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emotions, problems and sufferings. "Even if a Sparrow come before my Window I take part in its existence and pick about the Gravel." Or again, "When I am in a room with people, if I ever am free from speculating on creations of my own brain, then not myself goes home to myself, but the identity of everyone in the room begins so to press upon me, that I am in a very little time annihilated." As his brother became weaker, John felt that his own life was ebbing away. Thus, while his body was being exposed to the microbial agents of infection, he seemed to surrender his mind to disease through his identification with his brother. Tom died in December, 1818, at the age of nineteen.

For John, 1819 was a bad year. The memory of Tom haunted him. His poetry was attacked by the reviewers. His financial difficulties were increasing. And he was deeply in love with the vivacious, high-spirited Fanny Brawne, yet there had been misunderstandings between them. At the end of June he parted from her to go to the Isle of Wight, but this did not quiet the pangs of his jealousy. Back in London, he continued to seek refuge and inspiration in nature, seemingly unaware of creeping illness. On a February day of 1820, he returned from a short trip, coatless on the top of a coach in cold, snowy weather. Chilled to the bone, he was seized by high fever, and became so flushed and nervous as to appear drunk. Getting into bed, he coughed and suddenly tasted blood in his mouth. "Bring me the candle," he called to Brown, with whom he was staying, "and let me see this blood." He looked at the bright red spot on his pillow and then, his excitement and intoxication gone, he said calmly, "I know the color of that blood. It's 'arterial' blood. . . . That blood is my death warrant, I must die." Brown ran for the surgeon, who, according to the honored medical practice of the day, bled John from the arm, the first of the many bleedings that were to hasten his course to the grave.

It was not in a romantic attempt to dramatize his fate that Keats had forecast his early death, but from precise and painful

experience. He remembered his own mother dying of some ill-defined consumption, and more acute in his memory — indeed, in his very flesh — was his brother Tom spitting the death blood of the pulmonary phthisic.[3] In the course of his medical experience, he had seen countless young men and women become sick and go into a "decline." Often, this became a wasting consumption, the body burning away in a relentless fever; and in many patients the disease underwent its inexorable evolution to pulmonary phthisis, with a destruction of the lung that usually meant death.

And now there was on the pillow of John Keats, twenty-four years old, that telltale, brilliant red blood. It is probable that he had been agitated and in poor health long before this acute attack. "For six months before I was taken ill I had not passed a tranquil day," he wrote. Six months previous was the time of his first parting from Fanny Brawne.

During the following spring Keats suffered repeated pulmonary hemorrhages. Doctors continued to bleed him frequently from the arm — and believed that they were combatting the progress of the disease by keeping him on a starvation diet. In order to brighten his spirits, Armitage Brown had moved him onto a sofa bed in the living room; there Keats received visits, night and day, from his neighbors, and in particular spent many hours with Fanny Brawne.

Despite the progress of his disease, Keats now and then pretended to hope. He began to consider his doctor's advice that he escape from the inclement weather of England and move toward brighter skies. In August, 1820, he wrote to Leigh Hunt: "'Tis not yet consumption, I believe, but it would be were I to remain in this climate all winter; so I am thinking of either voyaging or traveling to Italy." Accompanied by his devoted friend, the young painter Severn, he started for Italy in September, 1820, aboard the *Maria Crowther*. She was a small cargo boat, equipped with one single cabin for the five passengers,

CHAPTER IV

Contagion and Heredity

UNIVERSAL as was the dread of consumption, it affected human behavior differently in various parts of the world. The diverse theories concerning the nature and spreading of the distemper determined the ways in which society tried to protect itself.

In certain countries the disease was regarded as catching, a contagion communicated through the air to the well person by some material emanating from the breath of the consumptive patient or from his belongings. In other places, by contrast, consumption was believed to be the product of a constitutional defect, often inherited from one's parents along with color of the hair or facial features.

