ANIMAL EXPERIMENTATION AND TUBERCULOSIS

"The humanity which would prevent human suffering is a deeper and truer humanity than the humanity which would save pain or death to animals."—*Charles W. Eliot.*

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ETIOLOGY

Everything that we know to-day of the etiology of tuberculosis, everything that has a direct bearing on the prevention and control of the disease, we owe to animal experimentation. Before the infectious nature of the tubercle became established by animal experimentation no advance was made in the knowledge of tuberculosis in any direction except in that of pathologic anatomy. From Sylvius,[1] who in 1695 first described tubercles and drew attention to their relation to pulmonary phthisis, up to the time of Klencke[2] in 1843, and even of Villemin[3] in 1865, who were the first to demonstrate by inoculation experiments on animals the infectious nature of the tubercle—that is, in a period of 170 years—no advance was made in the etiology of the disease, and this long period was wholly occupied by studies of the pathologic anatomy of tubercle, scrofula, caseation, pulmonary tuberculosis, and discussions of their relation to each other and their classification. Knowledge of the exciting causes of these pathologic processes remained theoretical; they were principally attributed to hereditary tendencies, perverted humors, and various types of inflammation.

Klencke,[2] in 1843, was the first to demonstrate the infectious nature of "tubercle" by inoculating rabbits in the vein of the neck with "tubercle cells" and producing general miliary tuberculosis in these animals. Klencke, however, hardly realized the importance of his own dis-

1. Sylvius: Opera Med. Traj. ad Rhenum., 1695.

2. Klencke: Untersuchungen und Erfahrung im Gebiete der Anatomie, Physiologie, Mikrologie und wissenschaftenlichen Medizin, Leipzig, 1843, i, Abschnitt 11; Mikropisch-pathologische Beobachtungen über die Natur des Kontagium, Paragraph 24. See also ii, Abschnitt 1, Par. 16.

3. Villemin, J. A.: Cause et nature de la tuberculose (first memoir), 1865. Etudes sur la tuberculose, 1868.

covery, and little attention was paid to his work until, in 1865, Villemin,[3] by extensive and carefully controlled inoculation experiments on rabbits, confirmed Klencke's views and demonstrated beyond doubt the infectiousness of tubercle by reinoculation from animal to animal. He also obtained evidence of specificity, as control inoculations with other morbid material, such as cancer, pus, bits of pneumonic lung, etc., remained negative. He was as successful with material derived from the *Perlsucht* disease of cattle as with human tubercle, and thus pointed out the identity of the tuberculous process in man and animals. From his experiments he reached the conclusion that the tubercle itself had nothing specific in its histology, and that the disease must be due to a germ. Scrofula he considered sometimes tuberculous and at others non-tuberculous, as he could not always produce the disease in his experimental animals with scrofulous products.

Animal experiments were first used as a means of diagnosis by Marcet,[4] in 1867, who demonstrated the tuberculous nature of material from suspected cases of tuberculosis by producing with it generalized tuberculosis in guinea-pigs, and Edwin Klebs[5] demonstrated by animal inoculations in 1868 that the sputum of tuberculous patients contained an infective element which was capable of producing the disease in guinea-pigs. Damsche,[6] in 1882, used animal inoculations to make a diagnosis of urogenital tuberculosis.

While Klencke's and Villemin's results were accepted, the strife for many years continued over the interpretation of these results. Meanwhile, the positive proof as to the infectiousness of tuberculosis, obtained by subcutaneous inoculation in animals, was supplemented by evidence brought to light by inhalation and ingestion of tuberculous material. Schweninger,[7] in 1866, at first failed to infect dogs by inhalations of phthisical sputum, but later—1886—he succeeded; and Lippl,[8] in

4. Marcet, William: The Inoculation of Animals as a Means of Diagnosis in Tuberculous Phthisis, Med.-chir. Tr., London, 1867, p. 437.

5. Klebs, E.: Ueber Entstehung der Tuberkulose und ihre Verbreitung im Körper, Virchows Arch. f. path. Anat., 1868, xliv.

