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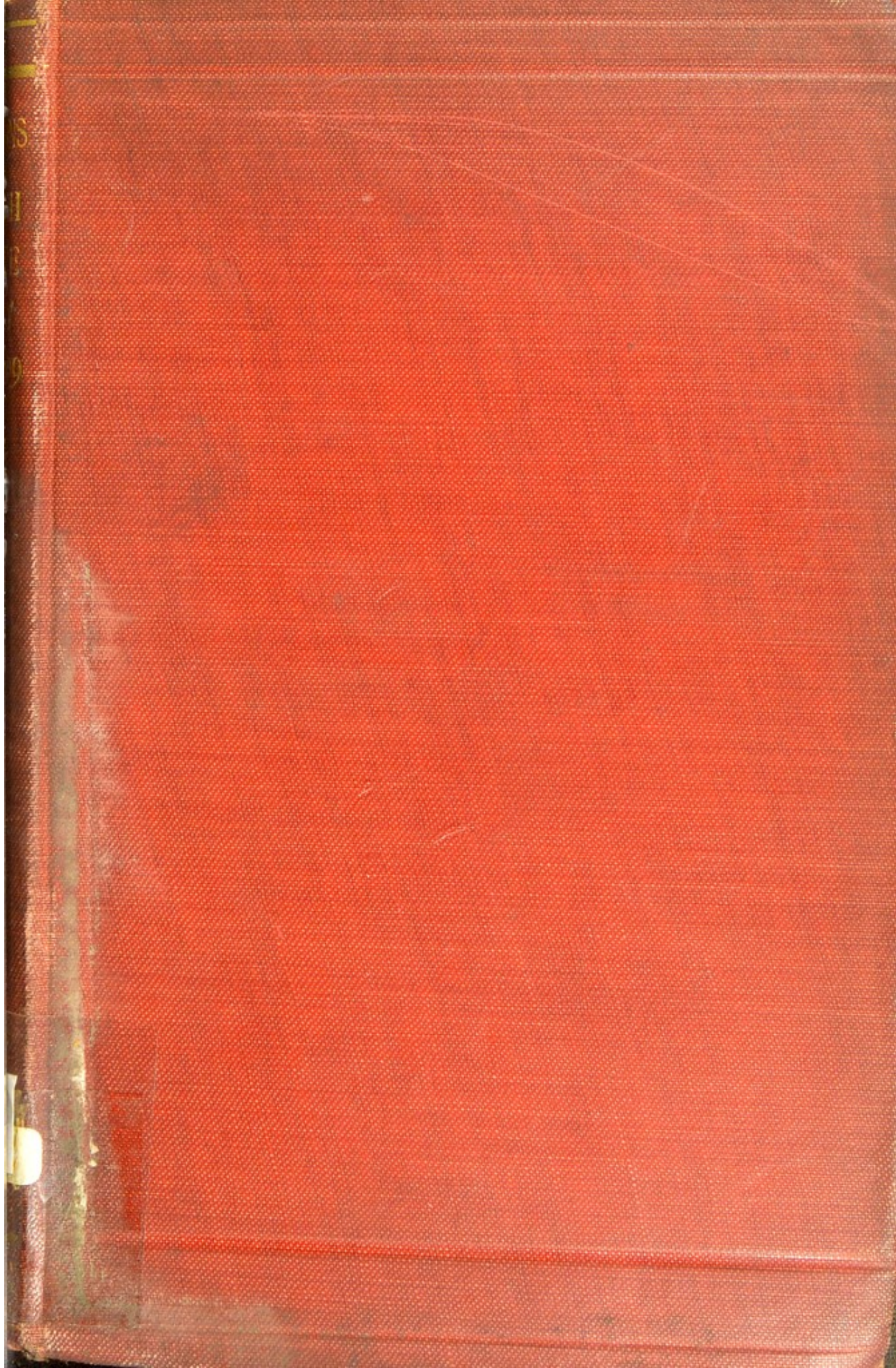
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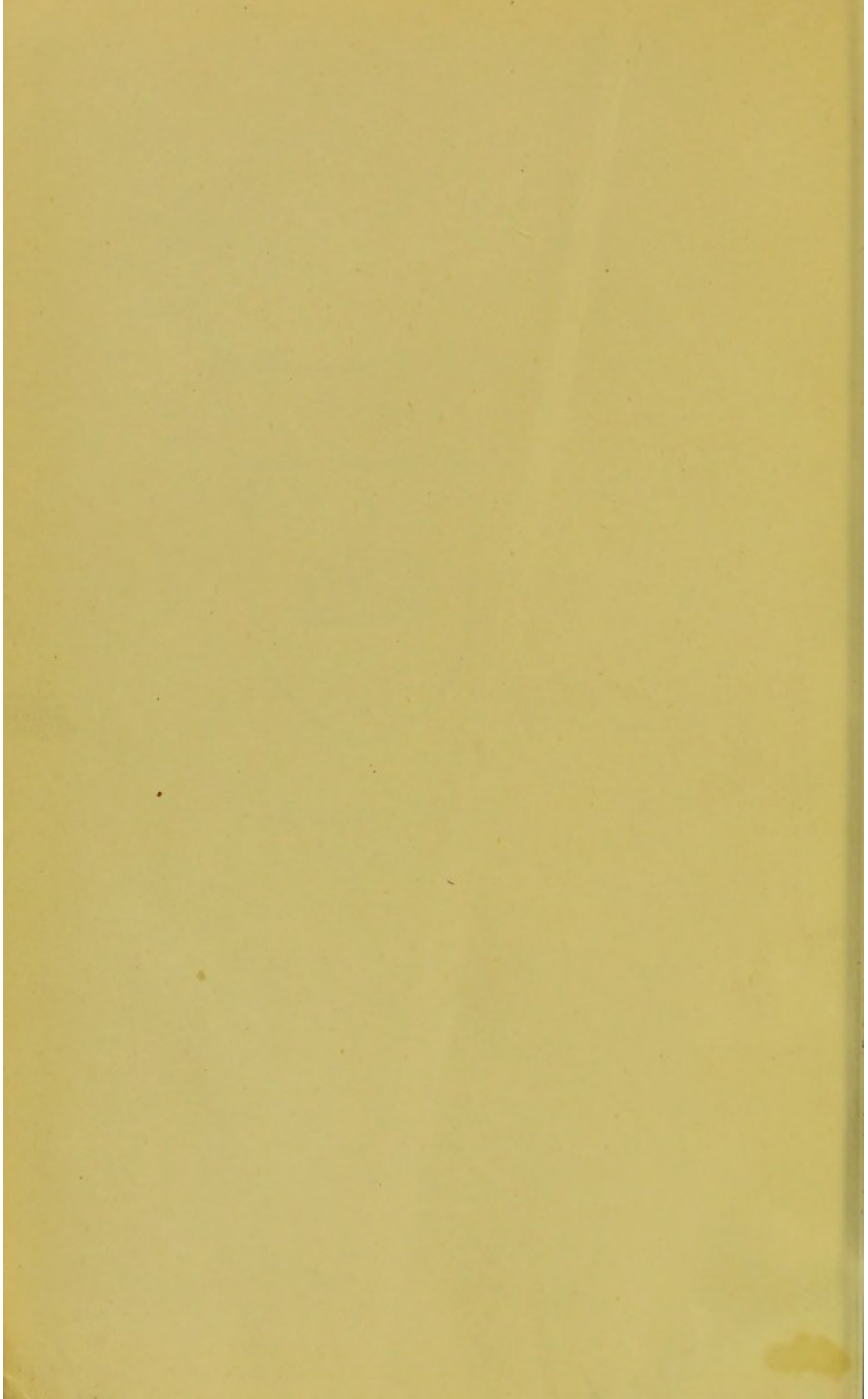