The theory of contagion had been clearly expressed by a Florentine physician, Hyeronymus Fracastorius, in 1546. So great was the prestige of Italian learning that the theory was at first generally accepted throughout Europe, and indeed many striking facts were presented to support it. For example, there was reported in 1648 the story of three young Brandenburg counts who had contracted phthisis from their teacher, and in 1697 that of a physician said to have become consumptive because he was in the habit of tasting the sputum of his patients for diagnosis. As human milk was often prescribed for the treatment of consumption, a practice still in favor late in the nineteenth century even in the United States, there were stories of nurses having caught the disease from their patients. More incredible tales found

credence. The celebrated physiologist Van Swieten stated that the kiss of a wife dying of phthisis took the hair off a spot on her husband's head. Panarolli, an Italian physician, was reported as having seen a man fall dead after stepping on the sputum of a consumptive, and another contract the disease after inhaling the fumes given off by sputum expectorated on burning coal.

So firm was the belief in contagion among Italian physicians of the eighteenth century that Giovanni Morgagni and other anatomists avoided performing autopsies on patients dead of phthisis in order to protect themselves and their students from contracting the disease. The most important consequence of the dread of contagion was to stimulate in Italy and Spain the enactment of regulations designed to prevent its spread. It was thus that in 1699 the Republic of Lucca promulgated the first decree of prophylaxis in the European annals of antituberculous legislation. The edict gave directives to protect the citizens from being "harmed or imperiled by objects remaining after death of a person suffering from phthisis," and it ordered physicians to "give notice of persons of either sex . . . treated for the suspected malady." The governing bodies of other Italian cities, and later Ferdinand VI of Spain, followed suit, the last edict being made in Naples.

The forceful statement by which a group of physicians of Naples recommended the new regulations to the Department of Health is not without interest. "Pulmonary consumption is of such a malignant nature in our country that even after the death of the sick person the seed of his malady remains hidden and unseen in many houses, with serious danger to those who move into them thoughtlessly; and indeed some of this seed is so penetrating that it can be communicated even without immediate contact with the infected person or thing."

The law ruled:

I. That the physician shall report a consumptive patient when ulceration of the lungs has been established. Failure

I have been sick as a dog the last two weeks; I caught cold in spite of 18 degrees C. of heat, roses, oranges, palms, figs and three most famous doctors of the island. One sniffed at what I spat up, the second tapped where I spat it from, the third poked about and listened how I spat it. One said I had died, the second that I am dying, the third that I shall die. . . . I can scarcely keep them from bleeding me. . . . All this has affected the Preludes and God knows when you will get them.

Soon the natives became aware of the fact that Chopin was consumptive and they refused to have anything to do with him or his party. George Sand, who accompanied him on this trip, has left a lively account of their ordeal.

At very great cost, we had succeeded in establishing ourselves in Majorca, a magnificent country but most inhospitable.

After a month there, poor Chopin's disease got worse, and we called in one, two, then three physicians — every one of them more asinine than the others and who spread through the Island the news that their patient was suffering from the lungs. The tale stirred up great terror. Phthisis is scarce in these climates and is regarded as contagious. . . . The owner of our small house threw us out immediately and started a suit to compel us to replaster his house on the pretext that we had contaminated it.

We went to take residence in the disaffected monastery of Valdemosa . . . but could not secure any servants, as no one wants to work for a phthisic. . . . We begged of our acquaintances that they give us some help — only one, the first, the last service! — a carriage to take us to Palma, from where we wanted to take a ship back home. But even this was refused us, although our friends all had carriages and wealth.

We had to go three leagues through deserted side roads in "birlocho," that is, in wheelbarrows.

When we arrived in Palma, Chopin had a terrifying hemorrhage; the following day, we boarded the only steamship that comes to the island and which is used to transfer pigs

to Barcelona. There was no other way to move out of this wretched country.

At the time of leaving the inn in Barcelona, the innkeeper wanted us to pay for Chopin's bed under the pretext that it was infected and that the police had given him orders to burn it.

Doubt as to the contagiousness of phthisis had been expressed by the Faculty of Paris around 1650. From there it soon spread over all Northern Europe. Northern physicians seem to have been led to believe that the disease was due to a constitutional hereditary defect rather than to contagion by the fact that it was particularly common and severe in certain families.