6. Damsch: Die Impfbarkeit der Tuberkulose als diagnostiches Hülfsmittel bei Urogenitalerkrankungen, Deutsch. Arch. f. klin. Med., 1882, xxxi, 78 ff.

7. Schweninger, E.: Ueber künstlicher Erzeugung der Tuberkulose, Gesammelte Arbeiten von Dr. E. Schweninger, Berlin, 1886, i, 242.

8. Lippl: Amtl. Ber. d. 50. Versamml. deutsch. Naturforsch. u. Aerzte, 1877, p. 268.

1877, produced pulmonary tubercles in rabbits by insufflation of fluid sputum from man through a tracheal fistula. Tappeiner,[9] in a series of experiments which lasted from 1877 to 1888, demonstrated beyond doubt the infectiousness of phthisical sputum by inhalation experiments, his results being confirmed also by Bertheau[10] in 1880. Tappeiner, in 1880, had failed to infect rabbits by exposing them to the breath of coughing consumptives, and concluded that the infection must be conveyed, if at all, by dried sputum arising as dust, and not by the breath of the patient. The danger of this mode of infection received practical confirmation when his servant, whom he had warned to protect himself from inhaling the dust of the room in which the animals were confined, developed pulmonary tuberculosis and died of it. Giboux,[11] in 1882, however, succeeded in infecting rabbits by making consumptives cough in the boxes in which these animals were confined, and thus demonstrated, long before Flügge's classical experiments, the dangers of sprayed particles of sputum from phthisical patients.

Feeding experiments also added irrefutable evidence of the infectious nature of tuberculous material, as well as bringing many facts to support the hitherto unsuspected identity of the *Perlsucht* disease of cattle and human tubercle, by proving that both produced tuberculous disease in animals when taken into the stomach. Chauveau,[12] in 1868, infected calves by feeding them bovine tuberculous masses, and Edwin Klebs,[13] in the same year, infected guinea-pigs by feeding them with the sputum of consumptives, and in 1870 by the ingestion of bovine tuberculous material, which led him to the conclusion that the *Perlsucht* disease of cattle and human tuberculosis were caused by the same virus. Gerlach,[14] in 1870, demonstrated the infectiousness of milk

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9. Tappeiner: Amtl. Ber. d. 50. Versamml. deutsch. Naturforsch. u. Aerzte, 1877, p. 269. Wien. med. Presse, 1877, No. 43.

10. Bertheau, H.: Zur Lehre von der Inhalationstuberkulose, Deutsch. Arch. f. klin. Med., 1880, xxvi, 523.

11. Giboux: Inoculabilité de la tuberculose par la respiration des phthisiques, Compt. rend. 1882, xciv, 1391. Centralbl. f. d. med. Wissensch., 1882, p. 716.

12. Chauveau, A.: De la transmission des maladies virulentes par l'ingestion des principes virulents dans les voies digestives, Gaz. de Paris, xlvii, 1868.

13. Klebs, E.: Beiträge zur Geschichte der Tuberkulose, Virchows Arch. f. path. Anat., 1868, xliv, 278. Zur Geschichte der Tuberkulose, Virchows Arch. f. path. Anat., 1870, xlix, 291.

14. Gerlach, A. C.: Ueber die Impfbarkeit der Tuberkulose und der Perlsucht bei Tieren, sowie über die Uebertragbarkeit der letzeren durch Fütterung, Virchows Arch. f. path. Anat., 1870, li, 297.

from tuberculous cows by ingestion experiments on animals, and concluded that such milk was dangerous for human beings. Chauveau,[15] in 1873, fed asses, horses, cattle, and 160 calves, with various kinds of tuberculous material for six weeks, and not a single animal escaped infection.