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## PREFACE

THE Research Defence Society was founded on Jan. 27th 1908, "to make known the facts as to experiments on animals in this country ; the immense importance to the welfare of mankind of such experiments ; and the great saving of human life and health directly attributable to them." It has now (March, 1909) over 2,250 members, of whom about 300 are ladies. Branch Societies have been established, or are in course of establishment, in Birmingham, Bournemouth, Brighton, Cambridge (University Branch), Dublin, Edinburgh, Leeds, Liverpool, Manchester, Norwich, Oxford, Shrewsbury, Torquay (Devon Branch), York and elsewhere.

The *minimum* subscription for the working expenses of the Society is five shillings annually ; but larger subscriptions and donations are gladly received. A donation of £10 constitutes life membership. Undergraduates and students of medicine are eligible for membership on payment of an annual subscription of half-a-crown. The Committee have decided also that there shall be Associates of the Society at an annual subscription of one shilling.

A considerable quantity of literature has already been distributed, and representatives of the Society have spoken at many public meetings and debates. The Society is always willing to send a representative to a debate arranged by any literary society, club, or debating



society, or to any public meeting, with this exception, that it does not propose to accept "challenges" from the anti-vivisection societies, or to arrange with these societies the terms of debate. A collection of lantern slides, with descriptive catalogue, has been prepared for popular lectures, and is in frequent use.

The chief objects of the Society's work were stated as follows in a letter from its President, which was published in the newspapers on April 24th, 1908 :—

"A Society has been formed, with the name of the Research Defence Society, to make known the facts as to experiments on animals in this country; the immense importance to the welfare of mankind of such experiments; and the great saving of human life and health directly attributable to them.

"The great advance that has been made during the last quarter of a century in our knowledge of the functions of the body, and of the causes of disease, would have been impossible without a combination of experiment and observation.

✓ "The use of antiseptics, and the modern treatment of wounds, is the direct outcome of the experiments of Pasteur and Lister. Pasteur's discovery of the microbial cause of puerperal fever has in itself enormously reduced the deaths of women in child-birth.