They had noticed, for example, that brothers and sisters often became consumptive at almost the same age. In 1688 Richard Morton wrote in his *Phthisiologia* the story of a Mr. Hunt, a citizen of London who had "lived almost from his youth to the seventieth year in a consumptive State, doing his business well enough by taking care." He had three sons, who all lived until they were about thirty, at "which time they were all, one after another, seized by the same inheritance with a consumption occasioned by Passions of the Mind and the drinking of Spirituous Liquors . . . the Distemper carried them all off before the emaciated old man died." More than a century later, Antoine Portal reported that in a family of Gaillac in the southeast of France all five children had reached the age of twenty-eight to thirty in perfect health, only to die of phthisis by the age of thirty-two; the first three had died within two years, and the last two some ten years later within six months of one another.[1]

History offers many examples of celebrated tuberculous families, the French royal Bourbon family being one of them. Louis XIII died of galloping consumption, his autopsy revealing extensive intestinal lesions and pulmonary cavities. His wife, Anne d'Autriche, also suffered from phthisis. Their son Louis XIV

had long suffered from fistula of the fundament, probably of tuberculous origin, and was operated for it by the surgeon Felix. It is told that after the operation the courtiers applied dressings to themselves so that they could imitate His Majesty's limp! As the operation was successful, and the royal anus cured, Felix received a farm and 300,000 livres, in addition to being created Seigneur de Stains.

The literary world of the nineteenth century provides many well-documented examples of familial phthisis, but none is more dramatic than the case of the Brontës.[2] The Reverend Patrick Brontë was born in 1777 (on Saint Patrick's Day) of a poor family in County Down, Ireland. After much struggle, he succeeded in going to Cambridge for his education and in being ordained to a curacy. He married Maria Branwell of Cornwall in 1812 and had six children, all born during the following seven years. Mrs. Brontë's health was failing when the family moved to Haworth in Yorkshire in 1820. She died the following year at the age of thirty-eight, of some vague ailment that was diagnosed an "internal cancer."

There is much that is obscure in the personality of the Reverend Patrick Brontë. His rise from a poor farm background in Ireland shows that he did not lack ability and enterprising spirit. But in Haworth, he kept himself and his family aloof from the village folk as if the humble social surroundings of his parish did not satisfy some unavowed ambitions. He professed and practiced extreme austerity of life, believing that his children should be brought up simply and hardily. There were no carpets in the parsonage except in the parlor, despite the cold dampness of the stone floors and stairs; little or no meat was served at table, and the Reverend forbade his wife and children to wear any colorful clothes or silk dresses that might lead to personal vanity. Yet there are vague rumors that he had changed the family name from Brunty to Brontë when he moved from Ireland, and he was wont to display before certain stran-

also the many theories that have been devised to account for their genesis and evolution.

We shall recount in the following pages how a few physicians succeeded in organizing this welter of information into an orderly system based purely on clinical and pathological criteria, long before the discovery of the tubercle bacillus. We shall note also that much theoretical and practical knowledge was gathered by those who regarded heredity, nutrition, climate, or emotions as the causes of tuberculosis. The progressive discovery of facts, and the unfolding of doctrines bearing on the causation of tuberculosis, constitute some of the most brilliant chapters in the history of medical science. They demonstrate that a disease can be described and analyzed in terms of many unrelated theories, each true at its own level, each fruitful in understanding and practical results. To him who follows her way, Nature reveals many roads that lead in the direction of truth.

Ancient knowledge of disease was derived almost exclusively from the observation of symptoms. As the initial stages of tuberculosis cause little discomfort, and usually remain unnoticed by the patient, the disease came under medical attention only in its very advanced form until modern times. Hippocrates, who lived about 400 B.C., and most physicians until the nineteenth century, taught that phthisis begins as a respiratory catarrh, with chest pains, increasing malaise and a dry cough yielding yellow sputum; but it is now known that, in many cases, these symptoms occur only after the lesions have become extensive. The Greek and Roman physicians recognized that evening fever and night sweats, blood spitting, a small pulse, clubbed fingers and curved nails, pleurisy followed by empyema, extinction of voice and diarrhea, were signs often associated with pulmonary phthisis. However, what impressed them most was the emaciation of the patient, an exhaustion of the reserves of the body that they

worth quoting his description of the discovery of pectoriloquy, the peculiar sound detected with the stethoscope over pulmonary cavities.