HISTOLOGY

Animal experimentation has also greatly advanced our knowledge of the histology of tubercle, and during the period from 1862 to 1882 the animal experimentation method was applied to its study, and many experiments were made to prove and disprove the specificity of tubercle from the histologic standpoint. In 1873 Virchow[16] considered giant cells a criterion of tuberculous tissue, and as late as 1880 had reached the erroneous conclusion that *Perlsucht* of cattle and human tuberculosis were not identical, and that bovine lesions should be classed with lymphosarcoma. The findings of pathologic anatomy, however, were reversed by animal experimentation when Heidenhain,[17] in 1872, and Weiss,[18] Rustizky[19] and Zielanko,[20] in 1875 to 1878, proved by experiment on animals that giant cells could be produced experimentally with powdered glass, muscle, bone, etc., and Cohnheim and Salomonsen,[21] in 1877, from evidence based on eye inoculations in rabbits, added irrefutable evidence to the view that *Perlsucht* and human tuberculosis are inoculable, and are caused by the same virus; and established transmissibility to susceptible animals as the true and only reliable criterion of the tuberculous nature of any pathologic lesions. By this criterion the unity of scrofulous and tuberculous disease in man and animals, so long opposed by Virchow, was established.

Thus animal experimentation demonstrated beyond doubt the infectiousness of tuberculous matter in man

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15. Chauveau, M.: Rec. de méd. vét., 1872, 1873. Cited by Johne, A.: Die Geschichte der Tuberkulose, Leipsic, 1883, p. 30.

16. Virchow, R.: Ueber die Perlsucht der Haustiere und deren Uebertragung durch die Nährung, Berl. klin. Wchnschr., 1880, Nos. 14 and 15. Die Uebertragbarkeit der Perlsucht durch die Nährung, Virchows Arch. f. path. Anat., 1880, lxxxii, 550.

17. Heidenhain: Ueber Verfettung fremder Körper, etc., Inaug. Diss., Breslau, 1872.

18. Weiss: Ueber der Bildung und Bedeutung der Riesenzellen, etc., Virchows Arch. f. path. Anat., lxviii, 67.

19. Rustizky, J. von: Untersuchungen über Knochenresorption und Riesenzellen, Virchows Arch. f. path. Anat., lix, 218.

20. Zielanko: Arch. f. mikr. Anat., cxi, No. 3, cited by Ziegler: Die Herkunft der Tuberkelelemente, 1875.

21. Cohnheim and Salomonsen: Sitzungsber. d. schles. Gesellsch. f. vaterl. Kultur, July 13, 1877.

and cattle, the danger of tuberculous sputum and milk, and the identity of scrofulous disease and tuberculosis in man, as well as tuberculous disease in animals, by subcutaneous injection, by inhalation, and by ingestion experiments on animals, and established the value of animal inoculations in the diagnosis of suspected tuberculous disease (a method which gives evidence from which there is no appeal) before the birth of bacteriology and before the tubercle bacillus was discovered by Koch.

Koch's[22] epoch-marking paper on the etiology of tuberculosis, announcing his discovery of the tubercle bacillus as the direct cause of all tuberculous and scrofulous diseases in man and animals, appeared in 1882. The unbroken chain of evidence forged by Koch in his logical demonstration of proof was obtained entirely by carefully controlled animal experiments, and gave the world a discovery of incalculable importance to the human race. Koch confirmed Cohnheim's views as to infectiveness being the best criterion of tuberculous disease, and by animal experiments established the value of microscopic search for the bacillus in diagnosis, and the identity of many lesions hitherto looked on as due to different diseases on account of the marked differences they presented both clinically and in the pathologic findings. He proved that all contained the same bacillus, which, when cultivated outside of the body, produced by inoculation in animals typical tuberculous lesions. Miliary tuberculosis, fibrous phthisis, caseous pneumonia, as well as scrofulous disease of glands, bones, and lupus of the skin, also *Perlsucht* in cattle, he showed to be due to the same cause—the tubercle bacillus.

