood, Natural History and the American Mind (New York, 1941), 73. MS. Univ. of Edinburgh, Rev. John Walker, "Lectures on Natural History", Lecture 2.

27. L. Mandl, Traité pratique du microscope...suivi de recherches sur l'organization des animaux infusoires par Dr. C. G. Ehrenberg (Paris, 1839), Pt. II, 195ff.

28. J. G. Millingen, Curiosities of Medical Experience (Philadelphia, 1838), 352-53. The "Gale" mentioned was possibly J.-C. Gales of Paris, who wrote Sur la diagnosic de la gale, sur ses causes, et sur les consequénces médicales pratiques à deduire des vrais notions de cette maladie (Paris, 1812).

29. Henry Holland, Medical Notes and Reflections (Philadelphia, 1839), 342-55.

30. Jacob Henle, "On Miasmata and Contagia", trans. George Rosen, Bulletin of the Institute of the History of Medicine, VI, No. 8, 948.

31. Ibid., 911-83. This essay comprises the first 82 pages of the Pathologische Untersuchungen.

32. René La Roche, Pneumonia: Its Supposed Connection Pathological and Etiological with Autumnal Fevers, including an Inquiry into the Existence and Morbid Agency of Malaria (Philadelphia, 1854), 318-19.

33. C. J. B. Williams, Principles of Medicine, Comprising General Pathology and Therapeutics (Philadelphia, 1844), I, 85.

34. Ibid., I, 79.

35. Julius Vogel, The Pathological Anatomy of the Human Body, trans. George E. Day (London, 1847), 441-42.

36. R., Southern Quarterly Review, N.S., I, Art. VII, 156 (April, 1850). Cf. J. G. Swayne, "An Account of Certain Organic Cells Peculiar to the Evacuations of Cholera," Lancet, 1849, II, 368-398, 410; F. Brittan, "Report on a Series of Microscopical Investigations on the Pathology of Cholera," London Medical Gazette, 1849, N. S., IX, 530-42.

37. R., South. Quar. Rev., N. S., I, 156.

38. For an interesting listing of advocates of a contagium vivum theory by an American, see La Roche, Pneumonia and Autumnal Fevers, 318-19.

Chapter 4 American Animalculists *

One of the most significant periods in the development of the animalcular hypothesis was the early nineteenth century. During the 1840's in particular, there was a definite animalcular school of thought in both Europe and America. In Europe, the hypothesis was gradually developed by first one scientist and then another until it culminated in the "germ theory" of infectious diseases. In America, the number of animalculists reached a peak in the 1840's and then declined - the miasmaticists meanwhile becoming more numerous. By 1875, when European ideas upon this subject once more began to receive attention they were treated as something entirely novel. The work of the early American animalculists was practically forgotten and scarcely a writer mentions one of them.

At the opening of the nineteenth century, America had reached the point of cultural development where it had a definite medical profession, with schools for training future physicians and a widespread literature to keep members of the profession in contact with modern developments. Although many physicians completed their education abroad, almost all began their studies at home and some relied entirely upon the education they received in American medical schools. The greatest medical center in America during most of the nineteenth century was Philadelphia. Here were the oldest hospitals and asylums in the country, and usually at least two medical schools were functioning - often four or five. Most American

medical books appeared with a Philadelphia imprint, and many journals were published in this city. Throughout the century, Philadelphia doctors were among the leaders of the profession.

Second to Philadelphia in importance were the medical centers of Boston, New York, Charleston and New Orleans. All these cities had schools, societies and scientific journals. The medical men of the two southern cities were famed for their work on tropical diseases, especially yellow fever. As westward expansion continued, Chicago and St. Louis also became medical centers, and the work of midwestern doctors appeared in journals published in these cities.

There was little government support for medicine during most of the nineteenth century, and all work of consequence was usually done on an individual basis. The views of American physicians, therefore, were not apt to be those of any special schools, but individual attempts at solution of the problems encountered in medical practice. Most of the theories presented by the American animalculists are of this nature.

The earliest Animalcular hypothesis published in America appears to have been that of John Crawford of Baltimore. Others may have had such ideas earlier, but none of these seem to have been printed.[1] Crawford expounded his views in a series of articles in a literary magazine, The Observer and Repertory, published by his daughter in 1807, and repeated them in an Introductory Lecture, printed in 1811. These pieces are now extremely scarce. Crawford may have been influenced by the work of Benjamin Marten and Sir Richard Blackmore, but his theory bears little

resemblance to theirs,[2] or, for that matter, to any other. Crawford's view was essentially that epidemics were caused by an animate contagion. By drawing upon analogies in nature he developed the thesis that disease "must be occasioned by eggs insinuated, without our knowledge, into our bodies."[3] He believed that these deposited eggs developed into parasites, which, like the eggs of ichneumon fly, grew at the expense of the host. His work attracted little attention from his medical contemporaries, though the Introductory Lecture of 1811 is cited by an anonymous reviewer in the American Quarterly Review for 1828. To most physicians his ideas probably seemed bizarre. His patients evidently thought likewise, for his practice suffered because of his unorthodox views.[4] Crawford was one of the earliest and most definite of the American animalculists.

The next animalcular hypothesis to appear in the United States was printed in the new series of the Medical Repository, a valuable little scientific journal edited by Samuel Latham Mitchill of New York. This hypothesis was hidden in a translation of Lancisi's book on marsh miasma made by Dr. Mitchill. The chapters dealing with Lancisi's theories on insect transmission and animalculae were printed in 1818. Though his animalcular hypothesis was generally ignored, nevertheless it was here made available to individual American readers. Lancisi had noticed that "moshettos" flourished in marshes and stagnant water, and he suggested that they brought infections of lethal particles of animate matter from the marshes to human beings, injecting the poisonous fluid in with their bites. Furthermore, he believed that extremely minute insects and worms

were bred in the marshes and that the eggs of these creatures were either swallowed or let into open wounds. He noted that drinking water was full of this "animalcular spawn" and food became loaded with it because insects were attracted to it. Lancisi probably hit upon the transmission of malaria when he said that mosquitoes injected the "insect" eggs with their saliva when biting. If he could have proved experimentally that the bite of a mosquito was actually letting in the spores of a parasite, he would have solved the malaria puzzle long before Laveran and Ross. It is remarkable how close to the truth he came, merely by using simple observation and thought. It was a long time before any other writer in either Europe or America developed as clear an idea of the etiology of malaria. Interestingly enough, Mitchill the translator, did not appreciate Lancisi's theory at all, and he concentrated his energies on "satanic septon."[5]

The views of Lancisi were very often misinterpreted by Americans as supporting the miasma hypothesis. An example of this is found in M. L. Knapp's essay on the medical topography of Illinois (1856). Said he:

> The hypothesis of different kinds of malaria, however, has never come to be generally acquiesced in, but rather the hypothesis assumed is, that obscure and diverse manifestations of disease, or masquerades of maladies, are ascribable to marsh malaria modified by place and circumstances. For the last century or more, this sweeping hypothesis of Lancisi has held domain over the records of medical philosophy, growing with its growth and strengthening with its strength; and upon it, as a foundation, are now erected the two superstructural hypotheses of the animalcular and the cryptogamous theories of the essential nature of malaria or miasmata.[6]

The term "malaria" here means a certain type of miasma, not the disease

we now know by that name. Other writers went even farther than Knapp in misinterpreting Lancisi and one doubts that they had ever read his work.

The animalcular hypothesis seems to have been seriously considered by Samuel Jackson of Philadelphia. In his volume on the "Yellow or Malignant" fever, published in 1821, he pointed out that Dr. Benjamin Rush Rhees, of Philadelphia General Hospital, had studied the black vomit of yellow fever victims with a solar microscope, and had found "innumerable quantities of animalculae" in it. These animalculae, which were probably blood corpuscles, were observed to be active if the victim was alive, passive if he was dead. "Comparative examinations were made of the discharges from the stomachs of patients, ill with autumnal bilious and remittent fevers, but no similar observations were discovered." If the observations had been significant, here would have been proof of the disunity of fevers. Jackson came to the conclusion that "these very curious observations require to be further and more extensively prosecuted and diversified in order to ascertain what relation those animalculae possess with regard to disease, either as cause or effect."[7]

An experimental approach to this problem was made by someone in Philadelphia between 1821 and 1828. The anonymous reviewer in the American Quarterly Review remarked:

> Dr. S. Jackson of Philadelphia, was so kind as to procure for us some decayed vegetables and water, from a miasmatous bank of the Schuylkill. On examination the next morning, by solar microscope, no animalculae were discoverable. No wonder, for to produce the disease in question the birds must have flown. They exist in the air; too small for human sight, unless with powerful apparatus.

A similar experiment was tried in the 1840's by Dr. Joseph Leidy, who examined the waters of the Schuylkill and the Susquehanna in the hopes of finding animalculae. He, too, was unsuccessful.[8]

One of the clearest of the American animalcular theories was expressed by the anonymous reviewer in the American Quarterly Review for 1828, during a discussion of John McCulloch's book on malaria. Nothing can be deduced about the author beyond the fact that he was a Philadelphian.[9] The text of the review itself at first seemed to favor the views of McCulloch and the unsuspecting reader was taken through what appeared to be a very favorable review of his theory that malaria (miasma) was a poisonous gas. The reviewer even remarked that the animalcular hypothesis was an ancient one, "at present not considered worth investigation." After two-thirds of the review had been devoted to McCulloch, the author suddenly announced that he was not satisfied with the gaseous theory and developed thirty-two arguments to show why the animalcular hypothesis suited the conditions of malaria better than any other theory. The terminology of this animalculist (and most others) is perplexing, because he used the word "insect" to mean "animalcule"; and the notion of the parasitic origin of disease is combined with a curious view of insect transmission (by swallowing or breathing them in) to the confusion of both. The anonymous reviewer desbribed his "insects" in the following terms:

> Insects are of all sizes, from the largest to the myriads of various kinds, which nothing but the most powerful microscope can exhibit to our sight. But large or small the laws of their production are the same. The circumstances that will produce a gnat, will produce an insect something less; and so on till we

> come to the animalculae infusoriae, and those that float on the atmosphere. Animalculae and miasmae are connected then: always in time, place and circumstance. What possible mode of connexion can the reader suggest or assign, but their sameness?
>
> Animalculae do exist in water, in the air, in the food we take in, in our bodies, Sometimes without ill effect. In disease, generally, of which they form a part. Tumours and abcesses contain animalcules.... It is probable they exist in the yellow fever: the physicians of Philadelphia are aware of Dr. Patterson's experiment at Bush Hill in 1820, where the ejection of black vomit exhibited, by the microscope, a congeries of animalculae. The experiment, we hope, will be repeated when it can be.
>
> Where the parasite animal is stronger than the life of the animal preyed upon, disease is produced, and the latter falls a victim. Hence the tendency to breed insects in weakly children, especially young females. —
>
> Does any man doubt that we inhale animalculae when we breathe: that we eat them and drink them? That when our constitution is vigourous, we destroy and assimilate them, and that when their constitution is more vigorous than ours, they live upon us, at our expense? Is not this the case with all the vermicular disorders? Is it not likely to be the case, when a new species of animalculae are suddenly generated in full vigour of existence, and when the circumstances that give energy to them, decrease our own? This is the case, not only with parasite animals, such as intestinal worms, but with the moss, the mistletoe, the ivy and other parasitic plants, which seize upon trees debilitated by old age, and live upon them.[10]

The reviewer notes the analogy between parasitic worm diseases and other diseases which seems very rarely to have occurred to any of his contemporaries, either in America or in Europe. So keen was he to establish the connection between animalculae in general and disease, that he neglected to bring in any doctrine of specificity. He acknowledged that he had read the work of John Crawford, but denied that he had been influenced by it. Though he believed in the parasitic origin of disease, he did not consider

insect transmission in the modern sense, and evidently had not had contact with the ideas of Lancisi.

The anonymous reviewer had a negative influence upon Usher Parsons of Brown University, who, though he included the animalcular theory in his work, rejected it in favor of the idea that disease was caused by the miasma arising from decomposing vegetable matter. Parsons, unfortunately, attributed so many diseases to miasmata from decaying vegetation that he almost defeated his own argument.[11] Even before research in pathologic anatomy came to America, authors such as Noah Webster and Edward Miller had found it necessary to differentiate between miasmata in order to account for the great difference in fevers.[12] Parsons, however, followed the older, vaguer pattern. Since the doctrine of specificity in disease required a long time to be successfully established, one should not be surprised at its omission from most of the early theories.

In the Middle West, far from the chief centers of medical practice, the celebrated Daniel Drake developed an interesting animalcular theory. In his Practical Treatise on the History, Prevention and Treatment of Epidemic Cholera, published in 1832, he indicated that disease could be caused by minute insects, which, like mosquitoes, deposited their eggs in damp places and stagnant water. The microscopic work of Derham (1727) and of Henry Baker (1764) confirmed his belief that there were insects in solid and fluid bodies as well as in the air. The minute ones, he thought, might have an extremely poisonous bite, much worse than that of the mosquito. His reasoning in regard to the action of invisible

life is interesting:

> As to the manner in which the supposed aerial animalculae might act on, or enter the human body, it may be the same, as that in which contagion, or malaria - admitting its existence - exerts itself. The ova of such insects may even be deposited and float in the air, to fall into the water and be hatched out, as the seeds of many of the most imperfect plants.... are disseminated; and these ova, as well as the perfect insects, may be inhaled or swallowed, and adhere to the mucuous membrane, or perhaps be absorbed into the blood or both; or, the ova, being deposited in the waters, may be swallowed, and the insects developed in our bodies.[13]

In view of what was then known about the proximate causes of fevers, Drake's idea seems quite advanced, in spite of limited and ambiguous terminology. Later he formalized his work and included it in the famous Diseases of the Interior Valley of North America, giving fourteen logical arguments for believing in a "vegeto-animalcular hypothesis." Of his earlier work, he said:

> Attempt was made to show, that the mode in which that disease [cholera] spreads was more fully explained by the animalcular hypothesis than any other .... The brief investigation then given to the subject, reinspired my respect for the opinion long before expressed, that autumnal fever, and many other forms of the disease, might be of animalcular origin; and the discoveries since made by the Ehrenberg school, have seemed to render that doctrine still more probable.[14]

Drake's theory is similar to that of "the anonymous reviewer", though carried somewhat further. He indicated that these "insects" which caused disease had the power of reproducing inside the body, and by this means he accounted for the period of delay or incubation between exposure to disease and its subsequent development. Neither Drake nor "the anonymous reviewer" went so far as to consider their insects as parasites which

might be conveyed to humans by means of a larger parasite. In this respect, they were less advanced than Lancisi. In most ways however, they were the equals of the average European animalculists of their day.

Following Drake's work in 1832, there was a lapse of about fifteen years, during which other theories, particularly chemical and atmospheric ones, occupied the attention of American physicians. Then, between 1847 and 1849, several new animalcular theories appeared. Elisha Bartlett, who wrote on the fevers of the United States, thought the animalcular hypothesis was the most reasonable of all the ones offered because it was "less embarrassed by objections which cannot be met, and by difficulties which cannot be overcome."[15]

Two textbooks in this period contained the animalcular hypothesis. Both were written by professors in the University of Pennsylvania Medical School. The first was A Treatise on the Practice of Medicine by George B. Wood, who informed his readers that "the microscope has laid open an otherwise invisible organic world, in which all the changes with which we are familiar in the visible may take place, beyond the cognizance of the senses, and lead to an aerial contamination inconsistent with health."[16] Wood first mentioned the possibility that there might be more than one theory of the contagium vivum type, writing:

> Two theories have been advanced... though further proof is required before either can be received. According to one of them, a peculiar product is generated... which is capable of acting as a ferment when it finds the proper materials to act upon, and of reproducing itself or a substance identical with it out of these materials, as yeast is generated... The other theory supposes the cause to be a living, organized, microscopic being, either

> animal or vegetable, which, produced out of pre-existing germs, under favorable circumstances, is capable of propagating itself indefinitely when these circumstances exist... In favor of the theory which ascribes the disease [yellow fever] to organic germs is the fact, that it is endemic or original only in a comparatively small portion of those regions of the world, where all the exterior circumstances appear equally to favor its production.[16]

By this time the achromatic microscope was available, and its value was recognized in America, even though it was not much used here. Wood's book went through at least five editions, so that there is probable that many students read of the animalcular hypothesis, even though they may not have accepted it.

The second textbook was Alfred Stillé's Elements of General Pathology, published in 1848. He noted that experiments had been undertaken to examine the contents of the air: "By condensing the vapours arising in certain malarious districts, small portions of mucus, containing animal matter, ammonia, and hydrochlorate and carbonate of soda have been obtained. This discovery would appear to countenance the hypothesis of Varro, that marshy emanations contain innumerable and invisible insects."[17] Writers in this period were almost always aware that the animalcular hypothesis was an old one, and they also knew which of their immediate predecessors had held it. In the period of the seventies such knowledge was more infrequent.

Stillé remarked that the insect idea had been revived by Dr. Henry Holland, but he himself was rather cautious about subscribing to it. He seems to have preferred the professionally safe miasma theory, though his intellect told him it was not very satisfactory. An explanation for the period

of incubation in disease puzzled him:

> How the virus acts during this period of apparent quiescence, and how it finally determines the reaction of the constitution, is altogether unknown... Liebig imagines this matter to consist of a sort of ferment, which, like the minute quantity of yeast that leavens a large lump of dough, gradually modifies the chemical relations of the fluid elements of the body. Other observers, upon the ground of an alleged discovery, that leaven acts by propagating germs, supposes the different sorts of virus to contain animal ova, or vegetable germs, which by rapid generation, fill the body with parasitic insects or invisible plants, whose presence constitutes the disease. When the microscope shall have revealed the existence of either of these sorts of bodies, in the fluids through which inoculable diseases propagate their kind, it will be time enough to give the hypothesis in question serious consideration.[18]

Thus Stillé rejected the obvious explanation for lack of experimental verification, yet he accepted what his contemporary, Julius Vogel, had refused: the idea that there must be something potent in the fluids used in inoculation. At one point Stillé noted that there were changes in the blood of malaria patients, a reflection of the work of Dr. Joseph Jones.[19] The best thing about Stillé's etiology was that it at least presented the animalcular hypothesis to his readers as a possible explanation. This was more than could be expected from most medical writers of the period.

The American medical observer of this period who came closest to Lancisi was Josiah Clark Nott of Mobile. Nott, writing of yellow fever in the New Orleans Medical and Surgical Journal in March 1848, ridiculed the marsh miasma theory. He observed that:

> It would certainly be as philosophical (as the malarial theory) to suppose that some insect or animalcule, hatched in the lowlands, like the mosquito, after passing its metamorphoses, takes flight, and either from preference for a different atmosphere, or impelled by one of those extra-ordinary instincts, which many are known to possess, wings its way to the hilltop to fulfill its appointed destiny.[20]

Nott credited the greater danger of night air to the presence in it of insects, which were rendered inactive by light and heat during the daytime, but emerged at night. In this catagory he mentioned moths, "musquitoes," aphids, and others. The insect hypothesis again would account for the "fact" that trees were a barrier to malaria, because the insects could use them for a resting place. Nott sarcastically added, "It should be borne in mind, too, that the very writers who... run their malaria up trees, are those who tell us that its specific gravity is so great that it lies on the ground!!" He believed that germs were responsible for contagious diseases, and he explained to his readers that heat, light, and alcohol destroyed them.

Nott carried his theories one step farther than other animalculists, for, noting the reproductive powers of the infusoria, he stated, "With these few facts before us, how much more easily may we account for the spread of yellow fever from a focus, by the insect, than by the Malarial hypothesis - here is something tangible and comprehensible."[21] He knew that plants had parasites, and vaguely inferred that a similar situation might hold for humans, but on this point his theory lacks clarity. It should be remembered that when Nott said "insects" he meant insects, and it is not clear whether he thought his insects did their evil work by biting the victim or by being swallowed or what. He did not have Lancisi's concept of the insect as a transmitter of the eggs of a smaller insect, but he did connect insects with malaria and yellow fever. In fact, he thought that different insects might cause different kinds of fevers, though not all

diseases could be of insect origin.

One other interesting point comes out incidentally in Nott's work. He suggested that dead animalculae could cause disease when rejuvenated by a congenial environment. This environment was not defined exactly, but probably lay outside of the body.[22] He had, of course, no specific data to go on to prove his conjecture, but it is interesting that he should even consider it. In giving his animalculae the power of lying dormant like seeds, he may have been influenced by the virus-like line of development of the contagium vivum theory, though this is not likely.

One of the most striking animalcular theories was that of John K. Mitchell of Philadelphia, who declared in 1849 that non-contagious, infectious diseases were caused by fungi. In his own words:

> The only theoretic view to which I incline, is that which refers marsh fevers, and some of the epidemic diseases, to a living organic cause, capable of reproduction by germs, as is alleged of contagious diseases; but unlike that latter in this, that the germs are not reproduced in the organism of the sick, but exteriorly to, and independently of, the human body. In other words, that as the germs of contagious diseases are reproduced in the body, the germs productive of malarious and other non-contagious diseases are elaborated and re-elaborated out of the body, and independently of its agency. One is the product of person, the other of place. This notion is sustained by the fact that organic azotized substances are the only things detected in marsh air or dew, which can possibly affect the health injuriously.[23]

Mitchell's theory has several interesting points. The spores of the fungi utilized to account for endemic diseases appear to have arisen spontaneously. He had evidently made some attempts at analysis of marsh air before working out his theory. Noting the presence of gangrene in many diseases, and adding it to diseases where it does not occur, he attributed

this condition to the action of a fungus. He thought that fungus spores could be swallowed, especially in the case of typhoid fever, producing gangrene inside the intestines. This conclusion may have been influenced by autopsy findings.

On the epidemiologic side, Mitchell noticed that fungi flourished in wet places and so did fevers; fungi spread at night and fevers were caught at night; fungi spread by means of spores, and disease could be better explained by this means than by any other. He ascribed most diseases, particularly fevers, to the action of fungi on different parts of the body. In view of the fact that the schizomycetes (bacteria) are a branch of the fungus family, Mitchell's theory is particularly significant.[24] Moreover, fungus infections themselves are now known to be serious.

Mitchell's cryptogamous theory had wide influence, both among his colleagues in Philadelphia, and among his contemporaries, particularly in the West. John Evans, writing in the Northwestern Medical and Surgical Journal in 1849, mentioned the many theories as to the origin of cholera, including the "cryptogamous". Daniel Drake hailed it as "almost irresistible", as did many others at home and abroad. It was reviewed by R. (probably Richards, the editor) in the Southern Quarterly Review in 1850. The reviewer was an expert mycologist and he checked Mitchell's statements against the latest developments in the field of mycology, to the complete vindication of Mitchell. The poor microscopes of the day made it difficult to check the hypothesis experimentally, but the medical scientists always hoped to get better equipment which would reveal more about

the invisible world. Joseph Leidy, the famous parasitologist, was opposed to the theory because he had swallowed quantities of "monas, vibrio, volvox, vorticella, etc." without any ill effects. In addition he has searched for animalculae spores in the waters, dews and air of malarious localities, but had found nothing. The Philadelphian, René La Roche, rejected Mitchell's theory because of his respect for the opinion of Leidy.[25]

Mitchell had introduced his theory in a series of lectures in 1846-47, but had refrained from publication because he was afraid that this would lead to controversy. He also feared he lacked conclusive proof, which was true. However, in 1848 a similar theory was presented in England by Charles Cowdell, and Mitchell's friends urged him to publish his own and claim priority. With the exception of Cowdell, Mitchell does not mention any others who also held fungus theories, although the idea had been published in a different form by Ludwig Boehm as early as 1838. Mitchell also claimed that the cryptogamous theory had "wide dissemination on this side of the Atlantic...," though he failed to elaborate this statement.[26] In 1876 and 1888, when certain later writers were enumerating forerunners of the germ theory of disease, Mitchell was the only American mentioned.[27]

A New York physician, Alexander H. Stevens, in 1850, speculated on the causes of cholera and suggested that animalculae or "seeds of fungus" might be involved.[28] By this time the views of European animalculists, such as Charles J. B. Williams, Henry Holland and J. G. Millingen, had received some attention in America and one would expect to find that the animalcular hypothesis had become more popular. Unfortunately this was

not the case, and only four or five American animalculists have been found for the period following 1850.