> In the very earliest period of my researches on mediate auscultation I attempted to ascertain the differences which the sound of the voice might cause within the chest. In examining several subjects with this in view I was struck by the discovery of a very singular phenomenon. I was studying the case of a woman affected with a slight bilious fever and a cough having the character of a pulmonary catarrh. When I applied the cylinder below the middle of the right clavicle while she was speaking, her voice appeared to come directly from the chest and to reach the ear through the central canal of the instrument. This peculiar phenomenon was confined to a space about an inch square and was not detectable in any other part of the chest. In order to elucidate the cause of this singularity I examined most of the patients in the hospital and recognized the same phenomenon in about twenty of them. . . . The subsequent death in the hospital of many of the individuals who had exhibited it enabled me to ascertain the correctness of my suppositions; in every case I found in the lungs excavations of various sizes, resulting from the dissolution of tubercles, and all communicating with the bronchi by openings of different diameters. . . . This circumstance naturally led me to think that pectoriloquy is caused by the superior vibration produced by the voice in parts having a more solid and wider extent of surface, and I imagined that, if this were so, the same effect ought to result from the application of the cylinder to the larynx and trachea of a person in health. My conjecture proved correct.

In principle and practice, the method of mediate auscultation is as simple as the method of percussion. And yet the invention of the stethoscope was at first received with as much indifference as was Auenbrugger's discovery. One of the only laudatory accounts was written by Chateaubriand, in reviewing some of the important events of the year; but the writer's interest prob-

ably came from the fact that he and his wife were Laënnec's patients.

Even those who professed great admiration for Laënnec's medical genius and were intrigued by his stethoscope regarded the instrument as merely a mechanical toy, out of place in the proud and dignified art of medicine. For example Forbes, who wrote the first English translation of the treatise on mediate auscultation, expressed a somewhat scornful skepticism in his preface.

> That it will ever come into general use notwithstanding its value, I am extremely doubtful; because its beneficial application requires much time and gives a good deal of trouble both to the patient and the practitioner; because its whole hue and character are foreign, and opposed to all our habits and associations. It must be confessed that there is something even ludicrous in the picture of a grave physician proudly listening through a long tube applied to the patient's thorax, as if the disease were a living being that could communicate its condition to the sense without. Besides, there is in this method a sort of bold claim and pretension to certainty and precision in diagnosis, which cannot at first sight but be somewhat startling to a mind deeply versed in the knowledge and uncertainties of our art, and to the calm and cautious habits of philosophizing to which the English physician is accustomed.[2]

But Laënnec was not one to be readily discouraged. To his cousin, Meriadec, who was preparing a thesis on auscultation, he wrote, "Do not fear to repeat what has already been said. Men need these things dinned into their ears many times and from all sides. The first rumor makes them prick up their ears, the second registers and the third enters." After a few years the celebrated French physician, Pierre Louis, introduced the stethoscope in his service at the Hôpital de la Charité in Paris. And before long the "Stethoscope Song," a sketch written by Oliver Wendell Holmes of Boston, served as a symbol of international

recognition.[3] Within a decade mediate auscultation came to be recognized as the most valuable of the diagnostic tools. Along with percussion it remained for a whole century, until the discovery of X rays, the only method available for the physical examination of the chest. Thanks to it, the knowledge derived from studies at the autopsy table could now be integrated with the results of physical examination of the patient, and thus the diagnosis and prognosis of disease became more objective and precise.

Laënnec's fame as scientist, clinician and teacher spread over Europe and America. In 1822 he was appointed Regius Professor of Medicine at the Collège de France. Every weekday he conducted his rounds at the Hôpital de la Charité and taught for about two hours, much of the time in Latin, both because he thought this ought to be the universal language of science, and because many of his students were foreigners; his observations on patients were also written in Latin. But his health was failing rapidly. He suffered from dyspnea, cough, anorexia, weakness, faintings and great depression of spirits. This illness was called "nervous fever," but there is little doubt that he was then afflicted with phthisis. On several occasions he had recovered some strength by returning for more or less prolonged visits to his property of Kerlouarnec in Brittany and engaging there in the life of a country squire.