PROPHYLAXIS, DIAGNOSIS AND THERAPY

In 1890 Koch[23] demonstrated by careful animal experiments the diagnostic value of tuberculin, pointed out its specific action on the course of the disease and on tuberculous lesions, and proposed the tuberculin test as a practical and efficient method of eradicating tuberculosis from infected herds, and tuberculin injections as a therapeutic measure in the treatment of the disease in

22. Koch, R.: Die Aetiologie die Tuberkulose, Berl. klin. Wchnschr., 1882, No. 15.

23. Koch, R.: Deutsch. med. Wchnschr., Nov. 13, 1890, No. 46a; Oct. 22, 1891, No. 43.

man. The discovery of tuberculin was entirely based on animal experimentation, and the value of this agent in the control of cattle tuberculosis, as an aid to early diagnosis of tuberculosis in man, and as a therapeutic agent in the more chronic types of the disease, can hardly be overestimated.

Animal experimentation has been of incalculable value in the diagnosis of obscure cases, and in teaching where the infectious material lurks and how to formulate effective measures for the prevention of the disease. By animal experiments the infectiousness of various secretions from the tuberculous was established. Edwin Klebs,[5] in 1868, proved the infectiousness of sputum; Gerlach,[13] in 1870, the danger to man from the ingestion of the milk of tuberculous cows. Cornet's[24] exhaustive animal experiments demonstrated the danger of dried sputum, and indicated one of the principal modes of infection to be by inhalation of dried particles of expectorated material contained in dust from rooms inhabited by consumptives. Flugge,[25] by animal experiments, proved the danger of droplet infection in the immediate neighborhood of the consumptive by the spraying of small particles of saliva in sputum in violent coughing. Animal inoculations of the dust of infected rooms have also been used to test the efficiency of the measures to guard against room infection. This was done by Hance,[26] at the Adirondack Cottage Sanitarium in 1895. The entire system of hygienic care of the sputum and other discharges has been built up on the results of animal inoculations.

Not only have animal experiments been used in demonstrating where the infectious material lurks, but, since the discovery of the tubercle bacillus, the same method has taught us the various channels by which the bacillus gains access to his host, and all that we already know of the mechanism of infection and the defensive resources of the living organism. To Cornet's[24] exhaustive animal experiments we owe much of our knowledge as to the sources of infection and the channels whereby the tubercle bacillus gains access to the living organism. Through his work on the channels of infection, he found that in most cases the pathologic evidence should

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24. Cornet, G.: Tuberkulose, Leipsic, 1890.
25. Flugge, G.: Ztschr. f. Hyg. u. Infektionskr., 1899, xxx, No. 1.
26. Hance, I. H.: Med. Rec., Dec. 28, 1895; Feb. 13, 1897.

furnish a clue to the site of invasion, but that tubercle bacilli are able to penetrate the macroscopically uninjured mucous membrane, and in rare cases even the skin, without leaving locally any evidence of their passage. This has been confirmed by many animal experiments in the recent exhaustive comparative studies of infection by inhalation and ingestion which have followed the world-wide discussion of the relative infectiousness of bovine and human tuberculosis.

Cornet[27] concluded that inhalation of infectious dust was the most frequent cause of infection, and that tuberculous infection progressed much more generally by the lymph stream than by the blood stream, and was rather a lymphogenous than a hematogenous infection.

Animal experimentation has taught us all we know of the complex, defensive mechanism by which the living organism resists the progress of bacterial infection and ultimately often heals the lesion and attains acquired immunity. Inspired by Pasteur's achievements in the field of acquired immunity, Daremberg,[28] Grancher, Martin,[29] Ledoux-Lebard,[30] Richet and Hericourt,[31] and others of the French school attempted (with, however, but indifferent success) the production of artificial immunization against tuberculosis in animals.