Three of these animalcular hypotheses appeared in the mid-fifties. A layman, J. Franklin Reigert, of Lancaster, Pennsylvania, held the notion that cholera was caused by very small yellow flies which he found in the spout of the town pump. Reigert used the words "fly" and "animalcule" indiscriminately, but is is interesting to note that he connected them through water with cholera. He also assumed that his fly might be the cause of "yellow jack," considering it "immaterial by which name renowned Doctors may choose to distinguish these two kindred epidemics, when preceded by the same yellow fly." His opinion of the medical profession was not too high, but he expected it to take notice of his discovery and act upon it. He also expected the doctors to solve the problem of how the poisonous flies did their work, favoring chiefly the possibility that they were swallowed by their victims.[29]

M. L. Knapp, a mid-western physician, also accepted an animalcular hypothesis, which he outlined in an essay of 1856 on "Etiological Deductions - Malaria." He reflected:

> It is analogically evident that the assumed miasmata must be animalculae, for the heat and slime of the bottoms force into existence nolens volens the products of decay, which like old cheese quicken with a sort of putrefactive vitality, and can surely be smelt if not seen, and easily be imagined to take wing by day and go to roost at night, seeking the interior of cabins in order to keep warm and dry like other well-bred fowl and insects. Furthermore the musquitoes, gnats, flies, devils-needles, toads, turtles, and turkey-buzzards are abundant as the insect swarms of an offended God sent upon the hosts under the hard-hearted Pharoah, therefore the miasmata must be of animal character or nature - a sort of

> animal stream or invisible quintessence of suspected animal life, well enough proved by its odor and poisonous effects, the fevers, as also by its being killed by the frosts, though never yet isolated or seen by the mortal eye aided by microscope![30]

This is a somewhat different point of view from that of the average animalculist. Knapp thought it possible that the invisible life could be either animal or vegetable in nature. In other words, he would subscribe to either animal or cryptogamous theories. He also had his own theory to the effect that, like scurvy, malarious diseases were due to deficiency of fresh fruits. He mentioned curing cases of "malaria" with oranges, lemons and fresh vegetables.[31] This is an interesting reflection on the diagnosis of the day.

In 1857, a commission in Norfolk, Virginia, submitted a report on the origin of yellow fever - following an epidemic there - in which the various members came to the following conclusion:

> In the present state of science, it is not possible to determine what is the material cause of yellow fever, in as much as it is not tangible, and cannot be subjected to examination and analysis. It is only by a careful process of induction from all known facts in relation to the disease, that we can hope to arrive at the correct theory of its origin and propagation. The hypothesis, which best explains most of the known phenomena of the disease, is that its material cause is some organic matter endued with the property of rapid reproduction, either in the soil or atmosphere congenial to it, but not capable of being reproduced in the human body. That this matter, whether of animalcular or vegetable character, is a production of tropical regions, and is only spread in climates when introduced into them by ships.[32]

This is a sort of semi-animalcular hypothesis. The "organic matter" is not considered capable of reproduction within the human body, although it could propagate itself outside.

A. B. Williman of the Norfolk group voiced a dissenting opinion, of possible animalcular significance, when he said, "Again, I think that the cause of yellow fever is some minute material germ, capable of reproducing itself when given off from the human body suffering under this disease."[33] Williman infers that his "germ" existed in the body but reproduced outside of it. Although actually animalculae or bacteria are capable under certain conditions of reproducing both within and without the body, what was intended in this case was a distinction necessitated by the split between the non-contagionist majority and the dissenting contagionist. In either case an organic poison, capable of reproduction outside of the human body, could have been intended. The situation is not at all clear, and this sort of confusion indicates a lack of understanding about the animalcular hypothesis, which may explain the subsequent loss of interest in the theory.

In 1866, following the cholera pandemic, there was considerable speculation about the cause of the disease. Nathan Smith Davis, discussing the epidemic in Chicago, mentioned that "seeds" or "germs" of cholera were scattered through the city and the "local and ... atmospheric conditions ... served to multiply and impart activity to the existing poison." He thought that the same forces which were needed to give activity to the supposed infection were also capable of originating it, thus agreeing with the general view that the disease was non-contagious. He noted the presence of "sporadic cases with other bowel-affections" as a possible factor in spreading the disease.[34] American writers on cholera of this period

were still unaware of the significance of the work of John Snow showing cholera to be a water-borne disease. Davis was not an animalculist or even a zymoticist, but he had adopted the idea of "seeds" of disease, being careful to have his seeds multiply in the atmosphere like a poison or miasma.

Very few genuine animalculists can be found for the two decades following 1860, and these will be discussed in a later chapter. The general run of American physicians were skeptical about the hypothesis during the whole period under discussion here - from about 1780 to 1880. Benjamin Rush in 1790 mentioned in his lectures that some people thought fevers were brought by insects from the marshes and that there was some reason to give this idea serious consideration. In 1828, J. W. Heustis called attention to the animalcular hypothesis in order to oppose it. Said he, "There are others again who, with still greater appearance of sagacity, pretend that the bilious or yellow fever is produced by countless myriads of animalcules, secretly introduced into the human system, and thence exciting it into morbid action." Some writers, like O. B. Knode, stated frankly that they had no idea of the nature of the malarial poison. R. S. Holmes admitted that he had heard of various theories of the animalcular type, but he added that "to mention [them] ... to persons who have really seen many locations of miasmata, would be but to abuse their patience." Nevertheless he added that "there are some medical gentlemen, however, who are even yet skeptical on the subject of miasmata." William H. Tingley claimed that "most etiologists endeavor to

explain the origin of disease by introducing some unknown external agent, - as miasm, malaria, fungus, decaying animal or vegetable matter - instead of searching for more rational causes." (In this case the "more rational causes" were climatic ones).[35]

S. Littell, who did not believe in the common miasma theory, calling it a baseless assumption, summarized the situation in 1866, when he admitted that the miasma theory was

> a doctrine which has become thoroughly incorporated with our literature, and forms a part of daily medical thought and expression. In books, in lectures, in conversation - everywhere - it is the organized language of physicians; and those who should have the temerity to intimate a doubt of the truth of a tenet thus universally admitted, would incur no small risk of having their own sanity questioned in turn.[36]

This situation was more true of America than of Europe, as will be noted in the following chapter. The influence of the animalcular school of thought was not widespread in the United States, and, to judge from the decreasing volume of literature, it appears to have been almost lost from sight by the late 1850's. The interest of the earlier period died out, and even those men who had espoused the animalcular views seem to have turned away from them.

One final consideration connected at this time with the theories of the causation of disease was the nature of the agent of transmission. The contagion controversy concerned itself with the question as to whether man or some external agent was primarily responsible. Holland and Evans suggested the agency of man in cholera, and Holmes, Barker and Semmelweis held the same thesis for puerperal fever.[37] None of these views was

generally accepted. Holmes in later years enjoyed reminding the medical profession of the soundedness of his early opinion. "I think I shrieked my warning louder and longer than any of them," he declared, "and I am pleased to remember that I took my ground on existing evidence before the little army of microbes was marched up to support my position."[38] At least one contagionist lived to see himself vindicated.

The most prevalent theory of agency, of course, was that of the air and its contents. Any causal factors - poisons, ferments, or animalculae - could be carried by this element. Closely confined air was thought to be particularly virulent. Water was a lesser agent and then only putrid water was considered, not water that looked pure. Some observers, such as Lancisi, went so far as to note that the air contained insects, which in turn might be either the cause of disease or the agent of transmission. The term "insect", as used in the sense of specific cause, was synonymous with "microbe". It is unusual to find it used in the sense of a transmitting agent, though a specific type of insect was suggested as such by Lancisi.

The English medical authority, Richard Mead, used "insect" to mean "microbe" and he believed that the eggs of his insects were transported from place to place by fomites, and they caused the disease where they hatched out.[39] Daniel Drake also thought that "insects" were the actual cause of disease,but he believed these were transmitted by airs rather than by fomites:

We assume the existence of malaria, of mineral exhalations, of

> meteoration, of contagion; let us, in like manner, assume the existence of poisonous, invisible, aerial insects, of the same or similar habits with the gnat; let us assume still farther ... that these have instincts which may direct their migrations ... and ~~what~~ that they are liable to be carried by high winds into elevated and dry places, which they would not frequent from choice; finally, let us suppose that some cause has augmented the number of individuals of some species, and we shall then have all the theory which is necessary to explain most of the facts connected with our Epidemic [cholera].[40]

In his later works on diseases, Drake made his "insect" analagous to "the smallest invisible gnat", a species of sand fly whose bite inflames the skin. From this he deduced that animalculae when introduced through the skin might have a poisonous effect.[41] The insect here is the transmitter of a poison rather than the actual causal factor in disease by itself. The insects of the "anonymous reviewer" in the American Quarterly Review were also of this type. Though this type of insect may be construed as a sort of carrier, it was really the poisonous bite itself (not the "germs" admitted with the bite) which was believed to be at fault. Although insects were mentioned by many writers,[42] their role as carriers of disease was suggested by none except Lancisi. Edward Miller of New York came very close to the theory of insect transmission as held by Lancisi when he supposed, about 1809, that miasmatic poisons might be "injected into the system by some venomous animal." His vagueness in the sentences elaborating the subject make it rather unlikely that he had any clear idea of the connection between insects and disease.[43] Drake, as noted above, had a much clearer conception, even though it was not the actual causation of the disease with which he was concerned.

Almost all the Americans who anticipated the germ theory of disease believed in some sort of an animalcular hypothesis. The virus-like line of development was rarely mentioned. Francis Peyre Porcher of Charleston was one of the exceptions to this rule. Porcher's work, Illustrations of Disease with the Microscope, appeared in Charleston in 1861. The pictures in it show what he found in his microscopic analysis of the blood and other body fluids, but none of the cells drawn appear to have been micro-organisms. Probably his microscope was not powerful enough to reveal them. In his text, Porcher stated that "scarlet fever, measles, small-pox, are each sui generis, are disseminated by exposure to special morbid poisons, working in the blood in the nature of a ferment, and which are peculiar in their nature."[44] He quoted Stillé to the effect that "many diseases ... arise from a retention in the blood not of substances actually foreign to it, but of some which have assumed a new form, rendering their presence in the system incompatible with health."[45] This suggests the action of a catalyst. Porcher's work is the only one which shows American acceptance of the doctrine of specificity, and his ferment idea is similar to the zymotic theory of disease. This reinforces the view that the doctrine of specificity belongs to the virus-like concept rather than to the animalcular one.

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At a time when a real science of bacteriology was being developed in Europe after 1860, American etiology was still in the same position it

had been when the century opened. The animalcular theory had not been accepted and, as Littell points out, it was virtually forgotten or mentioned only for ridicule. The interests of the 1840's, which led to scientific experimentation and eventually to the germ theory of disease in Europe, came to a dead end in America; and when the new ideas were later imported to the United States, they were treated as something entirely novel and their American forerunners usually ignored.

Why were Americans so slow in developing systematic medical research? And above all, why did American doctors fail to develop the science of bacteriology from etiology and pathology or even to keep abreast of European developments in this field after 1860, when they had the same background and the same raw materials with which to work as did the Europeans? Some of the answers to these questions are apparent.

In the early nineteenth century America lacked both public and private support for pure science and research. There was no patronage tradition. No organized research was carried on in the United States, only sporadic attempts, as in the classic case of William Beaumont. Some excuse for this state of affairs may be made on the grounds that the country was new, and that development and westward expansion took up the energies of men who might otherwise have turned to science. Cultural independence in the arts and literature was beginning to be apparent in the mid-century, and possibly this independent spirit was reflected in American attitudes toward European medicine just at the time when the greatest advances were being made abroad.

A more likely explanation lies in the fact that there was little prestige to be gained in research because the commercial spirit of the Anglo-Saxon world placed the emphasis on practice - reflecting the business man's sense of values. The dollar value of a man did (and does) carry more weight than his intellectual achievements. Furthermore, at that time, lack of financial support forced doctors into practice, regardless of their personal choices. Osler's "Alabama Student" was a typical example. Practice gave the physician his professional reputation. Even the university professors were chosen from practicing physicians, and a man who lacked a large and lucrative practice would have found it hard to attract students. There was no tradition of government support for science, as in France, and the tradition of private support had to wait for a generation of multimillionaires. The thought of patronage was repugnant to democratic ideals, and respect was accorded the sturdy, self-made scientist following in the Franklin tradition, but without Franklin's viewpoint on what should be done with amassed wealth.

The emphasis on the practical in the American outlook demanded utility at a time when the doctors could promise the least. The public was not interested in pure science, represented by etiology and the identification of diseases, but only in applied science, represented by treatments. Since the profession had no other source of income, it generally found it expedient to follow the public demand. This held back the development of medicine because treatment could not be successful, except by chance, when the causes of disease, or even the nature and identity of the

diseases themselves, were unknown. In this case emphasis on applied science over pure science was putting the cart before the horse, but one could scarcely expect the public to realize that.

Finally, there was a deterioration in quality of personnel in the medical profession itself. Sects, such as homeopathy and others more esoteric, discredited the profession as a whole. Medical education was at a very low level, with dozens of small, worthless colleges turning out students who had attended a course of lectures, but had never had any clinical instruction, and often had never seen or treated a patient. Most of the best doctors were educated abroad, at Edinburgh and Paris.[46]

Poor instrumental aids, legal hindrances and lack of facilities also impeded American medical development. Microscopes were rare and not of good quality. By the mid-century their worth as scientific instruments rather than toys was just beginning to be appreciated. In some states it was against the law to hold autopsies and everywhere dissections were seldom held. Hospitals were scarce and often poorly managed. In contrast to the European tradition, no experiments were made on the charity patients.[47]

In addition to the financial, philosophical, educational, material and legal impediments to medical research, there was one more great barrier which would have prevented progress even if all the other factors had been favorable. This was the mental barrier. The profession tended to oppose innovation and to be satisfied with the methods it had. As no great mental effort was needed to acquire its body of knowledge, and

prestige-satisfying additions could be made to that body from an arm-chair, there was little incentive to adopt the rigorous techniques of the scientific method. A sort of Baconian inductive system dominated medical thinking and long-winded arguments drawn from huge general collections of semi-classified observations took the place of experimentation as the foundation of truth. The result was a kind of latter-day scholasticism, well illustrated by the treatment accorded the animalcular hypothesis. By argument, American physicians felt that they had been able to dispose of this theory completely. It was so dead by 1875 that the discoveries of Pasteur and Koch then appeared as entirely new contributions. Abroad, the interest in etiology had led to the development of the science of bacteriology. At home, unable to make the transition for themselves, Americans had to follow the lead of Europe into intriguing new fields of medical science.

FOOTNOTES TO CHAPTER FOUR

* Much of the material in this chapter originally appeared in two articles, "Early American Animalcular Hypotheses," Bulletin of the History of Medicine, XXI, No. 5, September-October, 1947, pp. 734-43, and "Etiological Theory in America Prior to the Civil War," Journal of the History of Medicine and Allied Sciences, II, No. 4, Autumn, 1947, pp. 489-520. The subject has been discussed briefly in Erwin H. Ackerknecht, Malaria in the Upper Mississippi Valley 1760-1900 (Supplements to the Bulletin of the History of Medicine, No. 4, Baltimore, 1945), 12-15.

1. For example, Otho T. Beall of the University of Pennsylvania has drawn attention to an unpublished animalcular hypothesis formulated by Cotton Mather in a manuscript entitled "The Angel of Bethesda", belonging to the American Antiquarian Society, Worcester, Mass. Mather was influenced by the theory of Benjamin Marten (1722), and it is interesting that he gave serious consideration to it. His theory unfortunately appears to have had little influence upon his successors. A possible near-animalculist may have been Samuel Bard, who wrote to David Hosack in 1808: "Your first class of diseases is strictly and clearly defined; they can be communicated by contact only; is not the materies morbi of these diseases always generated within the body; and whether it consists of animalculae or a chemical mixt, are they to be found anywhere else?" --David Hosack, Observations on the Laws Governing the Communication of Contagious Diseases and the Means of Arresting their Progress (New York, 1815), Additional Notes, 83. Letter from Bard to Hosack, Hyde Park, July 27, 1808. In this case the animalcular hypothesis was secondary to the idea of contagion.

2. Benjamin Marten, A New Theory of Consumptions (London, 1722); Sir Richard Blackmore, A Discourse Upon the Plague with a Preparatory Account of Malignant Fevers (London, 1721). For a brief introductory account of the work of some of the American animalculists, see Erwin H. Ackerknecht, Malaria in the Upper Mississippi Valley 1760-1900 (Baltimore, 1945), 11-15. (Supplements to the Bulletin of the History of Medicine, No. 4).

3. Significant parts of Crawford's theory may be found in Palmer H. Futcher, "Notes on Insect Contagion," Bulletin of the Institute of the History of Medicine, IV, 549-557 (July, 1936).

4. Julia E. Wilson, "An Early Baltimore Physician and his Library," Annals of Medical Science, 3rd Series, IV, 68-69. (1942). Manuscript letters, John Crawford to Benjamin Rush in the Library Company of Philadelphia.

5. Medical Repository, N.S., IV, Appendix, 201-12, 322-32, 442-67. On Mitchill, see Courtney R. Hall, A Scientist in the Early Republic -- Samuel Latham Mitchill 1764-1831 (New York, 1934).

6. M. L. Knapp, Inquiry into the Nature of the Nursing Sore Mouth Affection (n.p., 1856) 226-27. Charles Caldwell wrote that the ancients had had an animalcular hypothesis and "Lancisi had only to exchange the generation of poison animalculae by putrefaction for the generation of a poisonous gas, and his work was done". (Essays on Malaria and Temperament (Lexington, Ky., 1831), 57-58). J. K. Mitchell listed Lancisi as a firm believer in miasma (The Cryptogamous Origin of Malarious and Epidemic Fevers (Philadelphia, 1849), Lecture I. In view of the fact that these men could have read Mitchill's translation in the Medical Repository, it is difficult to see how they arrived at such conclusions unless they took their information at second hand from some erroneous source. Similar misunderstanding took place in Europe, cf. August Hirsch, Handbook of Geographical and Historical Pathology, trans. Charles Creighton (London, 1883), I, 287.

7. Samuel Jackson, An Account of the Yellow or Malignant Fever as It Occurred in the City of Philadelphia in 1820 (Philadelphia, 1821),81.

8. American Quarterly Review, IV, 306; Joseph Leidy, Flora and Fauna within Living Animals (Washington, 1853), 14-15.

9. Amer. Quart. Rev., IV, 287, 304-306. This anonymous reviewer left few clues to his identity. From the content of his article it was evident that he was a Philadelphian and his mention of the solar microscope leads one to the conclusion that either there was one microscope in Philadelphia which many borrowed, or else this was the Dr. Rhees mentioned by Dr. Samuel Jackson. It might even have been Jackson himself.

10. Ibid., 303-304.

11. Usher Parsons, On the Comparative Influence of Vegetable and Animal Decomposition as a Cause of Fever (Philadelphia, 1830), 11.

12. Noah Webster, A Brief History of Epidemic and Pestilential Diseases (London, 1800), II, 338ff; Edward Miller, The Medical Works of Edward Miller, M.D., ed. Samuel Miller (New York, 1814), 183-202.

13. Daniel Drake, A Practical Treatise on the History, Prevention and Treatment of Epidemic Cholera (Cincinnati, 1832), 47.

14. Ibid., 25-50, 47; A Systematic Treatise, Historical, Etiological and Practical of the Principal Diseases of the Interior Valley of North America (Cincinnati, 1855), II, Pt. I, 723-27.

15. Elisha Bartlett, The History, Diagnosis and Treatment of Typhoid and of Typhus Fever; with an Essa on the D osis of Bilious Remittent and of Yellow Fever (Philadelphia, 1842), The History, Diagnosis and Treatment of the Fevers of the United States (Philadelphia, 1847), 347.

16. George B. Wood, A Treatise on the Practice of Medicine (Philadelphia, 1847), 146-47, 306.

17. Alfred Stillé, Elements of General Pathology (Philadelphia, 1848), 98.

18. Ibid., 104-105.

19. Ibid., 99-100. Joseph Jones of Savannah had some acquaintance with the work of Ehrenberg on infusoria. He used the microscope in connection with autopsies and with it he analyzed blood quantitatively. His most important observation was that the malarial poison destroyed red blood corpuscles. In regard to treatment he was opposed to the use of blood-letting and purging because he thought that malaria was depressing to the system and not an inflammation. (Joseph Jones, "Observations on Malarial Fever," Southern Medical and Surgical Journal, (June 1858), 5, 12, 178.

20. Nott, "Yellow Fever Contrasted with Bilious Fever -- Reasons for Believing it a Disease sui generis -- Its Mode of Propagation -- Remote Cause -- Probable Insect or Animalcular Origin -- &c.," New Orleans Medical and Surgical Journal, IV, 580. (March, 1848).

21. Ibid., 581-594.

22. Ibid., 590, 595, 597.

23. J. K. Mitchell, Cryptogamous Origin of Fevers, 31-32.

24. Ibid., 40ff. For the relationship of fungi and bacteria see Hans Zinsser and Stanhope Bayne-Jones, Textbook of Bacteriology, 8th ed., (New York, 1939), 143.

25. Evans, "Observations on the Spread of Asiatic Cholera and Its Communicable Nature," Northwestern Medical and Surgical Journal (Chicago, 1849), 21-22; Drake, Diseases of the Interior Valley, II, Pt. I, 727n; Southern Quarterly Review, I, 146ff; L y, Flora and Fauna, 14-15; René La Roche, Pneumonia: Its Supposed Connection Pathological and Etiological with Autumnal Fevers (Philadelphia, 1854), 319-20n.

26. Mitchell, Cryptogamous Origin, iii-iv; Cowdell, Disquisition on Pestilential Cholera; Ludwig Boehm, Die Kranke Schleimhaut . . . in der Asiatischen Cholera (Berlin, 1838).

27. Austin Flint, "Medical and Sanitary Progress", Harper's Magazine, No. CCCXIII, Vol. LIII, June, 1876, 83; Ezra M. Hunt, "Notes on Progressive Studies in Etiology," Medical News (Philadelphia), Mar. 17, 1888, Vol. LII, No. XI, 281.

28. Alexander H. Stevens, "On the Communicability of Asiatic Cholera," Transactions of the Medical Society of the State of New York, (Albany, 1850), No. 174, 34.

29. J. Franklin Reigert, A Treatise on the Cause of Cholera (Lancaster, Pa., 1855), 5-15.

30. Knapp, Inquiry into Nursing Sore Mouth Affection, 251-52.

31. Ibid., 226-27.

32. Report of the Origin of the Yellow Fever in Norfolk (Richmond, Va., 1857), 43.

33. Ibid., 44.

34. Davis, "How Far do the Facts Accompanying the Prevalence of Epidemic Cholera in Chicago, during the Summer and Autumn of 1866, Throw Light Upon the Etiology of that Disease?", Presented to the American Medical Society, May 1867, p. 18-19.

35. For Rush, cf. Richard H. Shryock, The Development of Modern Medicine, 2nd ed. (New York, 1947), 274; J. W. Heustis, "Remarks on the Endemic Disease of Alabama," American Journal of Medical Sciences, II, 32 (1828); O.B. Knode, "A Report on Malarious Fever," St. Louis Medical and Surgical Journal, XIV, No. 5, 410 (Sept., 1856): R.S. Holmes, "Malaria and Topography," St. Louis Med. Surg. Jour., V, No. 6, 520 (May, 1848); Tingley, "On the Action of Climatic Causes in the Production of Disease," St. Louis Med. Surg. Jour., XIV, No. 5, 386 (Sept., 1856).