He was much impressed by the fact that phthisis was practically nonexistent among the peasants and small-town people around him, whereas it was the most important cause of death in Paris; he felt convinced that there was in the marine air something that protected from the disease. This conviction led him to advocate fresh air in the management of patients, and, contrary to the notions of the times, he insisted upon having the windows open day and night during his own illness. Imaginative and enterprising as ever, he had seaweed brought from

Brittany and spread on the floor around the beds of his wards in Paris. Infusions made of the weeds were given to the patients. For a time he had the illusion that these measures somewhat reduced cough and sputum, an example of the difficulties involved in evaluating methods of treatment of tuberculosis.

In May, 1825, Laënnec was attacked suddenly with fever, sweating, cough and a diarrhea. Auscultation with the stethoscope revealed pectoriloquy, the sign that phthisis had reached the dreaded cavity stage. Realizing that he could no longer stand the strain of his professional studies in Paris, he decided once more to retire to Brittany in the hope of a cure. The trip was exhausting and the patient was compelled to dose himself with opium to control diarrhea.

After ten days Kerlouarnec was reached, and Laënnec, craving the out-of-doors and a view of the farming country, rode in his carriage around the estate. The diarrhea and sputum waxed and waned; fever persisted. Despite weakness and the heat of July, Laënnec contrived to walk daily in the garden. During August, violent fever and delirium set in. On the last day of his life, during a moment of lucidity, he removed the rings from his fingers and placed them on a table, stating that he wanted to spare others this melancholy task. He then sank into a coma and expired a few hours later, in August, 1826.[4]

After Laënnec had shown that the tiny area of infiltration and the tubercle constitute the first phase of phthisis, the next question was to determine the origin of these primary alterations. Around 1850 the study of tissue cells in health and in disease began to dominate medical research. More and more emphasis was focused on the microscopic structure of the tubercle, which was found to consist of peculiar cells different from those present in normal tissues and in other disease states. As Lebert stated in 1843, "Whenever examinations with the naked eye leaves

one in doubt as to the tuberculous, purulent or cancerous nature of a given lesion, the microscope will easily settle the issue."

Elaboration of this point of view occupied the attention of many eminent workers for several decades. In 1855 Rokitansky discovered the "giant cell," which he found to be one of the characteristic components of tubercles and which was further studied by Langhans in 1868. The most famous student of cellular pathology, Rudolph Virchow, contributed much to the knowledge of the cellular structure of tubercles, pointing out in particular the presence of lymphocytes and of the large epithelioid cells. Unfortunately, Virchow asserted also that only those lesions characterized by the typical gray, semitransparent tubercle were truly tuberculous, whereas those exhibiting caseation were of a different, nonspecific nature. In the same spirit, he stated that the caseating glandular lesions of scrofula were unrelated to true tuberculosis and merely the result of an inflammation due to some local "feebleness of the tissue." In other words, he claimed that tubercular phthisis differed in origin from caseous conditions, thus denying the unitarian theory expounded by Laënnec more than half a century before.

Virchow's views were wrong, but the very fact that he had been able to formulate and defend them points to a weakness in the edifice raised by Laënnec. The unitarian theory of phthisis was a brilliant concept based on precise observations of autopsy material; but Laënnec had never proved by experimentation that the different lesions of phthisis really did evolve one from the other in an orderly sequence, from the small tubercle, through the caseous ulcer, to the cavity stage. "How Laënnec hit on the facts," wrote one of his recent commentators, "we are unable to imagine. There is no doubt that he was either a superlative guesser or else an observer gifted in superlative degree with the power of generalization."

Laënnec could not prove his theory, because he did not know the primary cause of tuberculosis and, moreover, could not pro-

duce the disease at will in experimental animals. He was limited to the observation of its final results in the patient. The rigorous demonstration of Laënnec's inspired guess became possible only after techniques had been developed for the experimental production of the different forms of tuberculosis in laboratory animals.