The treatment of tuberculosis by tuberculin, as originated by Koch[23] in 1890, was the first adaptation of the knowledge acquired by him in artificial immunization of animals to the treatment of tuberculosis in man. In America, Dixon,[32] in 1889, made experiments in this direction with attenuated bacilli; Trudeau,[33] in 1892, produced a marked degree of artificial immunity in rabbits with avian tubercule bacilli; and in 1893 de Schweinitz[34] obtained similar results in guinea-pigs by the use of bacilli of human origin attenuated by prolonged cultivation. In 1895 Theobald Smith,[35] by ani-

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27. Cornet: Tuberculosis, in Nothnagel's Practice, pp. 104-106.
28. Daremberg, G.: Compt. rend. hebd. Soc. de biol., Dec. 30, 1893, v.
29. Grancher et Martin: Congrès pour l étude de la Tuberculose. 1891, 1896.
30. Ledoux-Lebard: Arch. de. méd. expér., 1898, No. 10.
31. Richet et Hericourt: Etudes sur la tuberculose, 1891, iii.
32. Dixon, S. G.: Med. News, 1889, lv; Med. and Surg. Reporter, 1890, lxiii, 281.
33. Trudeau, E. L.: Med. News, Sept. 3, 1892.
34. De Schweinitz, E. A.: New York Med. Jour., March 23, 1893.
35. Smith, Theobald: Tr. Assn. Am. Phys., 1896, p. 75; Jour. Exper. Med., 1898, iii, 451.

mal experiments, demonstrated the differences of virulence between human and bovine bacilli, and thus opened the way for further studies in cattle immunization. Pearson and Gilliland,[36] by animal experiments, were among the first in America to attain a high degree of immunity in cattle by the use of the human type of bacillus. In Europe, during the past decade, von Behring,[37] Koch,[38] Calmette[39] and their associates, by extensive animal experiments, demonstrated the possibility of producing immunity by preventive inoculations in cattle of living human cultures, and advanced our knowledge of this complex problem of such overwhelming importance in man's struggle against tuberculosis to a point which may lead to its ultimate conquest.

Far-reaching in the saving of human life as the new knowledge of tuberculosis is, it is difficult to define accurately what it has already accomplished, because it has so recently been acquired and has, owing to the vastness and complexity of the problem, been as yet so imperfectly applied to both prevention and treatment, and because the results offered by the falling death-rate are in this disease influenced by so many factors other than those which bear directly on preventive measures aimed solely at the specific infecting agent, the tubercle bacillus.

The death-rate from pulmonary tuberculosis has fallen steadily in most countries during the last forty years, notably in England, where a decrease of 50 per cent. has taken place in that time.[40] In many countries it has fallen only slightly faster since the discovery of the tubercle bacillus and the more or less complete adoption of preventive measures, while in others it has fallen much more rapidly since 1882, as in New York City, where there has been during the past twenty years a reduction in the death-rate from pulmonary tuberculosis of nearly 40 per cent.,[41] and notably in Prussia,[42] where

36. Pearson and Gilliland: Philadelphia Med. Jour., Nov. 29, 1902, p. 842.
37. Von Behring, E.: Beitr. z. exper. Therap., 1902, No. 5.
38. Koch, R.: Schutz, Neufeld and Miessner: Ztschr. f. Hyg. u. Infectionskr., 1905, li.
39. Calmette and Guérin: Compt. rend. de. l'Acad. d. Sc., 1906; Ann. de l'Inst. Pasteur, 1908, xxii, 689.
40. Osler's Modern Medicine, iii, 145.
41. Handbook on Prevention of Tuberculosis, Charity Organization Society, 1903, p. 165.
42. Kayserling: Osler's Modern Medicine, iii, 144.

the death-rate was 50 per cent. less in 1903 than in 1885. In some places, as in Boston, the death-rate during the twenty years preceding the discovery of the bacillus and the gradual adoption of preventive measures had shown no inclination to fall, while during the twenty years following this discovery it has fallen markedly and continuously. While it is true that the decrease in mortality began before any effective measures aimed directly at the infecting agent had been in force, the steady and continuous decrease in the death-rate makes it fair to assume that the brilliant results obtained have been due, in part at least, to the measures which aim directly at the limitation of the infection and the protection of the well from tuberculous dust.