36. S. Littell, Relations Which Electricity Sustains to the Causes of Disease (Philadelphia, 1866), 4.

37. Henry Holland, Medical Notes and Reflections, Chap. XXXIV; John Evans, "Observations on the Spread of Asiatic Cholera", N.W. Med. Surg. Jour., 1849; The work of Holmes and Semmelweis is well known, but that of Thomas Herbert Barker is not. It may be found in his book, On Malaria and Miasmata and their Influence in the Production of Typhus and Typhoid Fevers, Cholera and the Exanthemata: Founded on the Fothergill Prize Essay for 1859 (London, 1863), 162-64, 167.

38. O. W. Holmes, Letter to the American Gynecology Society in Philadelphia, 1893, printed in William Osler, An Alabama Student and Other Biographical Essays (Oxford, 1929), 66.

39. Richard Mead, A Short Discourse Concerning Pestilential Contagion, 6th ed. (London, 1720), 16.

40. Drake, Practical Treatise on Cholera, 44.

41. Drake, Diseases of the Interior Valley, II, 724.

42. James Lind, An Essay on Diseases Incidental to Europeans in Hot Climates, 4th ed. (London, 1788), 68; Robley Dunglison, Human Health, new ed. (Philadelphia, 1844), Sect. III, 58-94; William Currie, An Historical Account of the Climates and Diseases of the United States of America (Philadelphia, 1792), 57; Webster, Brief History of Epidemics, II 16-17; Benjamin Rush, Medical Inquiries and Observations, 2nd ed., (Philadelphia, 1805), IV, 175; James Copland, A Dictionary of Practical Medicine, ed. Chas. A. Lee (New York, 1845), II, "Epidemics," 777; Noah Webster, Jr., A Collection of Papers on the Subject of Bilious Fevers Prevalent in the United States for a Few Years Past (New York, 1796), 3, 76; Parsons, Comparative Influence of Vegetable Decomposition, 17-18; Copland, Dictionary, II, "Disease," 569; Medical Examiner, VII, 269 (1843).

43. Edward Miller, Medical Works, 47.

44. Francis Peyre Porcher, Illustrations of Disease with the Microscope (Charleston, S.C., 1861), 79

45. Ibid., 28; Alfred Stillé, Therapeutics and Materia Medica (Philadelphia, 1860), II, 641.

46. For details of material covered in the preceding paragraphs, see Richard H. Shryock, American Medical Research: Past and Present (New York, 1947), Ch, I, II. On medical education, see W. F. Norwood, History of Medical Education in the United States before the Civil War (Philadelphia, 1944).

47. New York Journal of Medicine, IV, 159 (March, 1859); Samuel Jackson, The Principles of Medicine (Philadelphia, 1832), pref., xvi-xvii.

Chapter 5 The Germ Theory of Disease in the Mid-Century

The failure of the animalcular hypothesis in America only serves to point up its success in Europe. It had long been known on both sides of the Atlantic that this hypothesis, or germ theory, as it was now increasingly to be known, required a more exacting proof than had hitherto been forthcoming. But while Americans were content with the rational and epidemiologic approaches to the problem, the Europeans, particularly French and German scientists, observed more carefully and verified observations by experimentation. They speedily grasped the importance of the microscope and turned it towards the investigation of animalculae, seeking proof of the germ theory in the laboratory. Ultimately, the use of these more exact scientific methods resulted in a successful demonstration of the validity of the germ theory.

I

This turning to more exact methods raises a pertinent question. Why are discoveries not recognized when they are made? The work of Lancisi, Plenciz, Henle and the unknown "Gale" has already been described, and it has been pointed out that these men were very close to the scientific solution of the problems of etiology. But it seems to be generally recognized that there are other factors involved which create a favorable milieu and set the stage for the acceptance of a discovery. For this reason inventions and discoveries are often made

simultaneously. It is difficult for example, to determine who invented the telescope, or to explain why Boyle's Law is called Mariotte's Law on the Continent, or to settle the Newton-Leibnitz priority on the calculus, or to determine who should get the credit for the discovery of oxygen. Only four examples have been given and there are dozens available in the history of science. A scientific discovery may be made at any time, but it is only accepted and adopted when the intellectual climate is ready for it.

This general conclusion is also true of the germ theory. Up to the mid-nineteenth century, animalculists in general had been content to formulate their hypotheses and omit experimental proof. The inconclusiveness of such laboratory work as was done raises the very real question as to whether techniques and instruments were good enough to make possible a satisfactory solution. In other words, with substantially the correct concept, it may have been physically impossible to prove it. Technological developments play an important part in the formation of an adequate intellectual climate.

The work of Louis Pasteur, who was a chemist and not a physician, and that of Robert Koch, who was a medical scientist but not much of a practitioner, serves to show that the European success was due as much to a favorable attitude as to a continuation of earlier work. The time was at last ripe for acceptance of significant discoveries. Henle's postulates returned as Koch's postulates, and this time they were seriously utilized to provide a completely satisfactory demon-

stration of the germ theory. Laymen such as Pasteur were able to get a hearing from the medical profession because their discoveries fitted in in such a way as to solve a medical puzzle.

The favorable climate of opinion which was developing during the mid-century was derived from many other sources besides technological improvements and the utilization of effective scientific methods. Advances were also being made in sciences either allied or soon to be allied with medicine, such as zoology, parasitology, microscopic anatomy, histology, cytology and taxonomy. In addition, one of the chief factors in creating a milieu which would encourage the germ theory was the fear aroused by the terrible cholera pandemics of 1832-38, 1848-59, and 1865-73.[1] These mass pestilential invasions created such a demand for sanitary reforms and clean-ups as had never been felt in Europe before. A voluminous cholera literature, only equalled by the plague tractates of earlier days, appeared on all sides. The search for causes of the dread malady was carried on with feverish activity. The filth theory of disease, in which disease was attributed to miasmata or other poisons arising from decaying filth of all kinds, had its hey-day during the mid-century, and resulted in sanitary codes -- not only in the national but in the international field.

The filth theory created a climate favorable to the acceptance of the germ theory, through the success obtained by the use of disinfectants. This suggested that there was some organic basis for disease, although its exact nature was unknown. In the 1860's and

after, the introduction of antiseptic procedures in surgery produced dramatic results. Here was something that was tangible. The problem then became that of determining whether the carbolic acid sprays kept air-borne germs out of wounds, as Lord Lister said, or whether they covered the open wound with a protective coating and isolated it from chemical poisons in the air, as certain miasmatists believed.[2]

While all these factors aided in preparing the way for the acceptance of the germ theory in Europe, the thirty years from 1850 to 1880 saw the theory itself advance from a nebulous and somewhat doubtful possibility into a scientifically proven explanation of the etiology of certain specific infectious diseases. At the beginning of this period the situation was still confused. John Snow, in 1853, wrote that various writers attributed epidemics to the atmosphere, to the presence or absence of ozone, to effluvia from a sick person, to the predispositions of certain people, to climate and season (particularly in unhealthy localities), to miasmata, and to contaminated water.[3]

To this list, Thomas H. Barker added cosmic happenings, the anger of God, geological conditions, the idea of a communicable poison arising spontaneously in a human body, and the germ theory. All these ideas are interesting in themselves. Some of the meteorological and geological writers tested the soil and Sir Ranald Martin came to the conclusion that a high temperature and a highly ferruginous soil were essential to the production of epidemic diseases. He also considered the electrical condition of the atmosphere and "observed" that a

negative electrical atmosphere weakened human resistance. M. Boudin determined the isosthermal lines delineating the limits of various diseases.[3]

Another well-known theory was that of the Bavarian, Max von Pettenkofer. Through English eyes in 1863, his views indicated that the excreta of cholera patients acted as a leaven on an impure soil in the neighborhood of human dwellings, and the special poison of cholera was a miasma produced by such a fermentation. The miasma hypothesis by this time had absorbed some of the earlier chemical or gaseous theories, and it became slightly more discriminating. Deseye analysed marsh air and found it to be composed of 78 parts azote (nitrogen), 21 parts oxygen, and 1 part carbonic acid. Oxide of azote, carbonic acid, carburetted hydrogen (methane), sulphuretted hydrogen (hydrogen sulfide), and phosphuretted hydrogen (phosphine gas), were all believed to arise from vegetable or animal decomposition and to be a gaseous end-product of decaying organic matter.[3] There appears to have been no clear distinction between organic and inorganic compounds. All of these theoretical solutions to the problem of etiology were but continuations of ideas put forth early in the nineteenth century.

In the middle of the century, the nature of miasmata was still such a problem that in his Fothergill Essay, Thomas Herbert Barker included the germ theory and the zymotic theory with other theories about the nature of miasma. He wrote:

> Some men have considered malarious agents to be matters of organic life, that is to say, invisible cells, germs, fungi, or animalcules generated under favouring circumstances, caught up by the atmosphere and conveyed to man through the respiration, or communicated to him in the soluble form by inoculation. They who espouse this view, as a primitive view in respect to cause, differ widely as to the course and consequence of the origin. One sect assumes that the germ introduced into the living organism is actually multiplied there: others think that the poison being organic primitively, does not necessarily act on the affected organism directly, but that coming into contact with decomposing matters in the soil, it gives rise as a ferment to the formation of compounds which become poisonous when breathed, malaria. A third class opine that the organic poison introduced into the blood, and favoured in its transmission into the blood by heat and moisture, has the power after its absorption, of exciting zymosis and producing decomposition of the blood itself, and of the tissues which are dependent on it for nutrition, of thus setting up an entire modification of the chemistry of life, and of inducing those departures from the healthy standard which we call, under different names, specific diseases.
>
> As to the method by which those changes are induced, but little has been advanced except by one author [Farr], who... argues that the symptoms of disease are not produced immediately by the organic poison, but are the result of a new poison, the product of the fermentation which the organic substance has called into action.[4]

According to this statement, the germ theory had acquired enough proponents to be labelled as a sect. The explanation of the zymotic theory given is not entirely satisfactory. What is really involved here is a Liebig fermentation theory -- since the factor of reproduction of the poison is omitted. Thus there were no less than three fermentation-type theories: one was a purely chemical concept involving a catalyst; another was entirely biological, requiring a living plant as the agent; the third (termed the zymotic theory in this thesis and roughly indicated above) involved an organic substance or ferment capable of reproducing itself within the human body. The mere fact that the etiologic theories were

becoming so complicated by the mid-century, indicates what a tremendous interest had been aroused by the whole subject.

Of all the theories of disease available in the 1860's, perhaps the zymotic hypothesis is the most interesting. As we have seen, this theory had its antecedents in the virus-like line of development of the contagium vivum theory. It was brought to a high degree of refinement by many hands. William Farr, in the Registrar-General's Report on Cholera for 1848-49, outlined some zymotic principles, placing the origin of infectious disease in a series of specific chemical poisons whose exact composition was not known. The scheme of Farr is worth reproducing because of its wholehearted espousal of the doctrine of specificity (the "zymes" are in the third column):

ZYMOTIC PRINCIPLES

Small-pox	variola	varioline
Cow-pox	vaccinia	vaccinine
Glanders	equinia	equinine
Hydrophobia	lyssa	lyssine
Syphilis	syphilis	syphiline
Infection in dissecting	necusia	necusine
Erysipelas	erysipelas	erysipeline
Puerperal fever	metria	metrine
Measles	rubeola	rubeoline
Scarlet fever	scarletina	scarletinine
Hooping cough	pertussis	pertussine
Dysentery	dysenteria	enterine
Diarrhoea	diarrhoea	
Cholera	cholera	cholerine
Influenza	influenza	influenzine
Typhus	typhus	typhine
Plague	pestis	pestine

The existence of gangrenine, ergotine, ophthalmine, tetanine, miliarine, diphtherine, parotine, aphthine, tracheine may also be admitted. 5

It should be emphasized that this differentiation among specific causes appeared before any general distinction was made among different types of germs, except by Jacob Henle. Farr's interpretation of the zymotic theory followed Liebig's views on the nature of yeast and other ferments. He believed that a specific enzyme-like chemical poison was responsible for each disease or collection of symptoms; and all infectious disease was therefore viewed as a kind of fermentation - initiated by the zyme but symptomatically due to chemical changes in the blood and other body fluids. His specific ferment did not multiply but acted as a catalyst.[6]

Farr's ideas were modified by his successors. Winslow has shown the gradual modification of John Simon's views from a zymotic theory similar to Farr's into one closely related to the germ theory.[7] A like case can be made for Thomas Herbert Barker, who lists both a well-developed zymotic theory and a germ theory. The zymotic theory is best illustrated by the six rules which he formulated to explain this hypothesis:

1. Specific epidemic diseases are derived from specific poisons, poisons reproductive in the animal economy, and reproductive possibly out of the animal economy, under conditions favourable to reproduction.

2. Such specific poisons received into the blood, whether by a wound in the skin, or by absorption from mucuous surface, produce the same specific effects.

3. The amount of poison is of little moment, when taken into consideration with the force of reproduction.

4. The poisons are diffusible only to a limited extent; for if they be gases, the diffusion process in the atmosphere disperses them; while if they be organic particles they float but for small distances, and remain active or inactive according to the medium with which they come in contact.

5. Meteorological influences do not assist in the diffusion of these poisons, but rather in the reproduction of them, -- inasmuch as those conditions of a meteorological kind are evidently connected with the prevalence of epidemics, such as high temperature, would rather favour the dispersion and removal of volatile poisons than their concentration and intensity.

6. As a consequence of the last-named position, matters on the earth exclusive of man, may be a constant storehouse of these poisonous agencies; the poisons may thus lie dormant for a time, like the seeds of a plant; at favourable seasons they may rise into full activity, and man subjected to their influence, may become the vehicle of their reproduction and of their further transmission.[8]

This passage has been inserted at some length because of the interesting idea it contains. The relationship between the zymotic theory and modern virology is quite apparent if one substitutes the word "virus" for "poison" throughout.

Sedgwick drew a very illustrative analogy between fermentation of apple juice and the course of an infectious disease:

The germ or zymotic (ferment) theory of disease

A Fermentation (apple juice)	An Infectious Disease (smallpox)
1. Exposure of the juice to air, dust, etc.	1. Exposure of the patient to infection.
2. Repose and then slow change (growth of the ferment).	2. Incubation (slow and insidious progress of the disease).

3. Active fermentation or "working". Evolution of gas bubbles, change of sugar to alcohol.	3. Active disease. Eruption, disturbance of the usual functions. Rise of temperature or fever.
4. Gradual cessation of fermentation.	4. Slow convalescence (or death).
5. No further liability to alcoholic fermentation.	5. Immunity to smallpox. 9

In this case no differentiation was made between the germ and zymotic theories, which is rather interesting as indicating how close the two became in their relationship. The fact that a virus disease has been innocently chosen in illustration of the point is doubly interesting.

It was more usual to find the zymotic theory posed as an alternate or even a rival to the germ theory. There seemed to many people to be no meeting place for the two. As the germ theory became better understood and more work was done on it, however, the zymoticists gave their ferments an organic body similar to the yeasts and gradually the two theories were merged. After the acceptance of the germ theory, the other hypothesis dropped out of medical literature. The zymotic idea itself, with its ferments of inert material capable of reproduction within the body, appeared to have no significance in bacteriology. Following the first decades of discovery of pathogenic micro-organisms, the problems raised by the germ theory turned out to be more difficult than had been anticipated. The discovery of the ultramicroscopic viruses (1892), too small to be seen by the most powerful microscope, but known for their potency in filtrates, opened up a whole new field.

The crystallization of the virus of tobacco mosaic (1935) subsequently raised the question as to whether the viruses were living organisms

or not. This question is still debated, but for the purposes of this thesis, Aristotle's teleologic definition of life has been adopted -- life is the combination of those forces which resist death, or, as it has been modified by E. A. Singer, a thing is alive which makes a self-preservative gesture. The viruses reproduce only in the living cell and here they multiply as the bacteria do in the living body. They definitely undergo modification and change when confronted with anything inimical to their continued existence. In other words, they adapt themselves to their environment in order to perpetuate their species. The factors of reproduction and adaptation make them resemble the ferments or zymes of the early zymotic hypothesis.

One may say, therefore, that the basic idea of the behavior of the ultramicroscopic viruses is not new, but is a transformation of the older zymotic theory. The intellectual relationship between this theory and the current knowledge of viruses is quite apparent now, but it has not been and could not be seen until recent developments had been made. Finally it may be observed that the two lines of development of the contagium vivum theory, which seemed so irreconcileable for such a long time, both have a place in the modern concept of the etiology of specific infectious diseases.

II

The story of the gradual development of the germ theory of disease in Europe has been well told by William Bulloch in his History of Bacteriology,[10] and therefore will not be repeated in any great detail

here. But it will be helpful to go back at this point to the general European story, in order to explain the final successes there. The main line of development in nineteenth century bacteriology began with the work of men not particularly interested in solving the problems of etiology. C. G. Ehrenberg, Baron Charles Cagniard de Latour, Theodor Schwann, and Agostino Bassi were at work on problems in general biology and chemistry. It continues through the work of those who were investigating the fungoid nature of skin diseases, and through that of the students of taxonomy and classification. The epidemiologists contributed a share in the general development of the germ theory, as did the zymoticists. The use of the experimental method as exemplified in inoculation experiments played a part. Study of the various forms of putrefaction, and the work of Lister in prevention of septic processes in wounds formed another important portion of the general development. All these factors taken together with the technological improvements in equipment and new advances in techniques finally produced satisfactory proof of the germ theory, but the process took a long time.

The beginning of work leading directly to the proof of the germ theory appears to have taken place with the posthumous publication of Otto Friedrich Müller's Animalcula Infusoria in 1786. Mandl, in 1839, recognized the publication of this work as marking the start of an epoch in the study of infusoria. Study of these microscopic creatures had been carried on in a haphazard fashion since the invention of the micro-

scope, producing such works as Henry Baker's Employment for the Microscope (1753), for example, but after the appearance of Müller's work, it was carried on in a much more systematic manner.[11] The systematization received further development at the hand of Christian Gottfried Ehrenberg, whose Die Infusionsthierchen als Vollkommene Organismen appeared in Leipzig, in 1838. Ehrenberg made a very thorough study of the infusoria, carrying on where Müller had left off. Working with the improved microscope, he classified hundreds of tiny animals and some micro-organisms which are now relegated to the plant catagory. The terms "spirillum", "bacterium", "spirochaeta", and "vibrio", used to classify bacteria, were established by Ehrenberg. He used carmine-and indigo-colored water as a stain to show up the nuclei and food vacuoles of some of the infusoria. This had been tried earlier by Trembley (1744) and W. F. Gleichen (1778), but their results were not as satisfactory as those of Ehrenberg.[12] This practice of staining micro-organisms to render them more readily visible was extended and utilized by microscopists, with varying degrees of success, for many purposes before William Perkin began the mauve decade with the synthesis of the first aniline dye. Later aniline dyes became the sine qua non of successful observation of bacteria.

Ehrenberg's contemporary, Agostino Bassi, was mainly concerned with finding a solution to the problem of the causation of the silkworm disease, muscardine. He found that a tiny microscopic plant was at fault. Unlike Pasteur, who made a similar study of a

silkworm disease, pébrine, some years later, Bassi was content to end his work by pointing out the possible analogy between a disease of silkworms caused by a cryptogamous organism and human diseases which might be due to a different member of the same tribe. The germ of cholera, for example, he thought might be "a cryptogam, mould or fungus more minute still than that of Calcino [muscardine], and consequently lighter, more slender and more volatile than the germ of Calcino."[13] Here was a speculative brand of specificity. All this work on infusoria was basic for any further developments in microscopic biology. In the field of chemistry, the study of the nature of fermentation proved to have a similar importance.

It has already been noted in a previous chapter that Robert Boyle thought the problem of the nature of the exact causation of disease would prove to be bound up with the true knowledge of fermentation. It turned out to be so, though perhaps not quite in the manner which Boyle had foreseen. Men such as Thomas Willis the physician, and the chemists George Ernst Stahl (phlogiston), Antoine Laurent Lavoisier, L. J. Gay-Lussac and the little known Adam Fabbroni had studied fermentation; but it is the biological period of the study, when yeast was considered to be a living thing, that is most significant. Cagniard de Latour, Schwann, and Friedrich Kützing independently studied the microscopic yeast cells of fermenting wine and beer during the 1836-38 period, and made the discovery that the yeast cell was organized, living matter. Schwann's careful work laid the groundwork for modern knowledge of

the process of fermentation. The chemists of the same period, J. J. Berzelius, F. Wöhler, and Justus von Liebig, opposed the biologists' idea that yeast was a living organism. They considered it to be a catalyst only, and Liebig in particular believed that animalculae were a result and not a cause of fermentation, and that the "ferment" was not an actual substance in itself, but a part of a chemical process -- material in an unstable and changing state. The problem of the nature of fermentation was finally settled by the researches of Louis Pasteur, in spite of the violent opposition of Liebig. Pasteur, though a chemist, showed that the views of the biologists were correct.[14]

About the time that the work on infusoria and fermentation was being done, a serious study of parasitic fungi was also being made. As in the case of the work on yeasts, discoveries were made almost simultaneously or within a few years of each other. Johann Lukas Schönlein found the fungus of favus, for instance, in 1839, and Remak in 1840. Other discoveries followed thick and fast, including those of David Gruby, Johannes Müller, John Goodsir, A. Retzius, Eichstedt, and Hughes Bennett. An attempt to find organisms in cases of infectious disease had been made by Schönlein as early as 1836. He discovered a large number of crystals in the excreta of patients with typhusfever and thought that the presence of these might be a characteristic sign useful for distinguishing typhus from other, similar diseases. Johannes Müller, however, demonstrated that these crystalline salts were present in all excreta, as had been noticed earlier by Leeuwenhoek.[15] Schönlein evidently then sought

something more tangible and, with the example of Bassi's successful results in muscardine before him, he turned to the study of the skin disease, favus, with successful results. Other workers had more luck with infectious diseases than Schönlein. Alfred Donné noticed spirochetes and bacilli in genital tracts in 1837. Pierre F. O. Rayer and Casimir J. Davaine announced the discovery of rod-like forms in anthrax in 1850. Davaine also worked on entozoa in man and animals. One of the most significant discoveries in this pre-Koch-Pasteur period was that of Otto Obermeier, who announced his discovery of the relapsing fever spirillum in 1873. All this work preceded the great decade of discovery in bacteriology, the 1880's.

All the studies leading into modern bacteriology would have been handicapped without advances made in nomenclature and classification. As Karl Kisskalt points out, new concepts brought new words with them.[16] This nomenclature had the effect of creating a specific terminology for the new science and enabled the scientists to talk to each other with less misunderstanding. A better classification system was also developed and in this respect the work of Ferdinand Cohn especially stands out. The system of Müller had been extended by the studies of Ehrenberg. Ehrenberg's classification, however, was somewhat involved and a simplification was made in 1841 by Felix Dujardin, a French zoologist. Another new classification was proposed in 1852 by Maximilien Perty of Berne, noted as "the first to observe bacterial spores."[17] The most important work was done by Cohn, Professor of Botany at the University

of Breslau. As early as 1854, Cohn suggested transferring Ehrenberg's family of vibronia from the animal to the plant world. His greatest work in the field of bacteriology was a series of papers entitled "Untersuchungen über Bacterien", which appeared in 1872, 1875, and 1876. These embodied the results of years of careful investigation and laid the foundation of modern classification in bacteriology. Cohn himself became one of the foremost bacteriologists of his period.[18]

Contributions to the developing science of bacteriology also were made by men who used the epidemiologic approach. Of these, John Snow has been chosen in illustration, though the work of William Budd is equally significant. Snow's essays, On Continuous Molecular Changes (1853) and the more famous On the Mode of Communication of Cholera (1855), are good examples of an enlightened point of view on the part of an epidemiologist. In the first essay, Snow was groping towards the germ theory of disease. "The material cause of every communicable disease, he said, "resembles a species of living beings in this, that both one and the other depends on, and in fact consists of, a series of continuous molecular changes, occurring in suitable materials." This meant that he thought a living organized material was responsible for disease because it was capable of increasing its own kind, though he also thought it would be extremely difficult to differentiate between disease causes "like individuals of a species of plant or animal." The most interesting part of Snow's view was his notion that just as the "molecular changes" in the seeds of plants and in the ova of many animals were capable of being

suspended, so the same thing could happen in the case of the materies morbi of diseases; "they permit of being suspended, under certain circumstances, and recommence at the point at which they ceased." This seems analogous to spore formation. He recognized that the period of incubation in disease should be termed a period of reproduction of the material cause.[19] Snow's ideas on the communication of cholera were the same as the ones he elaborated in the later essay.