CHAPTER VIII

The Germ Theory of Tuberculosis

THE BELIEF in the contagiousness of phthisis first became firmly entrenched, as we have seen, in Italy, Spain and the South of France. But the earliest explicit statement of the germ theory of disease before the microbiological era seems to have been formulated by a forgotten English physician, Benjamin Marten. In a volume printed in London in 1722 he presented his opinion that "animalculae fretting or gnawing the Vessels of the Stomach, Lungs, Liver" were the immediate cause of disease.

Having reviewed the factors believed by his contemporaries to be the cause of consumption, Marten suggested that these factors merely . . .

> . . . promote some other Peculiar, Latent or Essential Cause which I suppose to be joined with them. The Original and Essential Cause, then, which some content themselves to call a vicious Disposition of the Juices, others a Salt Acrimony, others a strange Ferment, others a Malignant Humour, may possibly be some certain Species of *Animalculae* or wonderfully minute living creatures that, by their peculiar Shape or disagreeable Parts are inimicable to our Nature; but, however, capable of subsisting in our Juices and Vessels.

One hundred and sixty years were to elapse before Koch actually saw the "minute living creatures" postulated by Marten, and proved them to be the cause of consumption. But today we are still much in the dark concerning the "peculiar shape" and

"disagreeable parts" that make the tubercle bacilli so inimicable to our nature.

Marten reasonably deduced from his theory a number of conclusions which have stood the test of time. He suggested that . . .

> . . . the minute Animals or their Seed . . . are for the most part either conveyed from Parents to their Offspring hereditarily or communicated immediately from Distempered Persons to sound ones who are very conversant with them. . . . It may, therefore, be very likely that by habitual lying in the same Bed with a consumptive Patient, constantly eating and drinking with him or by very frequently conversing so nearly as to draw in part of the Breath he emits from the Lungs, a Consumption may be caught by a sound Person. . . . I imagine that slightly conversing with consumptive Patients is seldom or never sufficient to catch the Disease, there being but few if any of those minute Creatures . . . communicated in slender conversation.

This shrewd man knew well that a theory is of little use until documented and developed by facts and deeds. And wisely he presented his views as mere suggestions.

> I have said enough to evince the Reasonableness and Probability of my conjecture concerning the Prime and Essential Cause of Consumption as well as of many other Diseases; and to afford sufficient Hints to some abler hand whose abilities are more equal to the Task to carry the Theory much farther than I have done and, it may be, bring it to absolute Demonstration in an extensive Degree.

But the "hints" did not fall on fertile ground. Indeed, so unreceptive was eighteenth-century England to the contagion theory of phthisis that Marten's book was soon forgotten. When it was rediscovered in 1911, only four copies of it and very little concerning the life of the author could be found. It was not that the possibility of contagion was ignored by Marten's contemporaries, for throughout the eighteenth and early nineteenth century English and French physicians mention the theory in

their writings, only to dismiss it as unsound. Many reasons account for their error. Microscopic organisms were known to occur in several parts of the body, but it was hard to understand at the time, and, indeed, it is still very unclear today, how "the fretting and gnawing" of these "animalculae" could bring about the tubercles, ulcers and huge cavities found in the phthisical patient. No form of reasoning could make the theory plausible *a priori*. And physicians can well be excused for having refused to believe in the germ causation of tuberculosis until compelled by the evidence of experimentation, by the gross fact that the disease, with its many types of lesions, could be produced at will by injecting a few bacteria into a normal animal.

The very prevalence of phthisis helped to obscure its contagious nature. It is certain that during the eighteenth and nineteenth centuries all dwellers in large cities of Europe became infected at an early age and remained in contact with heavily contaminated objects, sputum, food and dust throughout their life. However, infection does not necessarily mean disease, and phthisis became apparent chiefly in those afflicted with great natural susceptibility to it. Thus hereditary disposition overshadowed, and even completely masked, infectiousness.[1] On the other hand, the fact that the disease was rare in certain parts of the world while so prevalent in others, led physicians to conclude that it was the result of physiological disturbances caused by the environment. It was well known that tuberculous lesions in the lung often spread and invaded other organs, as if they had some infectious property; but this did not necessarily prove that they were caused by an infectious agent. It might merely mean that tuberculous tissue could graft itself onto healthy organs as does cancerous tissue. Indeed, Virchow regarded the tubercle as a tumor, and found no difficulty in accounting for its genesis, evolution, and structure in much the same terms that were used for the description of cancer.