In Boston[43] the death-rate, which in 1862 was 42 per 10,000 living, after slight variations, in 1882 was still about the same; but from 1882 to 1902 it fell from 42 to 21 per 10,000, so that during the past twenty-one years the diminution in the death-rate from tuberculous disease in Boston has been approximately 55 per cent., this decrease representing, in actual saving, 14,412 lives.

The demonstrable results in preventive measures aimed solely at the specific infecting agent would naturally be most noticed first in children, and the results in New York City, where such measures have been most strictly enforced, bring evidence in support of the influence of such measures on the death-rate of tuberculous meningitis and pulmonary tuberculosis in children. Dr. Biggs points out that "during the ten-year period ending 1902 there has been a decrease of more than 40 per cent. in the death-rate from pulmonary tuberculosis and tuberculous meningitis in children under 15 years of age in New York City, and that during a period of twenty years the decrease has considerably exceeded 50 per cent."[44]

The results obtained, however, must depend greatly on the thoroughness and efficiency of the preventive measures adopted, and this perhaps has been best demonstrated thus far in the observations of Dr. R. W. Philip,[45] of Edinburgh. Dr. Philip, believing that partial measures were of little avail, and that effectiveness in preventive measures aimed at the control of the dis-

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43. Massachusetts State Committee International Congress, 1908, p. 119.
44. Biggs: Arch. Pediat., May, 1904.
45. Philip, R. W.: Lecture before International Congress, 1908.

ease depended greatly on cooperation and coordination of all the agencies which tend to control the infection, gradually instituted a more and more comprehensive program in Edinburgh, in which all these agencies cooperated.

A study of the death-rate during the last twenty years in that city bears witness to the fact that the death-rate varies with the thoroughness with which the preventive program is carried out. The death-rate in Edinburgh was 19.5 per 10,000 in 1887. During the next ten years, when partial and uncorrelated measures were in force, it fell from 19.5 to 17, a percentage fall of 12.82; but during the following ten years, when a more comprehensive plan was adopted, it fell from 17 to 11 per 10,000, a percentage fall of 42.1 as compared with 12.82 during the preceding ten years, when a less efficient and comprehensive plan of prevention was in force.

Judging by what has been added to our knowledge of tuberculosis by animal experimentation in the past, it seems not unreasonable to entertain the hope that its ultimate control will be accomplished by knowledge acquired through the same means, and will probably depend not only on a more thorough and comprehensive application of the knowledge already won, on which all preventive measures are based, but also on the discovery of some specific method of immunization or treatment—a goal that can be attained only through continued and painstaking studies on animals.

NECESSITY OF ANIMAL EXPERIMENTATION FOR FURTHER ADVANCE

From the foregoing review of the history of tuberculosis, it would seem evident that everything that has a direct bearing on the prevention of tuberculosis, everything that has changed mankind's attitude toward it from one of apathy and hopelessness, when the infectious agent which produces tuberculosis was unknown and the disease was thought to be inherited and always fatal, to the growing hope of its ultimate conquest—a hope which has resulted in the great antituberculosis crusade spreading over the world and culminating in the late International Tuberculosis Congress in Washington—we owe to animal experimentation. If it were not for the knowledge which science has won by animal experimentation in the field of this disease in the last twenty-five years, we should still be plunged in the apathy of ignorance and despair toward it which formerly prevailed, and tuberculosis would still be exacting its pitiless toll, unheeded and unhindered. Were it not for animal experimentation, the prospect of ultimately lifting this great burden of suffering and death from the human race would be as dark as it was before Klencke, in 1843, and Villemin, in 1865, succeeded in proving its infectious nature by experiments on animals with tuberculous material, and thus paved the way for Koch's discovery, in 1882, of the tubercle bacillus. The many researches which have flowed from the study of this germ have taught us already how to protect the healthy from infection and are daily teaching us how we may restore to health those already infected.

Thanks to animal experimentation, we know to-day that tuberculosis is not inherited; that it is communicable and, therefore, preventable; and that in its earlier stages it is curable.