On the Mode of Communication of Cholera is the essay in which the famous episode of the Broad Street pump was announced to the world. Snow's views on cholera are too well-known to need retelling.[20] His views on etiology in general, however, are worth some consideration. In a very shrewd guess he came close to the correct solution of the malaria puzzle. Snow believed that the morbid agent of the ague might have to undergo a process of "development or procreation" outside of the human body before it could enter another body and infect it. He considered that this might be analogous to the life processes of "certain flukes infesting some of the lower animals, and procreating by alternate generations."[21] How close this is to the actual reproductive cycle of the malarial parasite.

In a long and extremely significant passage near the beginning of the essay, Snow gave his views on etiology, repeating some of the ideas presented in his earlier essay:

> Diseases which are communicated from person to person are caused by some material which passes from the sick to the healthy, and which has the property of increasing and multiplying

> in the systems of the persons it attacks. In syphilis, smallpox and vaccina, we have physical proof of the increase of the morbid material, and other communicable diseases the evidence of this increase derived from the fact of their extension, is equally conclusive. As cholera commences with an affection of the alimentary canal and as we have seen that the blood is not under the influence of any poison in the early stages of this disease, it follows that the morbid material producing cholera must be introduced into the alimentary canal -- must -- in fact, be swallowed accidentially, for persons would not take it intentionally; and the increase of the morbid material, or cholera poison, must take place in the interior of the stomach and the bowels..... For the morbid matter of cholera having the property of reproducing its own kind, must necessarily have some sort of structure, most likely that of a cell. It is no objection to this view that the cholera poison cannot be recognized by the microscope, for the matter of small-pox and chancre can only be recognized by their effects, and not by their physical properties. . . .
>
> The period which intervenes between the time when a morbid poison enters the system, and the commencement of the illness which follows, is called the period of incubation. It is, in reality, a period of reproduction, as regards the morbid matter; and the disease is due to the crop or progeny arising from the small quantity of poison first introduced. [22]

In contrast to the animalcular-type views expressed by Snow in his earlier essay, his etiologic ideas in this latter work, with the emphasis on specific poisons, place him squarely in the ranks of the zymoticists.

Adoption of the concept of specificity in disease was surprisingly slow. Even when the diseases themselves were separated, there was a lag in similar differentiation of specific causes. Such classification as had been attempted-first an artificial listing of miasmata and then a separation among the aerial poisons, with the term "malaria" reserved specifically for the cause of intermittent and remittent fevers -- proved to lack any solid basis and was looked upon with disfavor. In Europe, at least, it was recognized that the germ and zymotic theories provided a

more secure basis for the doctrine of specificity than the miasmatic or atmospheric theories. The idea of specificity in disease seems to have been adopted more readily by the zymoticists than by the animalculists. The latter were most anxious to prove that the cause of disease was living, while the zymoticists contented themselves with admitting the fact of its reproductive powers in the human body and concentrated on finding a specific zyme for each ailment. Plenciz and Henle have already been mentioned as two of the few animalculists who entertained the doctrine of specificity. Some others considered the idea of specificity in respect to one or two diseases,[23] but none of them had as well-defined a scheme as these two men.

Scientists had to have some notion of the specificity of disease to attempt inoculation experiments. The endeavor to produce a disease by inoculation automatically implies that there is a specific virus or transmissable poison which causes the disease. Kisskalt gives a list of those who tried self-inoculation experiments, with varying degrees of success.[24] Eighteenth century scientists had used inoculations of smallpox to produce mild cases of the disease as a protection against virulent strains. In the nineteenth century, however, experiments were made with diseases not generally considered contagious. Casimir Davaine is known to have made the experimental inoculation of anthrax (1863). Jean-Antoine Villemin conducted a series of excellent experiments proving that tuberculosis was inoculable (1865). Many experiments had been tried before this time, but none had been conclusive. The proof of both the specificity of disease and

its successful inoculation came with Koch's work on anthrax in 1876.

There was another important question in the 1860's which had a bearing on the developing germ theory. This was the problem of causation in the "putrefactive" diseases. The theories of the etiology of pyaemia listed by W. Roser in 1867 are extremely interesting as an indication of the type of etiological reasoning then in vogue. There was a mechanical school of thought which believed that this condition was due to the entry of pus cells into the blood. A septic school thought pyaemia resulted from a decomposition of the pus. The zymoticists, of course, considered a specific infection to be responsible for the condition. An eclectic group chose a combination of various causes and a skeptic school said there was no such disease![25]

There was considerable confusion about "putrid" infections during most of the nineteenth century. Some writers regarded all diseases as caused by putrid emanations which affected the body in varying degrees. Others limited the putrid diseases to ones obviously putrefactive, such as the pyaemia-gangrene types. François Magendie, Bernard Gaspard, and others, had discovered that the injection of putrid matter into the blood caused an infection. Miasmatists seized upon this work as proof that putrid exhalations in the air caused fevers. A long series of experiments were carried out by Karl Thiersch (1855-56) and by O. Weber (1864-65) in which both came to the conclusion that putrid intoxications were caused by some type of ferment. P. L. Panum also made experiments in 1856, which led him to the conclusion that neither bacteria nor ferments were

involved, but a special active putrid principle which attracted the proteins in the putrid fluid. Schwann had believed that putrefaction was caused by microbes, and this view was supported by Pasteur in 1863.[26]

The work on putrid infections divided itself into two camps, just as that on fermentation had done. The chemists were sure that chemical poisons alone were involved. The biologists preferred to blame the infections on the actions of bacteria or some equivalent. L. Coze and V. Feltz of Strasbourg, for example, noted the occurrence of infusoria in infective diseases, and they obtained marked success in inoculating rabbits with the "bactéries en chainettes" of puerperal fever. Their work was carried on in 1872 by that of Casimir Davaine, who called the disease produced by his putrid injections septicaemia. Davaine inoculated twenty-five generations of rabbits, and found that the virulence of his injection increased during its passage through the animals. He noticed that different species of animals have different degrees of susceptibility. Finally he came to the conclusion that septicaemia was caused by a ferment.[27]

Clarification of the etiology of the putrid infections was continued by Robert Koch in 1878 in his famous work, The Aetiology of Traumatic Infective Diseases. He produced septicaemia, gangrene, pyaemia, erysipelas and spreading abcesses in experimental animals by the injection of putrid liquids. Alexander Ogston of Edinburgh completed Koch's work by proving that infective diseases of this type were caused by parasitic micro-organisms. Ogston invented the term staphylococcus, and held that pyaemia and septicaemia were not diseases, but different manifesta-

tions of a certain type of infection. Others who followed him showed that different micro-organisms besides the streptococci and staphylococci could cause such infective processes.[28]

The developing germ theory modified attitudes towards the putrefactive infections. "Laudable pus" was shown by Joseph Lister not to be laudable at all. Lister had read of Pasteur's work demonstrating that the noxious properties of the air were not caused by miasmata or injurious gases or other chemical content, but by the presence in it of minute micro-organisms, "long since revealed by the microscope, and regarded as merely accidental concomitants of putrescence, but now shown by Pasteur to be its essential cause, resolving the complex organic compounds into substances of simpler chemical constitution, just as the yeast plant converts sugar into alcohol and carbonic acid [sic]"[29] Beginning as early as 1865, Lister made use of this knowledge to exclude the germs from open wounds by means of carbolic acid dressings.

Unlike his later American followers, who utilized the antiseptic and disinfection systems without having a clear notion of what they were combatting, Lister based his work solidly on the germ theory. He observed that:

> The Germ Theory supposes that the organisms are the causes of the changes; that the germs of these minute living things, diffusible in proportion to their minuteness, are omnipresent in the world around us, and are sure to gain access to any exposed organic substance; and, having thus reached it, develop if it prove a favourable nidus, and by their growth determine the chemical changes; and further, that these organisms, minute though they appear to us, form no exception to the general law of living beings, that they originate from similar beings by parentage. [30]

Or, in other words,

> The Germ Theory tells us that these particles of dust [in a wound] will be pretty sure to contain the germs of putrefactive organisms, and if one such is left in the albuminous liquid, it will rapidly develop at the high temperature of the body, and account for all the phenomena [of infection.] [31]

From these statements, it is clear that, as early as 1873, Lister had made the philosophical adjustment from a world where all injurious elements were tangible to the senses to the world of the omnipresent invisible micro-organism. The practical implications of the germ theory itself had been proven or universally accepted. Lister himself believed that his method proved the theory as convincingly "as experiments performed in a laboratory."[32]

The final demonstration of the germ theory is probably best illustrated by the example of anthrax. The small rod-shaped bacillus of this disease had been discovered in 1849 by Franz Pollender, though he did not publish his discovery until 1855. It was found about the same time in the blood of sheep by Davaine, whose results were published by Rayer in 1850. Friedrich August Brauell found the bacillus in man in 1857, and demonstrated its inoculability from one species to another. From 1863 on, Davaine took up the study of anthrax again and came to the conclusion that the bacillus was responsible for the disease: no bacillus, no disease. He made inoculation experiments, but positive and conclusive proof of his interpretation was lacking. In 1871 Edwin Klebs showed that the bacteria of anthrax were non-filterable because the filtrate did not produce the disease. Numerous others worked in the field of anthrax

and pseudo-anthrax, but their results either led to blind alleys or were inconclusive, mainly because their laboratory techniques were not sufficiently exact.[33]

The real proof of the causation and transmission of anthrax came in 1876 and 1877 with the work of Robert Koch and of Louis Pasteur. Koch had been a student of Jacob Henle at Göttingen; and after graduation he became a country doctor in Wollstein, a town in Posen. He conducted researches on anthrax in his spare time and in 1876, wrote to Ferdinand Cohn to say that he had found the complete cycle of the life-history of the anthrax bacillus. Koch had isolated the bacillus from the blood of infected animals, had grown it in a culture medium, had transmitted this new growth by inoculation to mice, and had again recovered it from the mice, so that it could be grown again in culture media and propagated by inoculation from mouse to mouse. In each case the disease produced was identical with the original anthrax. He examined the bacillus of anthrax microscopically and had a set of slides showing its complete life-history from the ordinary bacillus to the completely formed spore. The following year, Koch published his method of fixing and dyeing bacteria, and this technique, together with the "postulates" of his method, explain his success.[34]

Koch's work was confirmed the following year by Pasteur. The career of Louis Pasteur coincides with the development of bacteriology to such an extent that one might even say the career of Pasteur <u>is</u> the history of bacteriology. Pasteur was a chemist and began his work with certain chemical discoveries in tartaric and racemic acids. In 1854 he

began to work on fermentation; and beginning in 1857, one paper after another appeared, embodying the results of his work. Among other things, he discovered the lactic acid bacteria, the anaerobic character of butyric fermentation, the nature of acetic and alcoholic fermentation, the necessity and nature of the pellicle in vinegar formation, and, of course, the place of living organisms in all these processes. In 1863 he was called upon to save the wine industry of France, and the results of his investigations, Etudes sur le vin, were published in 1866. The heat process now known as Pasteurization was developed by Pasteur at this time to sterilize the wine. In 1865 he was called upon to aid the silkworm industry, which was being ruined by some disease which killed the young silkworms. After five years of hard work, Pasteur discovered that two diseases, pébrine and flâcherie, both caused by micro-organisms, were involved. His book on this study, Etudes sur la maladie des vers à soie, was very significant.

After working on the silkworm diseases, Pasteur returned to fermentation once more and in 1876, published his Etudes sur la biere. By this time, however, he was becoming interested in discovering the causation of disease in man in order to prevent it. This attitude was not altogether new, but the methods used by Pasteur to solve the problem were based on the germ theory of disease, and the consequent developments were quite different. Pasteur confirmed Koch's work on anthrax and "disposed of the question of a separate virus by carrying the bacilli through a hundred generations and producing anthrax from the term of the series."[35] In the following decade he discovered the principle of

attenuation of the virus, and was able to develop preventative vaccines for a number of diseases, notably chicken cholera, anthrax, swine erysipelas, and rabies.[36]

By the time the work of Koch and Pasteur on anthrax had been digested, the acceptance of the germ theory was assured. In 1881 Koch's solid culture media were described, and the following year his postulates were formally set forth in his paper announcing the discovery of the bacillus of tuberculosis. In 1883 he made the celebrated discovery of the cholera vibrio and of the Koch-Weeks bacillus of conjunctivitis.[37] By the early 1880's others had seen the advantages of work in bacteriology and the stampede began. Discoveries followed thick and fast, often, as in the case of the Koch-Weeks bacillus, many occurred almost simultaneously. Each year added to the knowledge of the etiology of specific infectious diseases. Of course, some "discoveries" proved illusory, and some were prematurely hailed as the sole cause of the disease in question. In addition, the resulting enthusiasm for bacteria as the only factors in causing disease had unfortunate consequences.

Nevertheless, compared with the situation even ten years earlier, by 1885 or 1890 the etiologic picture looked a thousand times brighter so far as the infectious diseases were concerned. With an accurate knowledge of causation, one could now for the first time work intelligently on the prevention and cure of disease. The greatest battle against epidemic disease was fought in the last decades of the nineteenth century, and the forces of preventative medicine carried the day. Just as in the recent

war, the mental adoption of the philsophy and tactics of the blitzkrieg preceded successful action, so in the case of the conquest of infectious disease, victory was only made possible by the successful proof of the germ theory of disease.

FOOTNOTES TO CHAPTER FIVE

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2. Frank H. Davis, "Atmospheric Germs and their Relation to Disease," Chicago Medical Examiner, XII, No. 4, 193-99 (April, 1871).

3. John Snow Snow on Cholera, Being a Reprint of Two Papers by John Snow, M.D., Together with a Biographical Memoir by B.W. Richardson, M.D., and an Introduction by Wade Hampton Frost, M.D. (New York, 1931), "On Continuous Molecular Changes, More Particularly in their Relation to Epidemic Diseases," 159ff; Thomas Herbert Barker, On Malaria and Miasmata and their Influence in the Production of Typhus and Typhoid Fevers, Cholera, and the Exanthemata: Founded on the Fothergill Prize Essay for 1859 (London, 1863), 8-22, 40-49, 50-65, 66-72.

4. Barker, On Malaria and Miasmata, 68-69.

5. Great Britain, Registrar-General Report on the Mortality of Cholera in England, 1848-49 (London, 1852), lxxx-lxxxiii, chart on p. lxxxi. This was written by William Farr. The part on the zymotic theory was originally published in the Fourth Annual Report of the Registrar-General, Appendix, 199-205. See also Barker, op. cit., 31-32.

6. Barker, op. cit., 35.

7. C. E. A. Winslow, The Conquest of Epidemic Disease (Princeton, 1944), Ch. 12, 259-66.

8. Barker, On Malaria and Miasmata, 86-87.

9. [W. T. Sedgwick] Sedgwick's Principles of Sanitary Science and Public Health, rewritten and enlarged by Samuel C. Prescott and Murray P. Horwood (New York, 1935), 26.

10. W. Bulloch, History of Bacteriology (London, 1938).

11. L. Mandl, Traité pratique du microscope... suivi de Recherches sur l'organization des animaux infusoires par Dr. C. G. Ehrenberg (Paris, 1839), Pt. II, Sect. II, 422.

12. Ibid., 426-27; Bulloch, Hist. Bact., 30; F. H. Garrison, Introduction to the History of Medicine, 4th ed., (Philadelphia, 1929, 595.

13. Ralph H. Major, "Agostino Bassi and the Parasitic Origin of Disease," Bulletin of the History of Medicine, XVI, 103; Bassi's work was entitled: Del mal del segno calcinaccio o moscardino (Lodi, 1835-36).

14. Wade W. Oliver, Stalkers of Pestilence: The Story of Man's Ideas of Infection (New York, 1930), 163; Bulloch, Hist. Bact. Ch. 3, p. 41ff; Karl Kisskalt, Theorie und Praxis der Medizinischen Forschung, 2nd ed. (Munich-Berlin, 1944), 179.

15. Mandl, Traité pratique du microscope, 124; Bulloch, Hist. Bact., 165-66; Garrison, Intro. Hist. Med., 582-83.

16. Kisskalt, Theorie und Praxis, 189.

17. Bulloch, Hist. Bact., 171-78.

18. Ibid., 176-77, 192-95, 198-200.

19. Snow, "On Continuous Molecular Changes," Snow on Cholera, 156-57.

20. N. R. Barrett, "A Tribute to John Snow, M.D. London 1813-1858," Bull. Hist. Med., XIX, No. 5, May, 1946, 517-35.

21. Snow, "On the Mode of Communication of Cholera", Snow on Cholera, 133.

22. Ibid., 14-16.

23. For a discussion of the specific element in disease from a different viewpoint than that of the author, see Bulloch, Hist. Bact., Ch. 7.

24. Kisskalt, Theorie und Praxis, 148.

25. Bulloch, Hist. Bact., 142.

26. Ibid., 129-33.

27. Ibid., 141-44.

28. Ibid., 146-52.

29. Joseph Lister, "On a New Method of Treating Compound Fracture, Abcess, etc.", The Collected Papers of Joseph, Baron Lister (Oxford, 1909), II, 2, Originally printed in Lancet, 1867, vol. I, 326, 357, 387, 507; Vol. II, 95.

30. Lister, "A Contribution to the Germ Theory of Putrefaction and other Fermentive Changes, and to the Natural History of the Torulae and Bacteria," Collected Papers, I, 275-76. Originally printed in Transactions of the Royal Society of Edinburgh, XXVII, 1875. Delivered orally, 1873.

31. Lister, "An Introductory Lecture (On the Causation of Putrefaction and Fermentation) Delivered at the University of Edinburgh, Nov. 8, 1869," Collected Papers, II, 482.

32. Lister, "Contr. to Germ Theory," Collected Papers, I, 276.

33. Bulloch, Hist. Bact., 179; Garrison, Intro. Hist. Med., 581.

34. Bulloch, Hist. Bact., 208-10; Garrison, Intro. Hist. Med., 578-79.

35. Garrison, Intro. Hist. Med., 577; Paul de Kruif, Microbe Hunters (New York, 1926) is excellent for a popular account for both Pasteur and Koch. Titles of Pasteur's work cited: Etudes sur le vin, ses maladies, causes qui les provoquent, procédés nouveaux pour le conserver et pour le vieillir (Paris, imp. impériale, 1866); Etudes sur la maladie des vers à soie, moyen pratique assuré de la combattre et d'en prévenir le retour, 2 v. (Paris, Gauthier-Villars, 1870); Etudes sur la bière, ses maladies, causes qui les provoquent, procédé pour la rendre inaltérable; avec une theorie nouvelle de la fermentation (Paris, Gauthier-Villars, 1876).

36. Garrison, Intro. Hist. Med., 576; Bulloch, Hist. Bact., 57-62, Ch. X, 388.

37. Garrison, Intro. Hist. Med., 578-79.

Chapter 6 Controversy over the Germ Theory in Europe

The rapid development of the germ theory in the mid-nineteenth century, combining as it did work in many different lines, was not entirely uncontested. To prove the theory it was necessary first to see the micro-organisms suspected of causing disease, and secondly to produce sickness from them.[1] Many medical men, as has been noted, spurned the animalcular hypothesis because the existence of the minute organisms had not been demonstrated. Since the microscopes were not strong enough to reveal them until after about 1825, this is not surprising. Men who considered themselves scientists could not be expected to accept things on faith.

As for the experiment of producing disease from microbes, this was contingent upon the acceptance of the first assumption. One must admit that there was something tangible to be transferred, either animalculae or poisons. Also it was necessary to be sure that the disease produced was the same as the original disease. If the inoculated animal or person did not die, and therefore no autopsy was performed, one could not determine with certainty whether the disease produced in the second instance was the same as that in the original case. Koch's great contribution was that of recovering the micro-organisms between inoculations and cultivating them again, thus proving that the same organism produced the same disease in each case. In this way he guarded against the possibility of getting contaminated material or the introduction of the micro-organisms of another disease in addition to or instead of the one he was trying to produce.

Such details were important. It was partly the criticism of those who opposed the germ theory that led to more careful work on the part of the ones attempting to prove it. The great controversy over spontaneous generation, or heterogenesis, and the odd theories which were produced as an answer to certain weak spots in the germ theory, were extremely valuable in making the scientists take greater pains in performing their experiments and exercise greater caution in their interpretation of results. The stubborn conservatism of individuals was also a factor in the opposition to the germ theory. Sometimes this was hidden under the guise of science, but in the cases of Max von Pettenkofer and of Henry Charleton Bastian one wonders if such views were not carried to the point of absurdity. There is always the case, of course, of the far-sighted individual who turns out to be correct when the whole body of his contemporaries were wrong. Such an individual requires the same type of temperament as the diehard. The reopening of the question of heterogeneity by the crystallization of viruses, which suggests a definite relationship between living and non-living materials, may yet make a hero out of Bastian.

Among the major opponents of the germ theory were the men who supported the doctrine of spontaneous generation. While the germ theory rested upon the basic premise that the self-reproducing germs or animalculae, which produced the specific infectious diseases, were communicated in every case from a person suffering from the disease in question to a susceptible individual, even though the means was often obscure, the adherents of the spontaneous generation belief, on the other hand, thought

that germs could arise de novo, without parents, producing disease, which was then propagated from person to person. Such a view would account for the prevalence of sporadic cases of diseases such as cholera or typhoid between epidemics, and it would also explain the sudden beginning of an epidemic without apparent cause.

The doctrine of spontaneous generation of certain creatures in the lower part of the great chain of being is an ancient one. Aristotle gave his opinion in favor of spontaneous generation and this was the accepted view until after the Renaissance. Probably the first attempt to disprove the idea was made by Francesco Redi in the seventeenth century. Redi produced visible proof that maggots did not arise spontaneously by covering pieces of fresh meat with gauze to keep off the flies. The insects deposited their eggs on the gauze and maggots appeared here, but the meat remained free from them. This refuted the notion of spontaneous generation for visible creatures. After Redi's time the idea went underground and persisted with regard to microscopic creatures.

Leeuwenhoek, though not an educated man in the usual sense, appears to have had insight into the real nature of micro-organisms. He opposed the idea that his newly-discovered bacterial creatures were generated spontaneously, preferring the idea that they came from seeds or germs. Louis Joblot, the microscopist, also held such views. He boiled hay infusions and poured them into two vessels, covering one with parchment and leaving the other exposed to the air. Only the open vessel showed the presence of animalculae.[2]

Such demonstrations were opposed by the great Buffon. As Bulloch points out, George Leclerc, Comte de Buffon, was a fine type of man, "but his only bodily defect was myopia, which in a measure unfitted him for fine and continued microscopic observations." By reasoning therefore, instead of by observation, Buffon came to the conclusion that all organic matter was composed of indestructible molecules, capable of entering into new combinations, similar to the atoms of Epicurus. A theory of spontaneous generation was a natural consequence of this view, because the microscopic organisms were concerned as molecules freed from their former combinations and combined into new ones. Buffon had a profound influence upon John Turberville Needham, who worked closely with him. Needham experimented with sealed flasks and always managed to find infusoria which had spontaneously arisen in them.