Starting from the very same facts, it is easy now to arrive at

conclusions opposite to those reached by Virchow and his school. If tuberculosis spreads from one organ to another, it is not because the tubercle grafts itself like a cancerous growth, but because the germs of tuberculosis are disseminated throughout the body by way of blood or lymph. If several brothers and sisters in a given family become tuberculous, it need not be the result of a special familial disposition, a phthisical diathesis, it may be simply that they have all been exposed to a heavy and continuous source of infection in the familial household. These explanations, however, are based on the germ theory of disease, and this theory did not become established in medical thinking until 1880.

It was the prevalence of tuberculosis among the Negroes in England that converted the English epidemiologist, William Budd, to the contagion theory of the disease. Negroes who contracted pulmonary phthisis while working on British ships were often sent to Clifton and Bristol for treatment. Budd wrote:

> The idea that phthisis . . . is disseminated through specific germs contained in the tuberculous matter cast off by persons already suffering from the disease first came into my mind . . . while I was walking on the Observatory Hill at Clifton in the second week of August 1856.
>
> Everywhere along the African sea-board, where the blacks have come into contact and intimate relations with the whites, phthisis causes a large mortality among them. In the interior, where intercourse with Europeans has been limited to casual contact . . . there is reason to believe that phthisis does not exist.

It was from the famous missionary, Dr. Livingstone, that Budd had learned that phthisis was practically unknown in the interior of Africa where the whites had not yet penetrated. Budd meditated eleven years before publishing his theory in the *Lancet* of October, 1867, and he does not seem to have contributed any specific information on the causation of tuberculosis.

During the same period, a French army surgeon, Jean-Antoine Villemin, took a fundamental step by demonstrating that phthisis is inoculable from man or cow to the rabbit and guinea pig, and can be transmitted from one infected animal to another in unending series. He presented this discovery for the first time before the French Academy of Medicine in 1865 and developed it in his great book, *Études sur la Tuberculose,* published in 1868. Villemin's experience as a military surgeon had made him aware of the fact that tuberculosis was more frequent among the medical personnel and soldiers stationed for long times in barracks than among troops in the field. He knew, furthermore, that healthy young men from country districts often became consumptive within a year or two after their arrival in army posts; and he also pointed out that prisoners, industrial workers and members of religious cloistered orders were more apt to contract the disease than were ordinary civilians.[2] All these observations reminded him of the fact that young and healthy horses would frequently die of the fulminating form of glanders when brought from isolated farms to depots where many horses were concentrated. The analogy was obvious to him and in simple, direct language he summarized his interpretation of the natural distribution of tuberculosis by the statement that "the phthisical soldier is to his messmates what the glandered horse is to its yoke fellow."

In fact, glanders in horses presents many similarities to tuberculosis in man, and knowing that the former disease could be transmitted by inoculation, Villemin resolved to prove that tuberculosis was also inoculable to animals. He introduced under the skin of young rabbits fragments of caseous material and fluid obtained from a man dead of phthisis. Three months later the animals were killed, and countless tubercles were found in their lungs and other organs. When rabbits were inoculated in a similar manner with tuberculous material obtained from a cow, a much more rapid and severe disease ensued. "It is remarkable,"

said Villemin, "that none of our rabbits, inoculated with human tuberculosis, has presented a disease so rapidly and completely generalized as that obtained by inoculation with the tubercle of the cow. . . . This would suggest that tuberculosis of bovine origin inoculated into the rabbit shows a greater activity than that of man inoculated into the same animal." Here was the first evidence that the germs of the human and bovine disease, otherwise so similar, differ in their virulence for the rabbit. As we shall see, the problem was to become the subject of a great international debate thirty years later when it was necessary to determine whether the germ of bovine tuberculosis could cause disease in man.