Animal experimentation has taught us already much as to the different types of the tubercle bacillus, its virulence, the poisons it produces, and the manner in which it invades the living organism and destroys it. Slowly but steadily animal experimentation is teaching us the avenues of infection whereby the germ gains access to the organs of its living host; what are the defensive resources of the living organism; and the delicate mechanism whereby it combats the poison of the germ, tries to localize the bacilli, to limit their spread, and ultimately to destroy them. Animal experimentation is teaching us daily more of the complex and delicate processes which bring about acquired and artificial immunity, and through which the living organism wins the victory over the invading parasite. In the thorough knowledge and further study of these vital processes by animal experimentation lie the hope of applying to the protection of healthy human beings and the cure of disease, the knowledge won by science in studying Nature's methods of cure through long years of tireless and painstaking observations on animals.

During my lifetime all this knowledge, so practical in its bearing on the saving of countless human lives, has been won by animal experimentation. In my own personal experience, and as a result of my own observations, animal experimentation has led me to conclusions which have had a practical application in the treatment of my patients. In 1886 I was able to demonstrate on animals the influence of a favorable environment on the disease. Inoculated rabbits placed under the most unfavorable conditions attainable, so far as light, air, food, exercise and surroundings were concerned, succumbed to the inoculation, while those turned out in the open air on an island and supplied with abundant food recovered, with only traces of the disease at the site of inoculation. These observations on animals increased my confidence in the influence of a favorable environment on the course of tuberculosis in man, and confirmed my faith in the value of the sanitarium and open-air method, of which I was then trying to make a practical application in the establishment of the Adirondack Cottage Sanitarium. The open-air and sanitarium treatment has already saved and prolonged, and will continue to save and prolong, countless human lives.

In 1893 animal experimentation gave me indubitable evidence that the production of artificial immunity against tuberculosis, which has always been looked on as impossible, was not as unattainable as was generally believed, my vaccinated rabbits and guinea-pigs showing increased resistance not present in the untreated animals; and this strengthened my faith in the value of continuing the study and use of vaccines in the treatment of tuberculosis. Although the progress made in this direction has been slow, the results obtained by many experimenters in many lands have been in accord as to the hopefulness of this line of research; the goal has almost been reached already in the vaccination of cattle through the experiments of Koch, von Behring, Calmette, McFaydean, Heymans, Pearson, and others; and the application of vaccines to the treatment of various infections in the human subject is extending and giving encouraging results.

The conquest of tuberculosis in man and animals, like the conquest of smallpox, of diphtheria, of rabies, anthrax, and many other infections through the production of some safe method of artificial immunity, seems, even to those hitherto skeptical, no longer visionary and unattainable. More knowledge of the infecting agent, its poisons, its methods of attack, the various defensive resources of the organism and methods that will call them into action, can be obtained only by animal experimentation.

Inoculation experimentations entail no greater suffering to the animal than the prick of a hypodermic needle, and then a painless death if it be killed, or death from tuberculosis if it be allowed to live. Those who cry out against animal experimentation trust us with the lives of their families when sick, but fear to trust us with rabbits and guinea-pigs. Surely the motives of physicians who are trying to learn how to prevent and cure disease, when their livelihood depends on the practice of medicine, can hardly be called into question. Those who in their blind ignorance or through false sentiment are trying by legislative interference to stop or to restrict animal experimentation do not, as we doctors do, have to witness daily the ravages of this terrible disease and live in the midst of the suffering and sorrow which follow in its wake; they seem to be content that all this should continue indefinitely so long as they are not brought into contact with it.

The new knowledge of tuberculosis, of such overwhelming importance to the human race, a knowledge which already gives assurance that generations to come will not die of this disease to the extent that former generations have died, has been won in recent years by animal experimentation. For all this is the death of any number of guinea-pigs and rabbits too high a price to pay? Are we to stop on the threshold of this newly acquired knowledge, and are the fruits of ultimate victory to be denied to humanity? These would seem questions that could safely be left to the common sense of unprejudiced men.