The great Italian naturalist, Lazarro Spallanzani, disproved the work of Needham in a series of masterly experiments in which he took greater precautions in hermetically sealing his flasks. In addition, he boiled them to kill the infusoria and removed the air to take out any air-borne infusoria. The result was beautifully uncontaminated material. His methods were as good if not better than those used one hundred years later.

In the nineteenth century, the theory of spontaneous generation became elaborated into that of heterogenesis. This new and more accurate title implied the generation of living things from two main sources. The first suggested a mechanistic approach: "living matter may be produced by the spontaneous organization of animal or dead matter without the

agency of any previous living things." Bastian called this archebiosis. The second view involved was a vitalistic concept found in two forms: living beings may be formed (1) as "a result of dissociation of parts of previous living things now dead," or (2) by "physiological action of a living organism which transmits the vital principle without its organic characters."[3] The whole concept became greatly elaborated and involved. A chart given by Bastian quite effectively delineates all kinds of spontaneous generation, provided one accepts the prior assumption that such a process exists.[4] The doctrine of heterogenity was accepted by such famous figures in the scientific world as O. F. Müller, Lamarck, Cabanis and Kützing, but not by Ehrenberg.

In the early nineteenth century an interesting process of preservation was developed in France by Nicolas Appert. Appert wrote a book describing his method of preserving animal and vegetable substances over a period of several years. The technique seems to have been similar to modern cold-pack canning. Material to be preserved was placed in bottles with good corks and boiled in hot water for several hours. Gay-Lussac noted that this drove out the air and thus avoided fermentation. It also sterilized the material. Appert's wines and other conserves were very popular because of their excellent quality.

The real experimental period in the history of the idea of heterogenesis began with the work of Franz Schulze in 1836. Schulze obtained sterile cultures by boiling his infusion, and by forcing air to enter the flask through chemical solutions. This method was not always successful as the air sometimes went through the solutions too quickly

to be disinfected. Nevertheless, many heterogenists followed Schulz's technique, which may explain their results.

More careful experimentation was done by Theodor Schwann, who used mercury solutions and heated his air before allowing it to enter the flask containing the nutrient material. He obtained cultures free from any form of life. This type of experimentation was carried further by Heinrich Schröder and Theodor von Dusch in 1859. They filtered their air through cotton. Their work was only partially successful - some substances could be kept from decomposing, otherscould not. Schröder was only able to obtain one hundred per cent freedom from putrefaction by boiling material in his flasks at 100°C or higher for a considerable time. Such experiments illustrate the resistance of micro-organisms to heat, but to Schröder they indicated that there was some vital substance in whey, casein, albumen and egg yolks, which gave rise to putrefaction. This was too close to the idea of spontaneous generation for scientific comfort.

In 1858, F. A. Pouchet began to present his conclusions in favor of spontaneous generation to the Académie des Sciences de Paris, and these were published the following year in his Hétérogenie. This was the starting point of a keen controversy. Pouchet came to the conclusion that life arose spontaneously in solutions of organic material, under the influence of pre-existing life, and retaining properties of the original organisms. Thus the vital principle was transmitted somehow through a solution composed of organic matter, formerly organized but now decomposed

and ready for the formation of new life. This vitalistic concept was opposed by Charleton Bastian, who adopted a mechanistic viewpoint: life rose from non-living material by a new combination of molecules. In Bastian's system, called archebiosis, life could come from a mineral or inorganic solution. The similarity between this and the atomism of Epicurus has already been pointed out. Bastain might well have seized upon the crystallization of viruses as proof of his idea if such information had been available to him.

Pouchet realized that the real problem in spontaneous generation was to determine whether or not germs existed in the air. He repeated the experiments of Schulze and Schwann, but obtained diametrically opposite results. His conclusions were opposed by Claude Bernard and others, and his methods were criticized by Pasteur. Pasteur's work on yeasts and fermentation had shown that yeast was a living organism. The problem of determining the source of the yeast cells opened the most heated stage of the whole spontaneous generation controversy.

Pasteur's work on spontaneous generation in 1860 and 1861 was communicated to the Académie des Sciences.[5] He repeated the experiments of Schwann and improved upon the techniques involved, using elaborate precautions to insure that the air passing into his flasks was truly sterile. First he proved that germs or similar organisms exist in the air. Then he showed that a sterile infusion could become contaminated by the introduction of unsterilized air. He devised some bent-neck open flasks in which nutrient material could be sterilized, yet the germs kept out by the

tortuous passage. Pasteur also proved that not all parts of the air were uniformly contaminated with germs.

Meanwhile Pouchet searched the air and examined samples of dust from various quarters and found no germs, spores, or eggs of animalculae (1859). With his supporters, Joly and Musset, in 1863 he made a series of experiments which seemed to refute Pasteur's work. Pasteur, however, again criticized Pouchet's method of experimentation and his lack of numerically sufficient data.

The Académie des Sciences had presented its Alhumbert Award for 1862 to Pasteur, and in face of the attack upon him by Pouchet and his followers, the members of the Academie decided to appoint a commission to settle the question one way or the other. This commission called upon the antagonists to demonstrate their results, each group using sixty flasks of infusions. Pasteur put a special solution in his flasks, and, after sterilizing the contents by boiling, he sealed fifty-six of them, and drew out and bent down the necks of the remaining four, but did not seal them. All sixty remained sterile. He also opened balloons at various points in Paris, producing contamination in them in varying degrees, thus proving his former contention that germs were not uniformly dispersed in the air. Pouchet and his associates made some minor objections to the test proposed by the commission and withdrew from the contest. Later Pouchet published another book on heterogenesis, but in it he merely reiterated his former position without adding any new material to prove it. After this he took no further part in the controversy over spontaneous generation.

Though Pasteur's experiments drove Pouchet from the active field of battle, others took the latter's place. Some of these people drew their conclusions from results obtained by using imperfect techniques in experimentation, and promptly became converts to heterogenesis on the basis of such inconclusive evidence. Hughes Bennett, for example, and possibly the American, Jeffries Wyman, fit into this catagory. The prize example of a heterogenist is Charleton Bastian. Entering into the fray in 1872 with a book entitled The Beginnings of Life, in which he upheld the doctrine of spontaneous generation, this Englishman fought on for his views until his death (1915), long after all his contemporaries had succumbed to the idea that all living things have parents. Emile Duclaux, one of Pasteur's co-workers, praised the work of Bastian in opposing Pasteur because the objections of Bastian in many instances were well founded, and Pasteur was forced to improve his own work as a result of them. Bastian's own laboratory technique was often faulty, although he did discover that the degree of heat needed to kill the infusoria was greater than Pasteur and his associates had supposed.

Bastian also opposed the work of the physicist, John Tyndall, who investigated the floating particles in the air as a problem in physics. Tyndall was drawn into the spontaneous generation controversy by his discovery that a flame burned up the "dust" in the air and left an optically dark space in a beam of light. A space which was germ free and dust free was "optically empty." Tyndall then performed a series of experiments in which he showed that infusions remained sterile unless con-

taminated by dust and germs in the air. This type of work led him to develop a technique similar to modern asepsis. In order to keep his infusions free from contamination he had to have the walls and floor of the room in which he was working scrubbed down, and dress himself and his assistants in clean overalls. He was able to show that at times the heating needed to sterilize the infusion in a flask (not the air in it) had to be prolonged over a much greater length of time than had previously been used. This led him to the conclusion that bacteria went through different phases of development (1877).

Ferdinand Cohn confirmed this idea and demonstrated the resistance of the spore. His finding dealt the death blow to the doctrine of spontaneous generation. Cohn showed that Bastian's experiments with turnip and cheese infusions proved, NOT the idea of spontaneous generation, but the unusual resistance which spores of these bacilli offered to heat. From this time on, any experiment carried out with proper precautions should have disproved the idea of heterogenesis. When the matter was reopened by the crystallization of a virus, it assumed a different form. The question now is whether the viruses are possible links between the organic and inorganic worlds - which suggests Bastian's archebiosis more than spontaneous generation proper.[6] Any such doctrine is still regarded with considerable suspicion.

In addition to the spontaneous generation conflict, there were other controversies based on opposition to the germ theory. These were not as dramatic or as much publicized as the affairs of heterogenesis, but they are probably just as important in illustrating general attitudes

adopted towards the germ theory. Many of the books written to oppose the theory were reprinted in America, especially the ones by English medical writers. In fact, one might even suggest that more of these types of books were circulated on this side of the Atlantic than volumes or papers supporting the germ theory.

Some of the controversies over the germ theory involved modifications of the theory rather than outright opposition to it. The English doctor, Theophilus Thompson, writing on influenza in 1852, apparently was greatly influenced by the work of Ehrenberg on infusoria and he wholeheartedly accepted the animalcular hypothesis. He did not however, altogether understand the idea in its usual form, and so one finds him adapting it to an atmospheric hypothesis:

> The observations of Ehrenberg have shown the presence of animalcules in our atmosphere. Such organized matter, if existing, may suffer under the influence of magnetical or other changes, which by altering the relation of the atmosphere to living beings, may thus engender or diffuse some peculiar virus adequate to become a cause of disease. [7]

Nevertheless Thompson did prefer the animalcular hypothesis as an explanation of the causation of disease, provided one considered the animalculae in the nature of minute insects, capable of proceeding against the wind, and of indulging in great migrations. Since the numbers of insects varied from year to year, and since epidemics seemed to have some relationship to insect migrations, Thompson thought insect life might be a possible cause of influenza. He mentioned the work of Holland and Henle as supporting such a view with regard to other diseases.[8]

It has been already noted in an earlier chapter, that there was nothing new in connecting insects with epidemics. Even as late as 1883, the English edition of August Hirsch's Handbook of Geographical and Historical Pathology included the statement that when cholera was first prevalent in Europe "peculiarly-tinted, mist-like obscurities in the air" were thought to be "dense swarms of lower organisms - 'cholera animalcules' - that had been carried from India by the wind."[9] Here again one is forcibly reminded that the terminology of the pre-bacteriology period was considerably confused, and that the word "animalcule" might mean anything from a micro-organism of animal or plant nature to an insect of microscopic size. Bastian was able to make the same criticism of the early bacteriologists. He wrote that:

> the most discordant opinions have always existed as to the nature of these Bacteria. Naturalists have been in doubt as to whether they should be regarded as independent living beings of the lowest grade, having an individuality of their own; or whether, rather, they should be looked upon as developmental forms of some higher organisms--either animal or vegetal. There seem to be four principal views concerning them:- (1) that they are animal organisms of the lowest grade, having an individuality of their own, as conjectured by Ehrenberg; (2) that they are, as supposed by Hallier, of the nature of spores, produced from, and destined again to develop into, some of the simplest microscopic fungi; (3) that they represent, as Cohn thinks, the later free-swimming stage in the existence of certain algae, intermediate between Palmellae and Oscillatoriae; or lastly (4) that they are the first and more common developmental phase of newly-evolved specks of living matter, which are capable, either singly or in combination, of developing into many kinds of living things.[10]

In considering Bastian's comment upon contemporary views on bacteria, it should be noted that the idea that all living things have parents of the same species as themselves had not yet been accepted. Hence many

of the theories about bacteria considered these organisms as earlier stages in the development of higher organisms. This is another reason why the work of Koch, in demonstrating the complete life-cycle of the anthrax bacillus, was so important. The idea of the interchangeability of species had to be destroyed in the process of building the science of bacteriology.

An extremely interesting variant of the germ theory appeared in 1861 in the work of Horace Dobell, an English physician. Dobell came to the conclusion that the vestiges of one disease became the germs or seeds of the next. He compiled a series of charts to show the inter-dependence of various diseases and, by what was mainly a symptomatic analysis, he connected the remains of one disease with the beginnings of another. For example, he noticed that abortion may be caused by syphilis, so reasoned that the vestiges of one disease, syphilis, were the cause of another disease, abortion. One wonders how he knew that syphilis had been "cured" and still left "vestiges." It seems a bit odd, also, to include abortion in the catagory of diseases. In the case of typhus, typhoid and other forms of "continued" fevers, the essential antecedent was "a poison in the organism either arising in the individual attacked or communicated from another." The causes of the essential antecedent of these diseases were principally "Conditions of Life--overcrowding; destitution; imperfect ventilation; exposure to emanations from decaying organic matter; organic impurities in drinking-water; and other defects in the conditions of life."[11] In spite of calling his book Lectures on the Germs and Vestiges of Disease, Dobell apparently had no intention of

using the word "germ" in the restricted sense common to his day. To him germs were the poisonous remnants of one disease ready to produce another.

An odd theory in opposition to the germ theory was developed by Lionel S. Beale of King's College, London, in the 1870's. His view was that disease was caused by a contagious bioplasm, which had the following properties: it was a minute particle, specific for each disease, derived from normal protoplasm. A living, growing organism, introduced from outside the body, it grew in the blood, body fluids, and tissues. It was small enough to pass through the walls of these tissues and the capillaries, but "NOT in the nature of bacteria or akin to any low form of vegetable organism."[12] The concept of bioplasm needs clarification, for this was the crux of Beale's whole theory. Normal bioplasm was the living protoplasm of the human body. When this material was changed, by some alteration in the vital processes, it became corrupted and gave rise to disease. This altered material he called the disease germs, nicely confusing the terminology of his day. Beale seems to have mistaken the bodily changes which result from the actions of micro-organisms, for instance, the mucus produced by the common cold, for the causes of the disease itself.[13] His bioplasm concept is extremely difficult to grasp because it is so intangible. It was primarily a vitalistic concept and evidently fared badly at the hands of his contemporaries.

Beale's opposition to the germ theory grew more and more pronounced with each succeeding edition of his book The Microscope in Med-

icine. By the fourth edition (1878), he was really violent. In attacking first the spontaneous generation advocates and then the germ theoriests, he wrote:

> No one can prove that the higher animals did not originate spontaneously; but it seems clear that the arguments yet advanced in favour of the spontaneous origin of a bacterium are no better than those that might be adduced to support the idea of the spontaneous origin of a worm or a dog. Futile will be the determined and repeated efforts to force people to believe that these ever-present, growing and multiplying bacteria are actually disease germs. The evidence is unsatisfactory and many of the statements untrustworthy. I believe that never before in the history of science have been made such violent efforts to foist upon the mind doctrines that never had anything to recommend them as of late years. Some distinguished persons are now always trying to make us accept certain scientific views which are contrary to evidence... 14

And again:

> It is curious to observe how very easily in these days an untenable doctrine may be forced into notoriety, and taught far and wide as if it were actually demonstrated truth. A few authorities perhaps in Germany graphically portray what they please to call the results of observations, and after marshalling before the reader certain facts and arguments, remark that the evidence is perfectly conclusive in favour, say, of the view that certain contagious diseases are due to microzymes. Papers, with "new observations", soon follow, and confirm the original statement in every particular. Pupils, friends, admirers, accept and diffuse the new doctrine. Abstracts and memoirs multiply, and the conclusions arrived at abroad are supported and promulgated here, under the patronage of a government official, and published in a blue book. Those unacquainted with the art and mystery of transforming arbitrary assertations into scientific conclusions are easily convinced that the whole scientific world is agreed upon this one question at any rate, while in point of fact the speculative and far-fetched arguments would not have withstood careful and intelligent examination. 15

Beale's unhappiness over the pressure being brought upon heretics to support the germ theory may in part have had a personal basis. The "blue book" mentioned was John Simon's Report of the Medical Officer

to the Privy Council for 1874, in which Burdon Sanderson published an abstract of the current work on bacteriology. This did not include any mention of the work of Beale (for obvious reasons), so Beale complained about the inclusion of work of foreigners to the detriment of those at home:

> The advance of science may be much retarded if Government officials are permitted to publish in departmental blue-books scientific doctrines in which they are interested, and to ignore the facts and observations which happen to be opposed to their pet theory. I shall further express the opinion that if the researches and observations of German authors are to be published at the public expense, it is not right that the results of the labours of men in this country should be omitted. The compiler should be instructed to draw up careful report of the observations of all those who are known to have published memoirs upon the subject, and he should be informed that he is not to select only those which he approved and the special results which favoured his views. The public could draw their own conclusions if they were permitted to study the different results. 16

The amusing part about the whole affair is that Simon and Sanderson were not at this time wholehearted advocates of the germ theory of disease, and both exercised considerable caution in presenting it to the public.[17] Beale's bioplasm theory was an interesting possibility when it was first presented in the 1860's, but as evidence mounted in favor of the germ theory it became outdated. None the less, Beale closed his eyes dogmatically to any opposition and so awoke to find himself in an untenable position by 1880. The rest of his book was a satisfactory text, and it went through many editions both in England and in America.

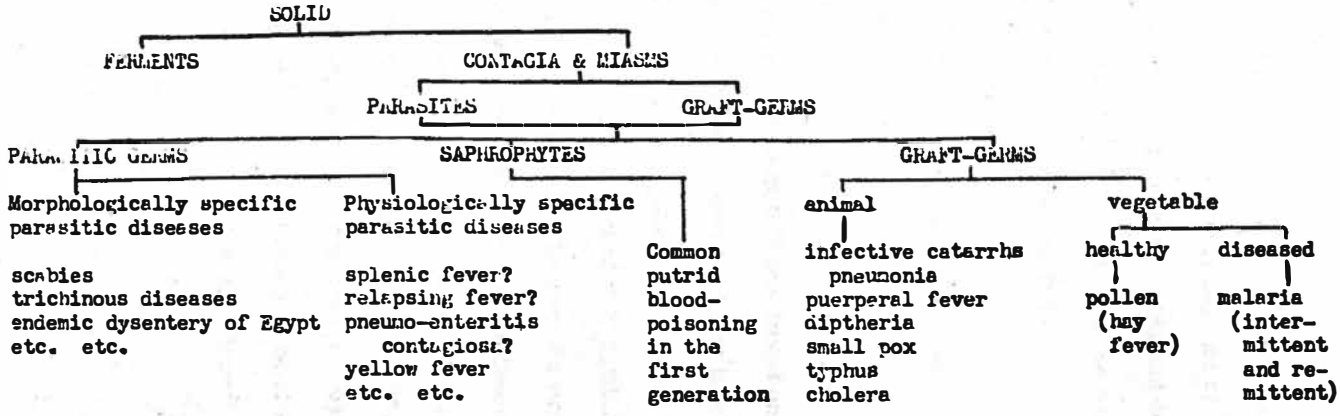
About the time that Beale was expanding his views, another Briton, John Dougall, published a little pamphlet in which he announced that germs were not the cause of putrefaction as was beginning to be believed, but

rather they prevented putrefaction. Germs were beneficial.[18] This was an interesting point, although carried a bit too far. A more interesting theory was presented by James Ross, also British, who applied Darwin's work to the germ theory. He accepted the germ theory to some extent, but also entertained the notion that portions detached from a living body might be the particles of contagion, in preference to living germs. His graft theory assumed that diseases such as small pox and scarlet fever "may have descended by successive slight variations from a disease which was different from both, but which presented characters intermediate between them."[19]

This hypothesis was modified by another English writer, John Drysdale, in his Germ Theories of Infectious Diseases. Drysdale accepted the germ theory for some diseases, and a graft-germ theory, based on the work of Beale, for others. The graft idea meant that disease was due to transplanted particles of living, detached matter (bioplasm or degraded protoplasm) grafted on to a new body. The author preferred this explanation for diseases which we now know are caused by viruses, though the choice was probably wholly accidental. Drysdale's elaborate chart is reproduced herewith, in abridged form, to illustrate his ideas (Fig. 1). This chart shows the intermediate position which it was possible to take with regard to the specific causal factors in infectious diseases.

During the 1880's, textbooks appeared in which the germ theory was utilized for diseases known to be associated with micro-organisms, but retaining the old miasma idea for those whose causal factors were as

FIG. 1 John Drysdale, The Germ Theories of Infectious Disease, frontispiece (abridged)



[The author connected saphrophytes with erysipelas, peritonitis, pyemia, diptheria, smallpox, thyphoid, malignant septicemia in this column.]

yet unknown. Drysdale, as may be seen by his question marks, was still not convinced that the correct explanation had been given in the case of anthrax (splenic fever) and that of relapsing fever. The connection he made between the saphrophytes and septic diseases is interesting and self-explanatory.[20] All in all, the work of Drysdale forms an enlightening and often overlooked link in the chain leading to the acceptance of the germ theory in general.

The development of the germ theory of disease from the animalcular hypothesis into a scientific explanation of the specific causal factors in infectious disease did not take place without considerable controversy and argument. Some of this was based on good scientific work, but often criticism of the developing germ theory was made by scientists whose work had led them to honest, but mistaken conclusions. In other cases it was the result of a man's desire to establish a pet theory or to support a favorite hypothesis. Whatever the origin, the consequence of all the argument was to place the germ theory on a sound scientific basis by forcing its proponents to answer questions and seek answers which they might not otherwise have done. The arguments against the theory began to disappear in the late seventies in Europe and by the early 1880's there was little questioning of it. The continuing work of Paster, Koch and their associates assured the successful establishment of the science of bacteriology.

FOOTNOTES TO CHAPTER SIX

1. Karl Kisskalt, Theorie und Praxis der Medizinischen Forschung 2nd ed. (Munich and Berlin, 1944), 58.

2. The material in this chapter on spontaneous generation is drawn from William Bulloch, The History of Bacteriology (London, 1938), 67-119, except where otherwise noted.

3. Bulloch, Hist. Bact., 79. The mechanist-vitalist interpretation is the author's, not that of Bulloch.

4. H. Charleton Bastian, The Beginnings of Life: Being an Account of the Nature, Modes of Origin and Transformations of Lower Organisms (London, 1872), 252.

5. "Mémoires sur les corpuscles organisés qui existent dans l'atmosphère. Examen de la doctrine de générations spontanées," Ann. chimie et phys., 3me série, LXIV, 5-110 (1862), also Ann. des sciences naturelles, XVI, 5-98 (1861).

6. The germ theory of crystallization which appeared in this period was a sort of reversal of archebiosis. This theory assumed that a germ acted as a ferment and initiated crystallization in chemical solutions. It is rather interesting as an indication of the intellectual climate of the mid-nineteenth century. (Bastian, Beginnings of Life, I, 301.)

7. Theophilus Thompson, Annals of Influenza or Epidemic Catarrhal Fever in Great Britain from 1510 to 1837 (London, 1852), 385.

8. Ibid., 383-89.

9. Geddes Smith, Plague on Us (New York, 1941), 52.

10. Bastian, Beginnings of Life, I, 268-70.

11. Horace Dobell, Lectures on Germs and Vestiges of Disease and the Prevention of the Invasion and Fatality of Disease by Periodical Examinations (London, 1861), 92-101, 73.

12. Lionel S. Beale, The Microscope in Medicine, 4th ed. (Philadelphia, 1878), 319-21. American edition.

13. L. S. Beale, Disease Germs: Their Real Nature. An Original Investigation (London, 1870), 152; The Mystery of Life: An Essay in Reply to Dr. Gull's Attack on the Theory of Vitality in his Harveian Oration for 1870 (London, 1871), 49-50.

14. Beale, Microscope in Medicine, 145.

15. Ibid., 286.

16. Ibid., 315n.

17. Beale practically admits this in his footnote on page 286.

18. John Dougall, On the Relative Powers of Various Substances in Preventing the Generation of Animalculae or the Development of their Germs; with Special Reference to the Germ Theory of Putrefaction (London, 1871), 19-25.

19. James Ross, The Graft Theory of Disease, Being an Application of Mr. Darwin's Hypothesis of Pangenesis to the Explanation of Phenomena of the Zymotic Diseases (Philadelphia, 1872), 267. American edition.