For several years Villemin accumulated evidence of the inoculability of tuberculosis to rabbits, guinea pigs, dogs, cats and other animals. He found that the sputum and sometimes the blood of patients contained the virulent principle. He proved also that the material taken from a scrofulous gland could induce in guinea pigs and rabbits the general picture of tuberculosis, thus demonstrating the etiological relation between scrofula and tuberculosis and giving to Laënnec's theory of the unity of phthisis the sanction of experimental evidence. Villemin's experiments demonstrated beyond doubt that tuberculosis does not originate spontaneously in man or animals as a result of emaciation, physiological misery, atmospheric disturbances, bad heredity, unhealthy occupations, or prolonged debilitating maladies. Its cause was some germ, living and multiplying in the body of the patient, and transmissible to a well person by direct contact or through the air.

Surprising as it may seem, Villemin's reports were received with such indifference that not even William Budd became aware of them. In part this was because the causation of disease by microorganisms had not yet been demonstrated. Even more, however, it was the belief in an innate susceptibility to tuberculosis which prevented the medical profession from being re-

ceptive to evidence of contagiousness.[3] The extent of this belief appears in the report of the commission appointed by the British Government to repeat Villemin's experiments. The English scientists inoculated fifty-three guinea pigs with tuberculous material and, in accordance with Villemin's claims, found that tubercles appeared in fifty of them. As controls they inserted setons of unbleached cotton in the shoulders of two other guinea pigs. One of these remained well, but the other died and was found riddled with lesions that appeared to be tuberculous. In the light of present knowledge, there is no question that the second animal either had been accidentally infected with tuberculosis by the inexperienced investigators, or had died from another disease, "pseudo-tuberculosis rodentium," which is common in guinea pigs. But this one exception was sufficient to rule out the theory of contagion in the minds of the investigators, and they worded accordingly the conclusions of their report, "M. Villemin's fact is established as unquestionable: certain of the lower animals, if inoculated from the human subject with the morbid products which are called 'tubercular,' will in consequence develop . . . a disease which is identical or nearly identical with the so-called 'tubercular' disease of man." But, the report went on, "A slight open wound such as that of a seton run beneath the skin . . . is capable of being the first step in a series of changes which gradually infect the creature's whole body with imitations of the human 'tubercular diathesis' and thus at last create such 'tubercular' disorganization as necessarily destroy life." Thus, the results in one guinea pig had been sufficient to bolster the official dogma of "diathesis" against the strength of all Villemin's inoculation experiments.[4]

Little by little, however, improved experimentation in Germany and in France added further evidence that tuberculosis was a specific, inoculable disease; and when the germ theory of disease gained widespread acceptance, the search for the germ of tuber-

culosis began in earnest. It seems certain that three German workers saw the tubercle bacillus in infected tissues almost simultaneously and independently in 1882. But so overwhelming was the mass of evidence, so masterly the experimentation, so convincing the demonstration presented by Robert Koch that to him goes the entire glory for demonstrating that tuberculosis is an infectious, bacillary disease.

In brief, Koch demonstrated the constant presence of the bacilli in the tuberculous lesions of men and animals; he cultivated these bacilli in pure culture on blood serum, and produced tuberculosis at will by inoculating the cultures into normal animals. These findings were first presented in a paper read before the Physiological Society of Berlin on March 24, 1882, then in a detailed description published in 1883, and later translated under the title, *The Etiology of Tuberculosis*. It seems that Villemin suffered much in his pride from seeing his work contemptuously ignored by Koch and all but forgotten by the rest of the world. He would have been wise to accept the cruel law of scientific life: "He becomes the true discoverer who establishes the truth: and the sign of the truth is the general acceptance. . . . In science the credit goes to the man who convinces the world, not to the man to whom the idea first occurs."

Koch was only thirty-nine when he discovered the tubercle bacillus.[5] While a medical officer in the small isolated town of Wollstein, he had started alone, with homemade equipment, his spectacular studies on contagious diseases. Anthrax of cattle was prevalent in the farms around him. In 1870 Koch startled the scientific world by reporting that he had found the bacteria that caused the disease, had cultivated them in the test tube, photographed them, followed their evolution throughout their life cycles, and produced anthrax by injecting them into laboratory animals. Then he had gained further laurels by developing techniques of elegant simplicity and perfection which are still in use today in bacteriological laboratories all over the world. In 1880,