20. John Drysdale, The Germ Theories of Infectious Diseases (London and Liverpool, 1878), passim.

CHAPTER 7 THE GERM THEORY COMES TO AMERICA

The European controversies over the germ theory of disease made little impression on American minds during the post-Civil War period. In fact, the theory itself was scarcely mentioned, and it certainly was not accepted by any great number of Americans. In discussing contributions to the science of bacteriology in his history of that subject, William Bulloch cites only two instances of American participation: work on spontaneous generation by Jeffries Wyman, famed comparative anatomist of Harvard University, and original investigations of fungi as causal factors in infectious disease by James Henry Salisbury of Cleveland, Ohio. Salisbury's studies on the various fungi believed to cause different diseases were probably the only original American work on the germ theory of disease to appear in the 1860–1880 period.

Salisbury began his work early in the 1860's and his first contribution, inoculation of measles by means of a straw fungus, appeared in 1862. Several other contributions followed, notably the work on the spore of the palmella plant as a supposed cause of malaria in 1866. Two years after this he published a little volume on microscopic examinations of the blood, in which he presented his views on the various forms of fungi found in the blood in cases of smallpox, cow-pox, typhoid, intermittent and remittent fevers. The form of his argument is quite convincing, and his illustrations are very interesting. As late as 1883 a work of similar nature appeared from his pen, "Original Investigations in Diphtheria and Scarlet

Fever, showing their Kinship and Cause to be the Mucor Malignans (a fungus in the exudations, blood, urine and sputa), Cured by Quinine Topically Administered in Powder, on the Tongue, and by Inhalation."[1] Of all this work, perhaps that on the palmella plant is the most typical of Salisbury's investigations.

Working in malarious areas on the banks of the Ohio and Mississippi Rivers, Salisbury discovered that there was a kind of algae or cryptogamous plants called the palmella whose spores were easily found in the nearby air. Since these plants were always found in the ague lands, Salisbury came to the conclusion that if he could prove that malarial fevers always occurred after exposure to the spores of the palmella and, conversely, if there were no fevers where there were no palmellae, then he might have the solution to the malaria puzzle. He therefore made a series of experiments to attempt a proof of his hypothesis. He suspended bodies in the night air of malarious places and found the cells of the palmella. He found similar cells in the urine of patients suffering from malaria. To connect the two sets of observations, he tried a more drastic form of experimentation. In his own words:

> With a view of obtaining still more positive evidence of the intimate relation between the cause of intermittent fever and the cryptogam developing upon drying humid soils, etc., I filled six tin boxes with the surface earth from a decidedly malarious drying prairie bog, which was covered completely with the palmellae previously described. Cakes of the surface soil were cut out, the size and depth of the boxes, and fitted carefully in without disturbing more than possible the surface vegetation. The covers were then placed on, and the boxes transported to a high hilly district, some five miles distant from any malarious locality, and where a case of ague had never been known to occur. The locality was over three hundred feet above the stream levels, was dry, sandy, and rocky. I here placed the boxes of cryptogams on the

> sill of an open second-story window, opening directly into the sleeping apartment of two young men; removed the covers and gave particular directions that the boxes should not be disturbed and the window left open. On suspending a plate of glass over the boxes on the fourth day, during the night, the under surface of the plate, the following morning, was found covered with palmelloid spores, and numerous cells of the same kind adhered to a suspended plate in the room, which was moistened with a concentrated solution of chloride of calcium.
>
> On the twelfth day one of the young men had a well-developed paroxysm of ague and on the fourteenth the other was taken down with the disease. . . .
>
> The experiment was repeated at another point in the same neighborhood, where one young man and two boys were exposed in the same way as described in the previous case. In this instance, the two boys were taken down with the disease; one on the tenth and the other on the thirteenth day of the exposure; while the young man escaped.
>
> On account of other duties, and the difficulty of obtaining the consent of parties for experiments, I have been unable to conduct this part of the examination further. [2]

In a footnote to the above statement, Salisbury added that he did get one more accidental example. He left a box of soil in the office of another doctor, forgetting to carry it with him, and the doctor was taken ill with malaria. Salisbury used the microscope to search for his cryptogams, and his experimental method was good, even though he did have the wrong organisms and the wrong disease. Had he tried such a method with a disease like anthrax, he might have had more success.

Encouraged by the reception given his work, especially in Europe,[3] Salisbury carried his idea over to the etiology of other diseases, but his work was indecisive and not much came of it. As it was, after initial acceptance, his experimental evidence was refuted by others who found

the palmella in localities where there was no malaria, showing it to be a very common plant.[4] One of the most effective of these refutations was that of Horatio C. Wood, who opposed the cryptogamous theory in general and Salisbury in particular. He cited the work of Joseph Leidy, which has been mentioned earlier in connection with opposition to J.K. Mitchell's theory. Wood himself swallowed the palmellae without ill effects, and he used the microscope but he could not find any of the cells in question. He was particularly disgusted with Salisbury's contention that he had found the fungi of syphilis and gonorrhea-pointing out that "of all the known diseases, the one, the natural history of which is most irreconcilable with the idea of a fungus as the cause, is syphilis. Why is contact necessary for its passage from one individual to the other if spores or fungi be the cause?"[5] Wood's objections were repeated by others, and by 1872, Christian W. Rauschenberg, who was well acquainted with the work going on in France and Germany, termed Salisbury's theory "unreliable."[6]

Rauschenberg wrote an article in the Atlanta Medical and Surgical Journal on "Microscopic Organisms as Instigators of Disease" in September, 1872, which was cautious but favorable towards the germ theory. The article was written "with a desire to consolidate into a palatable form the most important general facts" known at the time, and it certainly achieved its purpose. Rauschenberg was interested in the work on anthrax being done by Pollender, Brauell and Davaine, Ferdinand Cohn's work on single-celled organisms, and above all, Edwin Klebs' demonstration that the material which would not pass through an earthen filter contained "the living virus producing the disease, pyaemia and septicaemia." He wrote

in the article that Klebs had found in wounds and pus

> more or less microscopic organisms - as minute round cells, either single or in live motion or attached to each other, forming lengthy filaments, or crowded together as thick quiet clusters, or elongated as staff-like bodies with oscillating motion. [7]

There can be no doubt that the micrococci, streptococci, staphylococci and bacilli are being described here. The fact that they are called "more or less microscopic organisms" by Rauschenberg is amusing, but it indicates his reservations towards the bacteriologic work. He does not appear to have tried to verify Klebs' discoveries himself.

Two Canadian articles on animalculae and germs also came out in 1872. J.P. Brown of Galt, Ontario, had several patients who had been poisoned by contaminated buttermilk. Chemical analysis revealed no traces of any poison, but microscopic examination showed that it contained animalculae. Brown came to the conclusion that the animalculae had caused the ill effects.[8] John Bell, in an article on "Disease Germs" in the same year, believed that these germs were not cryptogams, but living particles of animal origin. He liked Lionel S. Beale's bioplasm idea thought that this was probably the answer to the problem of causation of disease because it indicated a change coming from within the body, not disease germs from the outside - a non-contagionist's approach. Nevertheless, Bell did not entirely reject the germ theory, and wrote:

> The great objection to the Germ Theory of disease is, that the distinction between healthy and diseased Germs has not hitherto been satisfactorily made with diseases supposed to be thus propagated. The reason for this appears to be that they are so minute as to require microscopes of such high powers as have been hitherto but seldom employed by investigators. Dr. Beale has delineated germs so small as the 1,000,000 of an inch requiring a microscope

> of from 2,000 to 5,000 diameters linear for their demonstration, and states they are invisible by less powerful glasses. It is not therefore surprising that the germinal theory has been hitherto chiefly hypothetical but recent investigations are clearing up this interesting subject and showing that morbid powers originating within and without the body are, at least in many instances, due to germs. 9

The Canada Medical Journal, in which this article appeared, had a section on "Medical News" in which the work of a Belgian on disinfectants is printed. This man accepted the germ theory and said that the disinfectants killed the germs and thus inhibited the putrefaction caused by them.[10] The Canada Lancet of the same year reproduced parts of Tyndall's lecture on "Disease and Smoke" given at the Royal Institution. In this lecture Tyndall reiterated his views on the germ theory. He regarded knowledge of certain parasitic diseases, together with Pasteur's work on the silk worm diseases of France as extremely important to proof of the actions of pathogenic parasites. Canadians reading this journal would certainly be well-acquainted with the philosophical reasons for accepting the germ theory.[11]

On the whole, however, little attention was paid by American physicians to European bacteriology during the early 1870's. The American journals of 1872, to take a sample year, were characterized by a primary concern with medical affairs in the United States. Foreign intelligence was reported, particularly in the American Journal of the Medical Sciences, but this work was taken in the form of abstracts of books or articles in foreign journals, or as letters from American students abroad. As a rule, there were no foreign contributors or reproductions of foreign work in toto.

When Americans mentioned foreign work on the germ theory, a rare occurence, they often chose to accept the arguments of those opposed to it -- Beale, Pettenkofer, and others. The only mention of Tyndall in any of the four representative journals examined in detail, related to his visit to the United States, rather than to the details of his work.[12]

Non-medical journals carried news of medical interest. A later paper of Tyndall on germs, read before the Royal Society, was abstracted in the first volume of the American Journal of Microscopy in 1876. In this paper Tyndall explained his views on the prevalence of germs in the air, to which his experiments had led him, and his work on the refutation of the doctrine of spontaneous generation.[13] The readers of this journal were as apt to be laymen as physicians.

Some knowledge of the work on bacteriology abroad was beginning to seep into American thinking by 1875, but it was still very imperfect. For example, in a discussion in the Philadelphia Medical Times in July of this year, Joseph C. Richardson wrote that different disease germs were microscopically indistinguishable, yet capable of developing into totally diverse diseases.[14] A short note on "Fungi in Disease" in the American Journal of Microscopy in 1876, connected fungi with diphtheria, and observed that at the Newark, New Jersey, Scientific Association, a Dr. Edwards reported that he had found a parasitic fungus always present in the diphtheria membrane. He was not sure whether this was a "cause or simple accompaniment of the disease."[15]

The real acceptance of the germ theory began with the appearance of an English translation of Hugo W. von Ziemssen's Cyclopedia of the Practice of Medicine in 1874-48. By 1878 the influence of this work was apparent at the meetings and conventions, as illustrated by the paper of John T. Carpenter given at the 29th Annual Session of the Medical Society of the State of Pennsylvania.[16] Before that time, it was a rare American dictionary or encyclopedia or even a textbook which contained any mention of the germ theory.

A study of some of the representative textbooks between 1860 and 1885 shows clearly how long it took for the new concept to be presented. Some authors were very far behind, missing even the purpose and results of the work in pathologic anatomy. Robert S. D. Lyons, in 1861, was still identifying fevers by their symptoms, classifying yellow fever as a kind of remittent fever. An appendix to volume twenty-three of the Transactions of the American Medical Association, "Nomenclature of Diseases", is interesting as illustrating a modified viewpoint. Disease classification is based mainly on symptoms, but listed by the anatomical parts affected.[17] This is similar to the present day listing of diseases not associated with either specific infections or poisons.[17]

Henry Hartshorne's Conspectus of the Medical Sciences, in the second edition (1874), contained some interesting comments on the etiologic theories of the day. He accepted the usual human effluvia (contagion) or "crowd poison" and filth origin of typhus, and the relation of high temperature, decaying vegetation and moisture to yellow fever. He followed Mitchell's cryptogamous theory so far as intermittent fever was

concerned, which is an indication of the length of time that this idea survived. His most interesting comments were made in connection with typhoid fever and cholera. The widespread character of this first disease caused him to be skeptical about Murchison's "pythogenic" theory, (in which typhoid fever was always referred to foul air like that of sewers), and about William Budd's water-transmission hypothesis. As to cholera, Hartshorne did not accept the work of John Snow and he refused to believe that this disease was dependent upon human agency and contaminated drinking water. Instead he followed the ideas of Pettenkofer and Thiersch in thinking that "the specific cause of cholera either exists in the 'rice-water' discharges, or is formed by a process of change in them after evacuation." This material got into the ground water and water-courses above the ground, and into dried dust from infected soils, which passed into the air, infecting large areas at a time.[18] Hartshorne knew of the work of most European writers on the subject of etiology, but he accepted that of those opposed to the germ theory of disease.

Similarly, a reporter in the Boston Medical and Surgical Journal for 1872, outlining "The Etiology of Typhoid Fever", preferred Pettenkofer, while Joseph G. Richardson, of Philadelphia, writing on "Certain Human Parasitic Fungi" in the same journal, accepted the work of Beale, saying that germs merely preyed upon the body like vultures after the disease had struck.[19] Americans appear to have been prone to favor the wrong side in the European controversy over germs.

A French text on hygiene by A. Proust, Traité d'hygiène publique et privée, published in 1877, was used to some extent in America. In this book, the opinions of those on both sides of the controversy over the necessity of specific micro-organisms as factors in causing disease were included. Proust accepted the germ theory, however, and he pointed out that there was no logic in sanitation without the idea of specificity. Furthermore, if one had some knowledge of the specific causes it would be possible to prevent the disease or infection, as illustrated by the practice of antisepsis. Proust also pointed out that the period of incubation and the known immunity of some subjects to certain diseases also confirmed the theory. In spite of his insistence that the germ theory provided the correct answer to the problem of specific causation in infectious diseases, Proust defined miasmata and contagia ("viruses") in his treatise, and apparently saw nothing unusual in ascribing one disease (such as anthrax) to a bacillus; another (such as malaria) to a miasma; and a third (such as small-pox) to an air-borne particle of contagion. The new ideas were slowly replacing the old, but until a satisfactory demonstration was effected, the old remained in the textbooks.[20]

Some of the texts in the early 1880's illustrate this fact very nicely. For example, in 1884, there appeared an American edition of Edmund A. Parkes' A Manual of Practical Hygiene, intended for military use. According to the preface, some Americans had expressed disappointment because earlier editions did not have any material on the germ theory. By this date Americans were anxious to hear of this work. The new edition did not answer this criticism, and in spite of the date of publication, there is not

one word about the work of Robert Koch on cholera, although Pettenkofer was mentioned frequently. Where the "germ theory" was mentioned, the author either included material to prove it was not correct, or else he chose in illustration ideas, such as the Klebs Bacillus malariae, which proved to be incorrect or premature.[21] Altogether this was not a very satisfactory text, even for the military.

An American medical dictionary by Wesley M. Carpenter, An Index to the Practice of Medicine, printed in 1884, but written two years before, turned out to be somewhat better. The doctrine of specificity seems to have been well-understood and the author includes "specific viruses" for dengue and hydrophobia, special "poisons" for typhus and malaria, and spirilli in the blood for relapsing fever. That marvelous disease entity, typho-malarial fever, was believed to be caused by the combined poisons of malaria and typhoid fevers.[22] A few of the entries under the heading "etiology" will suffice to give some indication of what information the student received:

Fever, Typhoid

Etiology - A specific poison. Infection, which may be conveyed by water, milk, sewer emanations, and putrefying animal matter.
Predisposing causes - Youth and adolescence; autumnal season; defective sanitary arrangements; idiosyncrasy.

Phthisis Pulmonalis

Etiology - Inflammation, tubercule, or a combination of the two; heredity; age (twenty to thirty); malnutrition from any cause, especially in a person having an hereditary tendency to the disease; previous or existing diseases, such as measles, ...; diathesis; anti-hygienic influences; climatic agencies; infection (?); mechanical irritants (with various occupations): conditions of the soil (moisture); the bacillus (?).

Pneumonia

Definition - . . . Is it an inflammatory affection or is it a general disease with local manifestation?

Pustule, Malignant (Charbon)

Etiology - Direct inoculation with matter from animals suffering from "joint murrain", "black quarter", etc. It is believed that the poison may be absorbed by the broken skin. Flies and other insects have also been supposed to be carriers of it. Possibly from eating the flesh of infected animals.

Treatment - . . . Inoculation with attenuated virus (Pasteur) (?).

Pyaemia-Septicaemia

Etiology - Purulent or septic material in the circulation; or a chemical poison derived from pus and other matters in wounds; or microscopic organisms.

Tetanus (Lockjaw)

Etiology - Occurs without assignable cause. Wounds and injuries of various kinds; exposure to cold and wet; epidemically....
23

The etiologic sections now seem a mixture of old and new, and in some cases a fairly complete account of the factors causing disease is given, while in others there is almost a complete misunderstanding of the causation of the disease. The old adage that it takes ten years for a new idea to get into the textbooks and another ten to get it out, appears to be realized here. One can see traces of the miasmatic, atmospheric, zymotic and germ theories, but no definite preference among them is indicated.

The question then arises: if the germ theory was generally not considered seriously in the United States during the 1865-1880 period, what thoughts did Americans harbor on the subject of etiology? Their ideas were of two main types. First, there was a continuation of the old miasmatic ideas; and secondly, of the filth theory of disease.

These views were interrelated. In 1859, as one might expect, typhoid fever was believed to be caused by idio-miasmatic effluvia, or personal infection."[24] The Third and Fourth National Quarantine and Sanitary Convenions each had a committee investigating "The Nature and Sources of Miasmata", which faithfully turned in reports in which fevers were attributed to decaying vegetation, to an invisible but detectable (method unstated) "malaria" or miasma, and to the presence of offensive effuvia from slaughter-houses, swamps, cesspools, and sewers -- mostly the same old factors previously enumerated by Benjamin Rush, and other eighteenth century authors.[25]

A typical view in 1866 was that of an anonymous reviewer in the American Journal of the Medical Sciences. In a review of work on cholera, the writer, identified only by his initials D.F.C. (probably D. Francis Condie of Philadelphia) brought out two ideas, which will be recognized as those of Snow and Pettenkofer. He wrote:

> The opinion that cholera is propagatable through the medium of a specific poison contained in the dejections of patients labouring under the disease, is one entertained by a large number of writers on cholera, and many very imposing facts have been adduced in support of its correctness. By a few, however, it is maintained that the recent discharges from cholera patients are not infectious, but become so only after they have undergone decomposition. [26]

The reviewer then described the work of Snow, but he himself preferred the view that cholera was a contagious disease, introduced by persons infected by or formerly in contact with it, or through the medium of their personal goods (fomites). This infection acted as a ferment in affecting the atmosphere, if the latter was in "an impure and stagnant state", and

turned it into a general carrier of the "morbific" poison.[27] Such an idea is merely a repetition of the old atmospheric hypothesis, and the author had picked up nothing new from reading Snow or the others.

A possible clue as to why Americans generally turned against the animalcular hypothesis, after some of them had supported it earlier, was given by Horatio C. Wood in 1868:

> In conclusion, perhaps it is allowable to state that some two or three years since the writer of this paper was very strongly inclined to believe in the doctrine of animate contagion, having imbibed it during his student life, and that this essay has not been the result solely of studies especially undertaken for the purpose; but that during the prosecution of other microscopic investigations, the evidence so gathered itself in his mind as to lead him into this by-path, and to leave him no doubt that general diseases are not caused by organic entities. There is a vast accumulation of negative evidence which repudiates the doctrine of animate contagion, either as taught by Linnaeus or by more recent authorities. There are no known facts establishing the doctrine; there are many such which strongly support the negative proposition.[28]

Wood's conclusion was maintained by him ten years later in a study on fever, but he did admit that in cases of fever there was a definite poison "sometimes having been formed in the system, sometimes having entered the organism from without."[29] This seems to be a hint of the zymotic hypothesis, though Wood never carried the idea very far. By the time the book was published, in 1880, his etiology was already out of date.

Rauschenberg, as has been mentioned, presented both the germ and zymotic theories in his paper on "Microscopic Organisms as Instigators of Disease." He was very careful to say that "no definite results have yet been attained and substantiated with absolute certainty. The subject, however, is daily gaining more interest and importance, and

deserves more and more the general attention of the profession."[30] If much attention was given to the work, the results were not apparent.

Austin Flint, whose work on typhoid fever in western New York state had been cited in evidence by no less authority than John Snow, published a popular article on "Medical and Sanitary Progress" in Harper's Magazine, in June, 1876. In it he dealt with the germ theory in the following terms:

> It is, indeed, claimed by some that the causation of certain diseases by specific organisms of microscopical minuteness has been demonstrated; by the majority of medical thinkers, however, the demonstrative evidence is not considered as complete. [31]

He also mentioned, as a matter of interest, that such a theory had been advocated a quarter of a century previously by "the late J. R. Mitchell." One wonders whether Flint waited until the early 1880's to regard the demonstrative evidence as complete.

It was still possible, in the late seventies, to write of disease without mentioning germs at all, and this was often done.[32] Some writers mentioned the theory only to condemn it. In 1879, the American Quarterly Journal of Microscopical Science carried a review of an article in the New York Medical Journal by one Dr. H. D. Schmidt. This physician observed that:

> The microscopical study of disease-germs has not been very prolific in practical results, and the question as to the existence of specific germs of this character is yet an open one. Investigations of the causes which produce disease are probably among the most difficult and unpromising of any which the microscopist can undertake. . .

> On the whole, it appears that the application of the hypothesis of contagium vivum to the explanation of the phenomena of disease, has had its day. 33

The reviewer of this article, probably a layman, accepted the views of this doctor without question.

Frank Wells, Cleveland Public Health Officer, writing on Filth and Its Relation to Disease, in 1876, thought it was not necessary to refer to the germ theory because it was as yet imperfectly understood. As to the origin of disease, he took notice of two schools of thought in Europe, preferring the second. According to Wells, the first school followed Liebig and Virchow and the majority of English writers in claiming that

> certain disorders, notably the zymotic diseases, spring spontaneously from filth; and hence, being entirely amenable to sanitary laws, have been designated by them "filth or preventable diseases;" the other [school], following Pasteur and upheld by Liebermeister, Pettenkofer and the greater portion of the German school, believe that filth does not directly originate these affections, but simply increases a tendency to their causation, by furnishing a nidus or resting place, a favorable soil, in which the living organisms of disease multiply and develop and without which they become as a rule inert and inoperative. In other words, the one class believe that filth alone, communicating the elements of decomposition, is sufficient to produce disease, while the other hold that there must be something more, viz. filth plus some particular poison. Pettenkofer, the warm supporter of the "germ" theory of disease, says that filth is like the charcoal in gunpower. It is necessary to have it, in order to produce the explosion. 34

If the first school is intended to be that of the zymotists, the author did not have a very clear idea of the zymotic hypothesis. In fact, his discussion of the second school shows little knowledge of the germ theory as presented by Pasteur. The inclusion of Pasteur and Pettenkofer as supporters of the "germ theory" shows no recognition of the basic

differences between their views. The spontaneous generation question is brought in in an unusual fashion to support the epidemiologists. Basically, it would appear that Wells had a fine misunderstanding of all the questions of the day: the germ theory, the ideas of Pasteur, the zymotic hypothesis, and the relation of the filth theory to epidemiology. The favorable mention of Pettenkofer again lends support to the view that Americans chose the wrong side in the European argument over the germ theory.[35]

It was during the seventies that the great preoccupation with the problem of sewer gas took place. The Canada Lancet reported that when the Prince of Wales contracted enteric fever in 1872, while on a visit to the home of Lord Londesborough, there must have been some defect in the drainage or pollution of the water involved. In this case both possibilities, one the presence of sewer gas, and the other of contaminated water, were given equal consideration. Frank Wells of Cleveland suggested that the noxious organic vapors of sewer gas were "either themselves the cause of disease, or... the medium by which the germs of disease" were propagated from "the sewers in which they float about." Serious writers in the Transactions of the College of Physicians of Philadelphia gave sewer gas and improper drainage (which allowed the sewer gas to get out) as causes of typhoid.[36]

In 1880, Benjamin Lee addressed the Medical Society of Pennsylvania on hygiene, and he blamed sewer gas for typhoid, rheumatism, pneumonia, parotitis, malaria, croup, and diphtheria. No mention was

made of germs, or any other possible contents of this gas. He stated:

> Whatever the agency by which it works, we know that it comes with the power and potency of death. Escaping into the free atmosphere, its deadly poison is quickly destroyed by the oxidation of its organic poisons; but when it mingles with the confined air of our unventilated living and sleeping rooms, it retains its deadly power long enough to do its work effectually. [37]

It will be recognized at once that this is merely the old idea of noxious miasmata transferred over to a new type of vapor. An effective refutation of this kind of thinking was made by George Hamilton and especially by J. M. Keating in a paper and discussion published in the Transactions of the College of Physicians of Philadelphia for 1883.[38] By that time, the germ theory was just beginning to be accepted.

One final element in the American picture concerns the use of the antiseptic system. This method of Lister was adopted in the 1879's, but the reason for it was not necessarily accepted. William Pepper in Philadelphia used the system because it was effective, still without knowing the causes of infection. Stephen Smith wrote an article, "Some Practical Tests of the Claims of the Antiseptic System", published in the Transactions of the Medical Society of the State of New York in 1878, in which he showed that the antiseptic system worked, but he had not the remotest idea why it did so. Articles in the Transactions of the Medical Society of Pennsylvania in 1880 and 1881, relating to disinfection in connection with puerperal septicaemia, show the same thing. This is one of the most interesting features of the whole problem of the general American ignorance of European work in the period following the Civil War.

Here the practical and visible results of the germ theory of disease were accepted without the theory itself. In fact, knowledge of the theory must have been very hazy if such a system could be adopted without the slightest hint, in some cases, of what lay behind it.[39]

Sometimes it seemed as if the laymen had a better grasp of the germ theory than the members of the profession. This was not strange when one considers the low status of medical education in America during most of the nineteenth century. Laymen were also among the forefront of the writers of books on the microscope, but this was partly because microscopy was an amusing pastime and not all of them thought of it as a scientific discipline. In 1875, a layman, F.A.P. Barnard, President of Columbia University, was called upon to speak before the first Convention of the American Public Health Association. His address, "The Germ Theory of Disease and Its Relations of Public Hygiene," was extremely interesting. He described the germ theory and the controversy over spontaneous generation. The latter he regarded as solved by Charleton Bastian, though he recognized that further work was necessary before it could be fully settled. He was well-acquainted with the work of Pasteur and Lister, and was sure that "the germ theory is at least partially true." He was one of the few Americans to mention such European leaders as Schwann, Tyndall, and Klebs, and he was entirely open-minded about the whole subject.[40]

Laymen did more than accept the germ theory - some of them made interesting contributions to it. In England, for example, in 1850, John Grove had introduced his theory of vegetable germs, which was

strongly influenced by the cryptogamous theory of John K. Mitchell. This was one of the rare instances of an American animalculist influencing Europeans. Grove disapproved of the zymotic theory and the animalcular hypothesis, preferring to believe that plant seeds, which had the power of lying dormant over periods of time, were responsible for disease.[41]

The theory of J. Franklin Reigert of Lancaster, Pa., in which the cause of cholera was considered to be minute yellow flies, has already been considered.[42] Reigert was also a layman and he was impatient with the medical profession for not taking up what he believed to be more promising lines of investigation.

In addition, there was another American layman who held an insect hypothesis, which was amusing though hardly constructive. This was William D. Riley, who published a small volume, Locusts and Grasshoppers: The Beginning and the End of the Febrile or Eruptive Diseases in Living Things, in Philadelphia in 1872. Riley was startingly ignorant of elementary biology and it is doubtful whether his work had much influence. It is a good indication of the dissatisfaction of laymen with the medical profession, but not a contribution to add much to the general picture of etiology. He attributed disease to the animalculae or eggs (germs) of insects "of the order of locusts and grasshoppers." These eggs got into the human body by being swallowed and

> the inflictions that follow the animation and the propagation of these germs in the bodies of winged fowls, and the animals, and beasts, and creeping things, and the human family, will be found

> classed under the names of consumption, bronchitis, pleurisy, discharges of blood from the lungs, convulsions, diseases of the kidneys and the liver, scarlet fever, piles, fistula, measles, the urinary and the venereal diseases, small pox, yellow fever, typhoid fever, and many others. In the infliction of the smallpox in the human family the animalcules eat into the linings of the throat. In some of the inflictions they enter the windpipe, and eat into the linings of the air cells of the lungs, and into the lining of the stomach and the intestines. 43

Towards the end of his discussion, Riley indulged in a little fanciful speculation. He wrote that flies deposit eggs, which were borne into the atmosphere and were transformed, becoming animalculae. These animalculae were deposited on earth as hailstones. They became animated as ground locusts in dead bodies, and these locusts then deposited eggs which were transformed into grasshoppers. The grasshoppers deposited germs which caused smallpox and other diseases and then flew up into the atmosphere to be changed into eels. Other germs which were deposited in living things caused cholera and other such diseases, then became animated into locusts, then grasshoppers, and finally frogs.[44] It may be seen that Riley had in mind here some kind of an interchangeability of species idea, which he may have entertained in order to avoid belief in spontaneous generation. He chose visible and known insects and higher organisms for his illustrations, which made his theory untenable.

In contrast to the general cautiousness of the medical profession in early post-Civil War period, and the bizarre ideas of some of the laymen, final acceptance of the germ theory came all of a sudden in the early 1880's. Examination of some of the journals of this period shows how rapidly the theory was made part of medical usage in these years.

For instance, there was not a word about germs and bacteria in the Transactions of the Medical Society of the State of New York until 1886. From that time the theory is constantly mentioned. Some of the Philadelphia journals were quicker to accept the new outlook. William Pepper, writing of typhoid fever in the Philadelphia Medical Times on February 12, 1881, was unaware of the germ theory and attributed the disease to the usual poisonous causes. One author in the same year was aware that there were animalculae in water, but believed these to be harmless. On the other hand, a discussion of the Philadelphia water supply indicated that the water might be impure because of the presence of disease germs in it. Another discussion in 1882, at the Philadelphia Medical Society, followed the presentation of a paper on the bacillus tuberculosis by Dr. H.F. Formad. Formad was opposed to the notion that the bacillus had any relationship to the disease, in spite of Koch, but by this time the atmosphere was generally hostile to those who opposed the germ theory, and Formad met rough treatment at the hands of his colleagues. By the middle eighties the germ theory seems to have been accepted by the medical societies of Philadelphia and of most other medical centers, although many individuals held out against it. The theory does not appear to have percolated into the small towns, as for example, Geneseo, New York, in spite of the fact that popular magazines wrote of it in favorable terms. As for the earlier proponents of the theory, few even remembered them, and a New Jersey doctor, Ezra M. Hunt, congratulated himself because he had traced the contagium vivum idea as far back as 1833![45]

So far as the regular medical profession and the general public were concerned, general acceptance of the germ theory of disease took place in the mid-1880's. However, there are still groups today which do not accept the theory. The most prominent among these are certain religious sects, particularly the Christian Scientists, various evangelical groups and some of the Pennsylvania German orders. The Christian Scientists came into being during the period when medical science placed an over-reliance upon the germ theory. Germs were then thought to be almost the sole cause of disease, and the factors of individual constitution, predisposition, susceptibility, immunity, mental attitude and other details, formerly termed "proximate" causes, were overlooked. Christian Science filled a genuine need for many people who could not be satisfied by the regular medical profession. Even William Osler himself recommended conversion to Christian Science in certain cases of psychoneurosis. Nowadays the medical profession is catching up with the psychosomatic and mental ills, and there are more satisfactory treatments available than religious conversion. Shryock has hinted that membership figures in the Christian Science Church show an inverse variation with medical progress against mental diseases.[46]

Christian Science is a rather intellectual undertaking and one which appeals to intelligent, well-educated, and generally prosperous people. The extreme evangelical sects, snake cults, faith healers and such, appeal mainly to the poor and ignorant. Ignorance, superstition and stupidityare greaterfactors in this respect than poverty, although all

are frequently found in conjunction. These cults often appeal to certain types of mental abnormalities, so that with the advance against mental disease, they may be expected to decline. Fortunately, all the minorities mentioned are protected from certain communicable diseases by the public health demands of the majority of the population. One would expect that the death rates from diseases not covered by public health regulations, but preventable by inoculation or early diagnosis, or curable by chemical therapy or antibiotics, would be higher among these people.

In addition to the religious groups which do not accept the germ theory, there are also some irregular medical sects, such as the osteopaths and chiropractors, which originally avoided this explanation. As in the case of Christian Science, osteopathy also had its origin in a very definite need. For instance, the prevalence of the type of ailments, now medically recognized, occasioned by a "slip-disc" in the backbone suggests that the osteopaths must have derived a considerable amount of their practice from the treatment of these and similar disorders. At the present time, treatment for rheumatism, arthritis, and similar conditions is not entirely satisfactory to the general public and the manipulative procedures of the medical sectarians, such as the chiropractors, who "cure" such ailments by bending a few bones are still sought by large numbers of people. It is most unfortunate when this type of aid is sought by those with specific infectious diseases, for the results are sometimes disastrous. There is a possibility that osteopathy, which is already studied in a four year course, may soon make the adjustments

necessary to be included in the regular profession as homeopathy has already done. The chiropractors, operating on a lower educational level, may always remain on the fringe, catering primarily to the ignorant. At the moment both sects belong in the ranks of the pseudo-sciences.

For the most part, in the 1870's the germ theory of disease was not believed to be of much consequence. A few men accepted it. A few more mentioned it with caution. As a rule, however, it was treated as a rather foolish idea, and variations of the older miasmatic theory held the attention of the medical profession.

During this period Americans began to realize that they needed better medical training and they went abroad to study in Germany, Austria and France. The result of this new training became apparent in the following decade, for when the students returned home they proceeded to spread the new learning which they had acquired. At that time, early instruction in bacteriology was begun by such European-trained men as George M. Sternberg and William Henry Welch. Sternberg's translation of Magnin's Bacteria in 1880 helped convince skeptical doctors at home of the truth of the germ theory. In fact, the publication of this book and the dissemination of the new science of bacteriology by returning students, together with the convincing work of Koch, turned the trick and brought the germ theory home to the medical profession in the United States.

The theory was accepted with comparatively little struggle in the early 1880's and it became a part of regular medical practice. Various groups still hold out against it, partly from ignorance and partly because

of the shortcomings of the profession. Some of these groups can be expected to be absorbed by the regular profession, or to be limited in numbers as the profession extends its practice to give aid in new fields. Other groups will probably always be with us because their independence of the regular doctors is based on factors over which the profession has little or no control. For the most part, however, the great struggle to establish the germ theory of disease is over, and Americans are now in the forefront of the movement to increase knowledge in the resultant sciences of bacteriology, virology and immunology.

FOOTNOTES TO CHAPTER SEVEN

1. Cf. J. H. Salisbury, "Remarks on Fungi, with an Account of Experiments Showing the Influence of the Fungi of Wheat Straw on the Human System: and Some Observations which Point to Them as the Probable Source of "Camp Measles" and Perhaps of Measles Generally," American Journal of the Medical Sciences, New Series, XLIV, 17-28 (July, 1862); "On the Cause of Intermittent and Remittent Fevers, with Investigations which Tend to Prove that these Affections are Caused by Certain Species of Palmellae," Am. J. Med. Sci., n.s., LI, 51-57 (Jan. 1866); "Description of two New Algoid Vegetations, one of which Appears to be the Specific Cause of Syphilis, and the Other of Gonorrhoea," Am. J. Med. Sci., n.s., LV, 17-25 (Jan. 1868); "On the Parasitic Forms Developed in Parent Epitheliel Cells of the Urinary and Genital Organs, and in their Secretion," Am. J. Med. Sci., n.s., LV, 371-80 (April, 1868); Microscopic Examinations of the Blood; and Vegetations Found in Variola, Vaccina, and Typhoid Fever (New York, 1868); "Original Investigations in Diphtheria and Scarlet Fever, Showing their Kinship and Cause to be the Mucor Malignans (a fungus in the exudations, blood, urine and sputa), Cured by Quinine Topically Administered in Powder, on the Tongue and by Inhalation," Gaillard's Medical Journal, XXXIII, 401-24 (1882). Also published in pamphlet form, New York, 1882, 1883, Detroit, 1883.

2. Salisbury, "On the Causes of Intermittent and Remittent Fevers," Am. J. Med. Sci., n.s., LI, 51-68 (Jan. 1866).

3. August Hirsch, Handbook of Geographical and Historical Pathology tr. Charles Creighton (London, 1883), 289, 291; A. Proust, Traité d'hygiène publique et privée (Paris, 1877), 728. See also The Canada Lancet, IV, 433-34 (1872).

4. Horace C. Wood, "An Examination into the Truth of the Asserted Production of General Diseases by Organized Entities," Am. J. Med. Sci., n.s., LV, 333-52 (Oct. 1868). See also W. H. Harkness, "Salisbury's Ague Theory," Boston Medical and Surgical Journal, n.s., II (whole vol. 79), No. 24, 369-75 (Jan. 14, 1869).

5. Wood, "Examination into the Truth of the Asserted Production of General Diseases by Organized Entities," Am. J. Med. Sci., n.s., LV, 333ff, 346, 349.

6. [Christian W.] Rauschenberg, "Microscopic Organisms as Instigators of Disease," Atlanta Medical and Surgical Journal, X, No. 6, passim (Sept. 1872).

7. Ibid., 358-59.

8. J. P. Brown, "Poisonous Effects of Animalculae upon the Human System," The Canada Lancet, IV, 554-55 (Aug. 1872).

9. John Bell, "Disease Germs," Canada Medical Journal, VIII, 65 (1872).

10. "Medical News," Canada Med. J., VIII, 336.

11. "Professor Tyndall on Disease and Smoke", Canada Lancet, IV, 42-43.

12. Am. J. Med. Sci., n.s., LXIV, "Quarterly Summary of the Improvements and Discoveries in the Medical Sciences"; Boston Med. Surg. J., LXXXVI, LXXXVII, "Foreign Correspondence", "Progress in Medicine"; Chicago Medical Journal, XXIX, "Selections". The Transactions of the American Medical Association for 1872 had nothing about foreign work in it. Tyndall's visit was reported in the Boston Med. Surg. J., LXXXVII, 208. A. G. Field published a little pamphlet called Footprints Made in the Dark or Forewords of the Present Status of Bacterial Etiology (Des Moines, Iowa, 1863-1910), which contained a series of papers purported to have been read before Iowa medical societies in 1866, 1876 and 1878. In these papers the discoveries of Pasteur and Koch were announced before they were made -- a remarkable bit of "foresight". Cf. pp. 8-10. 11-14.

13. "Professor Tyndall on Germs," American Journal of Microscopy, I, No. 4, 33-46 (Mar. 1876).

14. Joseph C. Richardson, "Discussion," Philadelphia Medical Times, July 10, 1875.

15. "Fungi in Disease," Am. J. Microscopy, I, No. 2, 22 (Jan. 1876).

16 John T. Carpenter, "The Local Origin of Constitutional Disease," Transactions of the Medical Society of the State of Pennsylvania, 29th Annual Session, 1878, XII, Pt. I, 140.

17. Robert S. D. Lyons, Treatise on Fever (Philadelphia, 1861), 53; Trans. Am. Med. Assoc., XXIII, Appendix, 1-77 (1872).

18. Henry Hartshorne, A Conspectus of the Medical Sciences, Comprising Manuals of Anatomy, Physiology, Chemistry, Materia Medica, Practise of Medicine, Surgery and Obstetrics, 2nd ed. (Philadelphia, 1874), 592-93, 603, 607, 612, 616.

19. "The Etiology of Typhoid Fever," Boston Med. Surg. J., LXXXVI, 58-60; Richardson, "On Certain Human Parasitic Fungi and their Relation to Disease," Boston Med. Surg. J., LXXXVI, 158-60.

20. Proust, Traité d'hygiene, Part XIII, Ch. 1, 714-24, Ch. 4, 735, Ch. 6, 753, Ch. 7, 768, Ch. 8, 784.

21. Edmund A. Parkes, A Manual of Practical Hygiene for the Use of the Medical Service of the Army, ed. F.S.B. François de Chaumont (New York, 1884), II, 134, 129-30.

22. Wesley M. Carpenter, An Index of the Practice of Medicine (New York, 1884), 66, 82, 87, 93-94, 135-36.

23. Ibid., 90, 217, 224, 230, 231, 265.

24. Charles A. Lee, "Account of an Epidemic Fever, which Prevailed at Somers and Yorktown, Westchester County, N. Y. during the Months of February, March, April, May and June, 1859," Am. J. Med. Sci., n.s., XXXVIII, 350 (Oct. 1859).

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26. D.F.C., "Review: Cholera, Its Pathology and Treatment," Am. J. Med. Sci., n.s., LII, 186 (July 1866).

27. Ibid., 187.

28. Wood, "Examination into the Truth of the Asserted Production of General Diseases by Organized Entities," Am. J. Med. Sci., n.s., LVI, 352 (Oct. 1868).

29. Horatio C. Wood, Fever: A Study in Morbid and Normal Physiology (Smithsonian Contributions to Knowledge, No. 357, Washington, D.C., 1880), 254-55.

30. Rauschenberg, "Microscopic Organisms as Instigators of Disease," Atlanta Med. Surg. J., X, No. 6, 350-51 (Sept. 1872).

31. Austin Flint, "Medical and Sanitary Progress," Harper's Magazine, Vol. LIII, No. CCCXIII, 70-84. For Flint on typhoid, see Clinical Reports on Continued Fever (Buffalo, 1852).

32. E. Darwin Hudson, "The Pathology and Etiology of Pulmonary Phthisis in Relation to its Prevention and Early Arrest," Transactions of the New York Academy of Medicine, 2nd series, II, 147-59 (1876); John T. Carpenter, "The Local Origin of Constitutional Diseases," Trans. Med. Soc. of St. of Pa., 1878, XII, Pt. I, 138-43; Harvey Cushing, The Life of Sir William Osler (New York, 1940), 164.

33. "Review: Dr. H.D. Schmidt on the Nature of the Poison of Yellow Fever and Its Prevention," American Quarterly Microscopical Journal, I, No. 4, 315-16.

34. Frank Wells, Filth and Its Relation to Disease. A Report Made to the Board of Police Commissioners of the City of Cleveland (Cleveland, 1876), 5-6.

35. There was an article by Max von Pettenkofer, "What We Can Do Against Cholera" in Public Health: Reports and Papers 1873 (New York, 1875), 317-35, in which he gave practical directions on the prevention of cholera and stressed the importance of cleanliness of water, soil and air, although he thought that drinking water had no influence on the spread of the disease.

36. Canada Lancet, IV, 233-34; Wells, Filth and Its Relation to Disease, 53; William V. Keating, "An Epidemic of Typhoid Fever from Defective Drainage," Transactions of the College of Physicians of Philadelphia, 3rd series, IV, 85-125 (1879).

37. Benjamin Lee, "Address in Hygiene," Trans. Med. Soc. of St. of Pa., XIII, Pt. I, 121.

38. George Hamilton, "Sewer Gas and Its Alleged Causation of Typhoid Fever", Trans. Coll. Phys. Phila., 3rd series, VI, 279ff (1883); J. M. Keating, "Discussion," Ibid., 301-2.

39. William Pepper, "The Sanitary Relations of Hospitals," Transactions of the American Public Health Association 1874-5 (New York, 1876), II, 1-10; Stephen Smith, "Some Practical Tests of the Claims of the Antiseptic System," Transactions of the Medical Society of the State of New York 1878, 106-30; William H. Parrish, "Puerperal Septicaemia," Trans. Med. Soc. of St. of Pa., XIII, Pt. I, 222 (1880); Isaac Snively, "Hygiene in Its Relation to the Medical Profession," Trans. Med. Soc. of St. of Pa., XIII, Pt.II, 666 (1881).

40. F.A.P. Barnard, "The Germ Theory of Disease and Its Relation to Hygiene," Public Health: Reports and Papers 1873 (New York, 1875), 70-87.

41. John Grove, Epidemics Examined and Explained: or, Living Germs Proved by Analogy to be a Source of Disease (London, 1850), 88-90, 128-37, 154.

42. J. Franklin Reigert, A Treatise on the Cause of Cholera. An Interesting Discovery (Lancaster, Pa., 1855).

43. William D. Riley, Locusts and Grasshoppers. The Beginning and the End of the Febrile or Eruptive Diseases in Living Things (Philadelphia, 1872), 4-5.

44. Ibid., 6-7.

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46. Richard H. Shryock, The Development of Modern Medicine, 2nd ed. (New York, 1947), 271, 354.

CHAPTER 8 SOME FACTORS IN THE EARLY AMERICAN NEGLECT OF BACTERIOLOGY

The American neglect of European bacteriology, followed by the speedy adoption of it when its value was at last appreciated, stands in sharp contrast to the slow, steady progress made in the science in Europe. While medical bacteriology was being developed abroad, between 1860 and 1880, all was quiet on the American scene. In view of the earlier American interest in animalcular hypotheses prior to the Civil War, this later indifference is surprising. Some attempt to explain it has already been made, but a fuller analysis of the situation is necessary before it can be fully understood. American attitudes towards science in general, and medicine in particular, must be analyzed in order to explain the American failure to continue work on the animalcular hypothesis.

The first factor which inhibited adequate research in this country was a matter of methodology. Americans failed to recognize the need of using the microscope and of making experiments to check their hypotheses. The proponents of the miasmatic theory, for example, thought that they had settled the matter and that there was no need of looking further. They assumed that simple observation of phenomena - as of epidemiologic data - and inductions based thereon, would provide the final answers. So, too, did those who believed in the animalcular hypothesis. Since these simple, Baconian procedures were quite inadequate for the problem in hand, neither theory could be finally established. It was impossible to raise the whole matter above an argumentative level.

The general prevalence of these attitudes was an American phenomenon, because the continental Europeans and many British scientists realized the value of the microscope. Among the British manuals of microscopy available in the mid-century were those of Gideon Mantell, intended for a popular audience, and of Jabez Hogg, a serious work for medical men. Mantell's book, Thoughts on Animalcules, appeared in 1846, and predicted a great future for microscopic work. Hogg, writing on the microscope in 1854, deplored public apathy towards microscopic science, and the attitude which viewed the microscope as a toy. He pointed out that the instrument was a very necessary part of medical equipment. Hogg had written his manual because he saw the need for a cheap and popular book on how to use a microscope. Evidently he judged the situation correctly because his first edition sold 5,000 copies in twelve months.[1]

Though these books were available in private libraries in the United States, evidently Americans were somewhat skeptical about the value of microscopy. Alfred Stillé, of the University of Pennsylvania, discussed both the ferment and animalcular ideas in his text on pathology, but he also wrote:

> When the microscope shall have revealed the existence of either of these sorts of bodies, in the fluids through which inoculable diseases propagate their kind, it will be time enough to give the hypotheses in question a serious consideration. Meanwhile, physicians may find abundant and more profitable occupation in investigating the relations of phenomena cognizable by the senses; in any other mode of searching for truth in our present subject, the most acute understanding is employed to little purpose. [2]

The last part of Stillé's statement throws some light on the usual American indifference to microscopy. It was suggested that physicians confine themselves to studying phenomena "cognizable by the senses" (by the naked eye) in preference to the microscope. Oddly enough, the very instrument which had been developed as an aid to the senses was rejected as untrustworthy for this purpose.

A more open-minded attitude was displayed by R (possibly the editor, Richards) in the Southern Quarterly Review in 1850. Not only did this man see the need for further microscopic studies on parasitic fungi, but he also recognized that technical improvements in the microscope itself were bound to reveal creatures whose existence was unknown. "For aught we know," he wrote, "there may be myriads of animal and vegetable atoms, far beyond the utmost range of microscopic vision, as there are worlds and systems of worlds which the telescope may never reach. . . ."[3]

In the spring of 1871, Dr. Frank H. Davis of Chicago became interested in the germ theory, though he had little knowledge of it. He realized that this theory had been "generally accepted by the scientific world" (most likely in Europe), but added that "microscopists have failed, however, as yet to demonstrate the existence of any such specific germs holding a definite relation to the origin of disease."[4] Here again one has an expression of American skepticism regarding the values of microscopy.

Davis did not rely entirely upon reason in arriving at his conclusions. He examined the air with a microscope, but was unable to find any germs

in it, so he concluded that either the germs had eluded him or else they did not exist. Furthermore, he justified his views by pointing out that these negative results were "confirmatory of the conclusions arrived at by those who have given the subject most attention"[5] - another instance of acceptance of the results obtained by groups in Europe which were antagonistic to the germ theory.

Observational work was also done by Francis Peyre Porcher of Charleston. In his book, Illustrations of Disease with the Microscope (1861), Porcher gave details and illustrations of his careful microscopic analysis of the blood and other body fluids. The pictures in the book show that his microscope was not powerful enough to see micro-organisms, but Porcher does not appear to have been looking for these. He was more concerned with the notion that the blood contained specific poisons (zymotic hypothesis), which he could not find.[6]

The attempt made by Frank Davis to settle the problems raised by the germ theory through microscopy brings up the question as to whether this was the general practice. The answer is a negative one. Only a few Americans attempted to apply the laboratory approach to the solution of the problems of causation of disease, although the need was recognized and a course in microscopy offered in Philadelphia in 1872.[7]

Mention has already been made of the occasional use of the experimental method (as distinct from microscopy) by Benjamin Rush Rhees of Philadelphia in 1821, by the "anonymous reviewer" of the American Quarterly Review in 1828, and by Alfred Stillé in 1848.

Experimentation was again tried in a Baltimore hospital during the cholera epidemic of 1849. Thomas Buckler described it as follows:

> With a view of testing the cryptogamic and animalcular theories, plates of microscopic glass attached to threads by means of sealing wax were dipped in solutions of sugar, starch, and gum acacia, and hung back of the north wall and in the cholera hospital. Other plates of glass were covered over with glycerine, remarkable for its property of remaining fluid for a long time when exposed to the air, and these, like the former, were suspended in various places about the establishment. Sugar and starch were selected because of the known tendency of vegetable germs to form on these compounds, and it was supposed if animalcula existed in the air that some of these would of necessity be caught on the moist and tenacious glycerine. These plates of glass, having been thus treated, were carefully examined by Dr. Christopher Johnston, aided by powerful lenses, but he was unable to detect the slightest trace of vegetable germs, animalcula, or microscopic organisms of any sort. 8

The experiment is an excellent illustration of both the technical and philosophical difficulties standing in the way of any possible proof of the germ theory at this time.

Similar and even more complex experiments by such an expert scientist as Joseph Leidy yielded the same kind of results. He admitted that animalculae could cause muscardine in the silkworm, and porrigo favosa in man, but as he himself had swallowed quantities of the cryptogams-monas, volvox, vorticella and others - without ill effects, he declined to accept these vegetable organisms as the responsible agents in causing fevers. Additional experimental work to test J. K. Mitchell's cryptogamous theory produced entirely negative results, and he concluded that "to assert, under these circumstances, that there are spores and animalculae capable of giving rise to epidemics, but not discernable by any means at our command, is absurd, as it is only saying in other words that such spores

and animalculae are liquid, and dissolved in the air, or in a condition of chemical solution."[9] This odd conclusion may explain why the formost American parasitologist failed to make any contributions to the developing germ theory. Such a viewpoint, unfortunately, would preclude a search for microscopic organisms.

A correspondent of R, the reviewer of the Southern Quarterly Review, found that he suffered from headache every time he worked with fungi and so he desisted, "being unwilling (with all my interest in the subject) to test Mitchell's theory by so strictly personal an experiment."[10] How different this attitude was from that of the Europeans practicing self-inoculation for purposes of answering similar questions.

A part of the difficulty with American observations and experiments in the 1850's and 1860's resulted from an imperfect knowledge of microscopy. Even with good microscopes, special techniques were needed to observe microscopic creatures with any degree of clarity. It is not surprising, therefore, to find that the mid-century was a period in which microscopic manuals were very popular. Most of these were English works, although a few French and German ones were available for those who could read them. Two of the early French manuals were Chevalier, Des microscopes et de leur usuage, and Mandl, Traité pratique du microscope. German manuals came later, notably Harting, Das Mikroscop, and Heinrich Frey, The Microscope and Microscopical Technology. The English ones were more popular and some of these went through several editions, all of which are readily available now in American libraries. Among these were John

Quekett, Practical Treatise on the Use of the Microscope, Lionel S. Beale, How to Work with the Microscope and The Microscope in Medicine, Jabez Hogg, The Microscope, and William Carpenter, The Microscope and Its Revelations. A strictly American text on the subject was that of John King, The Microscopist's Companion (1859).[11]

Similar materials for study were suggested in all of these manuals. The student was directed to look at yeast, leaves of plants, wings of butterflies, muscle fibre, skin, bone, hair, mucus membranes, epithelial tissue, blood, pus, saliva, intestinal secretions, urine, spermatozoa, infusoria, worms, the itch acarus (a favorite), milk, oil, and the circulation of the blood in the lower animals.[12] In Frey's volume (1872), considerable technical information was given about methods of "tingeing" or staining, and no less than ten different stains are given, including the red and blue aniline dyes.[13] All the manuals included pictures of the different types of microscopes then most popular and directions on how to use them. In the introduction of Frey's book the translator, George R. Cutter, did not hesitate to point out to his readers that microscopy, though very popular, was "delicate work" and few students or physicians were qualified to use a microscope in a satisfactory manner without adequate instruction.[14]

In addition to these manuals, three national journals of microscopy began publication in America between 1875 and 1880. These were The American Journal of Microscopy and Popular Science, The American Quarterly Microscopical Journal, and The American Monthly Microscopical Journal. Modelled after similar magazines in Europe, they covered all

the microscopic fields, and they also gave the latest information on technical procedures and new microscopes, as well as news from at home and abroad, including abstracts of articles in local microscopical journals and activities of clubs for microscopists. Local microscopical societies were established all over the country - in Boston and New York as might be expected, and also in small towns such as Dunkirk, New York. A microscopical section was added to the American Association for the Advancement of Science.

Amateur scientists were prominent in the post-Civil War period and some made important contributions to knowledge in all fields of biology. A large number of amateur scientific publications were put out between 1870 and 1900. Some of these ran for years. A few of them, such as Frank H. Lattin's Young Oologist, began as business catalogues and gradually added scientific articles. Others were purely scientific from the start. Their circulation was generally limited, as compared with popular magazines.[15] In addition, dozens of popular science books appeared. Some of those on the microscope were addressed to children, housewives, clergymen and other interested amateurs.[16]

It should be emphasized that the microscopical journals and societies (and, of course, the popular books) appealed to amateurs and to general biologists, and they do not seem to have been taken seriously by the medical profession. The amateurs at this time were investigating some of the fields which should have interested the doctors. These hobbists kept in closer contact with work in Europe than did their more learned contemporaries. Such a state of affairs may partly be explained

by the American attitude of looking upon the microscope as a toy rather than as a scientific instrument.

The value of the microscope as a device for amusement and profit of amateurs in science rather than for professional men was furthered by claims of its moral worth made by manual writers, notably John King. King's account is quite amusing:

> The most useful and fascinating study is that belonging to microscopic observation, and it is much to be regretted that means have not been heretofore employed to introduce its charms and value into the houses of the people - to their firesides. A more valuable gift from father to son, from husband to wife, from friend to friend, than that of a microscope, cannot be made; for unlike any other instrument, it can bestow upon its possessor, amusement, profit, instruction, health and happiness. Its astonishing and magnificent revelations are of so bewitching a nature, that the parent, son or the man of common sense, who has become fairly acquainted with them, would rather pass his unoccupied hours at home, in the circle of his family, displaying to its members the powers and excellencies of his microscope, thus cultivating in their minds a taste for scientific pursuits, than waste these hours away from home in the turmoil and strife of political excitements, in the mind and soul-destroying region of a porter-house, or in any of those many dens of dissipation, debauchery and vice, which throw out the most alluring temptations, to catch the indolent, the unwary, the careless and the ignorant; to rob wives of the affections of their husbands, to make sons rebel against and cause anguish to their parents, despoil wives and daughters of all self-respect, and render them among the vilest of all the vile. 17

Thus it may be seen that in making its devotees behave as paragons of virtue, the microscope was a rather powerful little instrument.

Other factors besides indifference to microscopy were involved in the American failure to use the laboratory methods systematically. Karl Kisskalt, in his recent Theorie und Praxis der Medizinischen Forschung, includes an interesting chapter on "Hinderances to Research", in which

various obstacles are outlined, some of which applied to the American scene.[18] There was, for example, a desire on the part of the public and press for sensational developments. This is probably always the situation, but the different sciences are not usually in a position to produce results of great magnitude every week or even every year. The public does not understand the years of preparation and tedious labor necessary to produce most "discoveries", so that when the announcement is made of something new, another "wonder drug" or antibiotic, for instance, it appears to have been found overnight and the public clamors for more of the same tomorrow. The medical profession in the doldrum years of the mid-nineteenth century had little to offer the public in the way of sensational developments; and in America, in particular, this lack of visible results was interpreted as evidence that the medical profession could not produce anything very useful and was not worthy of much confidence.[19]

The public naturally overlooked the meagre character of American facilities for research. It saw that inventors could work on a shoestring, and so why not medical men? Support of research before the establishment of the great foundations was haphazard.[20] The lack of means - no materials, no money, the necessity of using cheap and unreliable instruments, and above all, no time free from the constant drudgery of earning a living and no prestige for the laboratory hermit - all contributed to the lag in research in America. It is true that the lack of research facilities can be over-emphasized. After all, Robert Koch was only a small country

doctor when he made his studies on anthrax. There was one important difference, however. His work gained instant recognition and he was rescued from his country practice and given a position in a great research center where he was able to continue his work without the hindrance of having to keep up a practice. Such good fortune was rarely if ever experienced by the research man in America before the acceptance of the germ theory. There was no tangible reward for research as yet, either financially, professionally or socially, and so there was little incentive for independent work motivated by pure curiosity. In America, the spirit was lacking as well as the facilities.

In addition to these negative factors, there was positive opposition to new scientific outlooks. The physicians as a group provided even more opposition to new medical ideas than did non-professional sources.[21] The case of Semmelweis is an outstanding example of the opposition which a new idea may receive if it is advanced "before its time." Oliver Wendell Holmes met similar antagonism in America in connection with his work on puerperal fever. If new ideas were to be met with scorn, what was the use of undertaking a research project and carrying it to a successful completion? One might have to battle contemporaries for ten years in order to get the results accepted. This was true of even the simplest ideas. The necessity of combatting preconceived notions all down the line called for great personal courage in the researcher. Is it any wonder that many who might have been tempted to do research hesitated or fled when confronted by concerted opposition? Among Pasteur's greatest attributes

were his tenacity and his perseverance, for he most certainly met with opposition and attack from every quarter, some of which was entirely unjustified.

Among other miscellaneous reasons for the lack of research work on a large scale in America were several of cultural, social and economic nature. Misunderstanding, caused by language difficulties (expression of ideas, inadequate terminology), or lack of understanding of the ideas themselves because of their originality, or conscious opposition for political, religious or commercial reasons all played a part in holding back the development of new theories and the establishment of systematic experimental science.[22] In America, for example, knowledge of languages other than English was not widespread. Misunderstandings with the British in all areas of thought were well known, even within the same language. Many of these difficulties had their origin in nationalistic feeling. Trouble in comprehending the ideas themselves might have been due to inadequate or faulty education, as much as the uniqueness of the work. In the medical sphere this was very apt to be the case in the mid-century when medical education was at an extremely low level. Political opposition in some of the states was exemplified in the laws against autopsies, which assisted in keeping medical education at a low level. These laws were often based on moral rather than scientific values. Opposition to Darwinian thought is a prize example of the religious type of hindrance. Commercial opposition to the progress of medicine came from two sources. The first was the quacks and patent medicine companies, both of which would have lost

a good part of their market if medicine had been able to satisfy the intelligent members of the general public. The second source was the trading companies (expanding business) which suffered under the quarantine and public health restrictions. Extreme laissez-faire was the rule during the era of big business, and this affected all spheres. The removal of the "brutal" port quarantines from Boston and New York in 1859, as a result of the decision of the delegates to the Third National Quarantine and Sanitary Convention that the major fevers were non-contagious, was hailed as a great victory for commerce and "the welfare of mankind," second only to "the Declaration of Independence in Philadelphia, nearly a hundred years ago."[23]

In addition to all these factors, there was the interlude of the Civil War to be considered. Just before the war, in 1859, one of the delegates to the Third National Quarantine and Sanitary Convention remarked that the series of causes invoked to explain the rise of yellow fever included:

> every variety of exhalations from animal and vegetable decompositions, and from every possible compost; newly-made ground, and sunken lots, and pools of water, in every soil; soap-bubbles of unaccustomed appearance; animal poisons - prominent among which is the rattle-snake - the mephitic exhalations of marshes and swamps and church-yards; all these and more have been accused as the source of the pestilence. Nor is this all; the ichthyological source is formidable indeed, though it is difficult to ascertain which has the most noxious power - the fresh or the salt fish; conchology has also supplied causes of the malady.[24]

From this it may be seen that the situation was becoming highly confused. One is almost tempted to believe that the war was a blessing in diverting men's minds from such nonsense. There is no doubt that the war did divert attention from the problems of etiology - as from all basic research. Prac-

tically nothing new was written on the subject during the conflict; and afterwards the volume of work dwindled in comparison with what had gone before, which may be taken as an indication of the lack of interest in the whole question.

During the post-Civil War period, it appears that Americans turned away from Europe. Medical men, at least, had little knowledge of what was going on abroad in their fields. In contrast to the ante-bellum era, there were few references to foreign literature in American journals of the 1870's. It is difficult to find more than one or two articles containing data on the new work being done abroad in general biology or on the germ or zymotic theories. In contrast, Salisbury's work in this country on the cryptogamous theory was well-received in Europe, even being mentioned as late as 1883 by August Hirsch.[25]

The American ignorance of European work in this period can be accounted for in several ways. Most American physicians were poorly trained in medicine at this time and their general education also was often inadequate. Moreover, a considerable language barrier lay between them and the French and German publications. The older generation of French-trained physicians had gone, and the new generation of German-trained men had not yet arrived. During this interlude, Americans relied largely upon British accounts for their information.

Here again there was a problem. At that time there was considerable antagonism in the North towards the British because of their attitude during the Civil War. In contrast with the Canadian doctors, who adopted the

ideas of Tyndall and others, and were open (if colonially) minded about the germ theory, Americans were inclined to be skeptical and reserved - all in the name of science, of course. The culmination, in the post-Civil War period, of a strong nationalistic trend led to a sort of intellectual declaration of independence from Europe, which is reflected in the development of a distinctly American literature and in American education in general.[26] For the medical sciences, this attitude of independence reached this apex at exactly the wrong time. Some of the most important developments in the whole history of medicine were taking place in Europe just at the time when Americans turned their backs on that continent.

In the physical sciences, the independent feeling led to pioneering work in the various branches of geology, and in navigation and engineering. The development of a native industry and the exploitation and settlement of the West emphasized the value of new inventions, particularly machinery, technical processes and in communications. In the economic sphere, fortunes were made and lost almost overnight, and great emphasis was placed on monetary values. The garnering of wealth for reasons of prestige rather than for personal need led to cutthroat competition. It was every man for himself and self-reliance was the watchword of the era.

This self-reliance doctrine had one major qualifying factor. The equalitarian form of democracy which developed in the United States during the nineteenth century, in theory opened the doors of success to anyone who was willing to work hard for it. In contrast to the more philosophical type of democracy in Britain and France, American democracy included a de-

gree of social equality (in addition to the political and legal sort) undreamed of in Europe. The difficulty of securing submissive servants in America, so often commented upon by foreign visitors, was due to such an attitude. Under a system where the phrase "all men are created equal" was taken seriously, there could be no effective aristocracy based on birth. Aristocratic status, therefore, had to be based on achievement, measured in turn by either brains or material possessions. In America, the latter was easier to acquire, and with wealth one could buy brains. Lacking a fixed hierarchy of classes, status in this country came to be measured largely by wealth alone.

The medical men of the nineteenth century emulated their contemporaries and strove for large and lucrative practices which would give them the prestige of wealth denied them for their intellectual efforts alone. In the present age, when the DOCTOR is almost akin to the gods, it is difficult to realize the lack of confidence which mid-nineteenth century Americans displayed toward the medical profession. Hence the physician who desired prestige must needs acquire it through a fashionable practice which brought wealth, rather than through research achievements.

In addition to placing a monetary value on men and their work, the Americans of the mid-nineteenth century had taken over the old Puritan ideal of usefulness. This meant that the value of a study, practice, technique or science was based on its immediate usefulness, and hence the applied sciences were preferred to theoretical work because they produced results.[26] Here was another trait which helps account for the non-acceptance

of ideas from abroad. There seemed to be no immediate use in them. Needless to say, Pasteur's work on wine, beer and silkworms had strictly practical results; but the American liquor industry ran to distilled beverages, and the textile industries were those based on cotton and wool. Had his work touched a field of economic consequence here there is little doubt that it would have been accepted immediately.

In presenting his work on the microscope to the American public, John King felt it advisable to emphasize its usefulness. He presented the microscope as useful in detecting adulteration of foods, and in the investigation of crime, saying that "the microscopists... are always well paid for their services in those cases where legal or medico-legal questions are to be determined...."[27] He also pointed out that with a microscope the non-professional man could diagnose himself and "learn certain unhealthy conditions of the system, without having immediate recourse to a physician." In this connection he was thinking primarily of microscopic urinanalysis, whereby the microscopist could catch a serious illness before the symptoms had developed, and of skin diseases due to parasites.[28] To modern eyes this looks like an open invitation to the hypochrondriac to get a microscope and see what he could find to worry about.

The final consideration is a philosophic one. The type of scientific method used was also involved in the problem of American backwardness in the development of the germ theory. Americans, like the medieval scholars and even the ancient Greeks, were too prone to ask "why", when the solution to the question could be better obtained by asking "how" or

"what". William Harvey would never have discovered the circulation of the blood if he had asked why the heart beats instead of counting the heart beats and measuring the amount of blood involved in relation to each beat. Galileo's contributions to physics were notable in that he knew what he could leave out. The "why" to the nature of the universe came later, unsuccessfully with Descartes, more successfully with Newton. The European biologists, and especially Pasteur and Koch, answered the "what" in the etiology of disease, but the "why" has not been settled yet.

Americans were also bound to the extreme form of the inductive system advocated by Francis Bacon. All kinds of facts were collected, regardless of their significance, in the pious hope that they would make sense in some grand collection later on. As a result, there are literally thousands of reports on yellow fever or malaria or typhoid-typhus fever, and all kinds of extraneous situations were reported which might have a remote bearing on the case. The interpreters of Bacon overlooked his rule that facts unnecessary for the problem should be omitted, which implied a certain degree of hypothesis-making. For instance, the contagionists and non-contagionists employed the inductive system, each group beginning with its initial, incomplete hypothesis (Bacon's "indulgence of the understanding") either for or against contagion in certain diseases. Then the adversaries collected all the evidence, in a neutral sort of way, yet each side managed to use practically the same material to prove diametrically opposite ideas. A more critical and sophisticated approach was radically needed.

The lack of interest in the germ and zymotic theories of disease after 1860 was a striking example of American neglect of the basic sciences in the nineteenth century. In the early part of the century, American medical writers were not only able to keep abreast of current developments in Europe, but they also made original contributions to the theories of etiology. This was true in the case of the miasmatic and atmospheric concepts as well as the animalcular one. American writers were frequently cited in European works on yellow fever, malaria and other epidemic diseases. In contrast, by the mid-century and after, European work was not mentioned in America to any great extent and few American works were cited abroad. The old question "Who reads an American book?" applied to fields other than that of literature.

The American scene was a strange contrast to that of Europe. An isolationist spirit appeared at an unfortunate time for medicine. In the various fields in which microscopy and experimentation were being used to work towards the science of bacteriology in Europe, little was being done on this side of the Atlantic. The task of assigning reasons for the American neglect of European work in this period has been attempted. These reasons lay in the cultural pattern of a developing American civilization. A basic change in these American attitudes towards science was necessary before any substantial contributions could be made in theoretical science. The sudden acceptance of the germ theory may have aided in producing such a change.

FOOTNOTES TO CHAPTER 8

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2. Alfred Stillé, Elements of General Pathology: A Practical Treatise on the Causes, Forms, Symptoms and Results of Disease (Philadelphia, 1848), 105.

3. R, "Review of J. K. Mitchell's Cryptogamous Origin of Fevers," The Southern Quarterly Review, n.s., I, Art. VII, 151 (April, 1850).

4. Frank H. Davis, "Atmospheric Germs and their Relations to Disease, " Chicago Medical Examiner, XII, No. 4, 194-5 (April, 1871).

5. Ibid., 197-8, also especially 193-99. In the Chicago Medical Journal for 1872, I. N. Danforth wrote that the microscope might solve the problem as to "Whether miasmatic diseases are caused by specific germs or not." He believed that this work would take months or even years of painstaking study. - "Disease Germs," Chicago Medical Journal, XXIX, No. 8, 453 (Aug. 1872).

6. Francis Peyre Porcher, Illustrations of Disease with the Microscope (Charleston, S. C., 1861), passim.

7. An advertisement in the American Journal of the Medical Sciences for July, 1872 (Vol. 64) announced that Joseph G. Richardson, M.D. was offering a course in medical microscopy. This instruction was to consist of fifteen lectures for $15.00.

8. Th. H. Buckler, A History of Epidemic Cholera... (Baltimore, 1851), 23.

9. Joseph Leidy, Flora and Fauna Within Living Animals (Washington, 1853), 14-15.

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12. Cf. Mandl, Traité pratique du microscope, 68ff; King, Microscopist's Companion, Ch. 9.

13. Frey, The Microscope, 150-60.

14. Ibid., viii.

15. Phyllis Allen, "Amateur Scientific Publications in N.Y. State," Museum Service (Rochester Museum of Arts and Sciences, Rochester N. Y.), XVII, No. 8, 71 (Oct. 1944).

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17. King, The Microscopist's Companion, 12.

18. Karl Kisskalt, Theorie und Praxis der Medizinischen Forschung (Berlin and Munich, 1944), Ch. 18, 170-86.

19. See Richard H. Shryock, The Development of Modern Medicine, 2nd ed. (New York, 1947), Ch. XIII.

20. Richard H. Shryock, American Medical Research: Past and Present (New York, 1947), Ch. 1, 2.

21. Stern, Society and Medical Progress, Ch. 9.

22. Kisskalt, Theorie und Praxis, Ch. 18, passim; Bernhard J. Stern, Society and Medical Progress (Princeton, 1941), Ch. 10; Richard H. Shryock, "American Indifference to Basic Science during the Nineteenth Century," Archives internationales d'histoire des sciences, No. 5, 1948, 50-65.

23. Proceedings and Debates of the Fourth National Quarantine and Sanitary Convention Held in the City of Boston, June 14, 15, 16, 1860 (Boston, 1860), 14.

24. Proceedings and Debates of the Third National Quarantine and Sanitary Convention Held in the City of New York, April 27th, 28th, 29th, and 30th, 1859. Doc. No. 9 (New York, 1859), 33.

25. August Hirsch, Handbook of Geographical and Historical Pathology tr. Charles Creighton (London, 1883), I, 291.

26. See Shryock, "American Indifference to Basic Science", Arch. int. d'hist. d. sci., No. 5, 1948, 50-65.

27. King, The Microscopist's Companion, 7, 159, 200.

28. Ibid., 10-11, 157-59, 197. King was a doctor.