✓ "The nature of tuberculosis is now known, and its incidence has materially diminished.

✓ "We owe the invention of diphtheria anti-toxin entirely to experiments on animals.

✓ "The causes of plague, cholera, typhoid, Mediterranean fever, and sleeping sickness, have been discovered solely by the experimental method.

"Not only have a large number of drugs been placed at our disposal, but accurate knowledge has replaced the empirical use of many of those previously known.



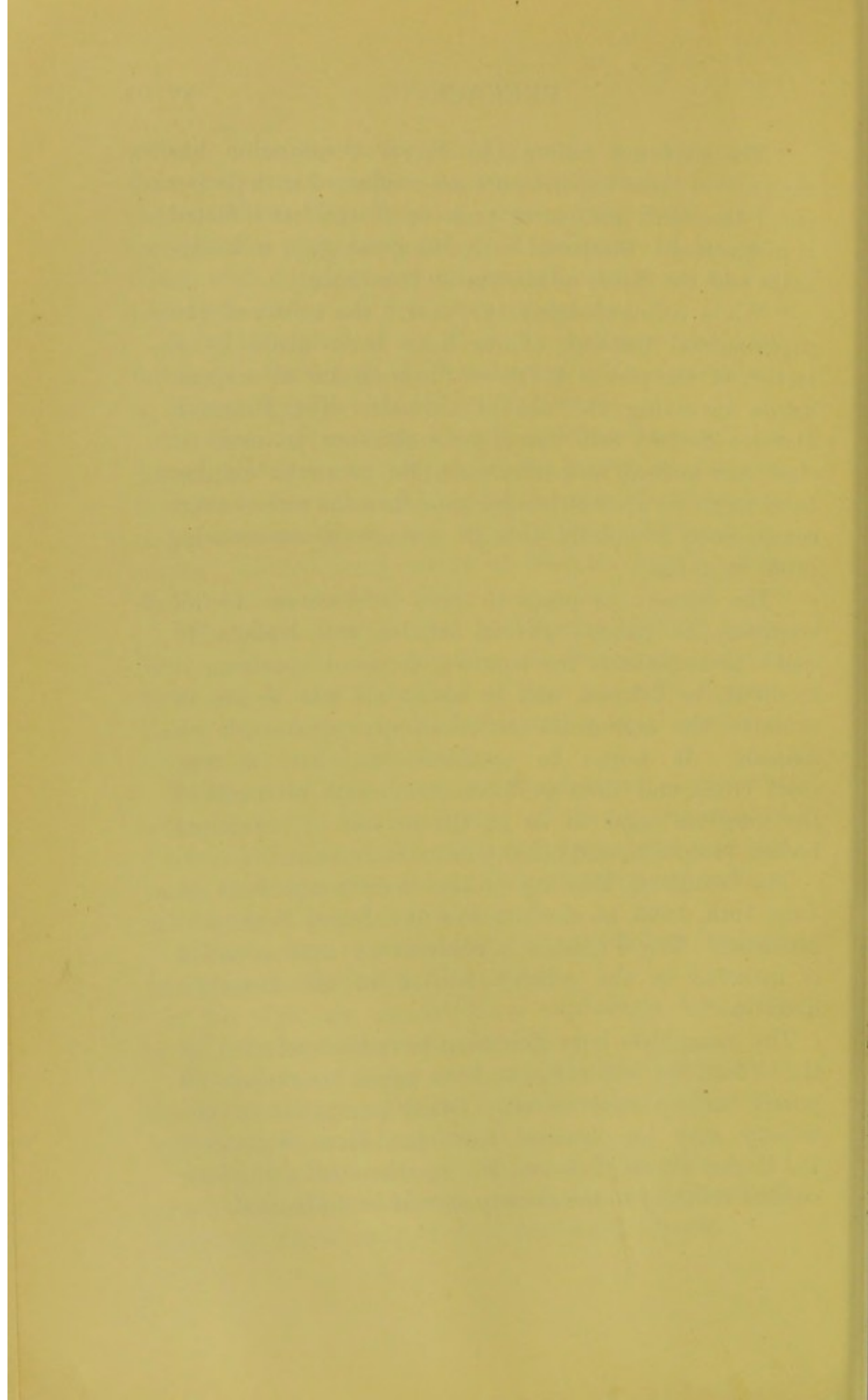
"The evidence before the Royal Commission has shown that these experiments are conducted with proper care; the small amount of pain or discomfort inflicted is insignificant compared with the great gain to knowledge and the direct advantage to humanity.

"While acknowledging in general the utility of the experimental method, efforts have been made by a section of the public to throw discredit on all experiments involving the use of animals. The Research Defence Society will therefore endeavour to make it clear that medical and other scientific men who employ these methods are not less humane than the rest of their countrymen, who daily, though perhaps unconsciously, profit by them.

"The Society proposes to give information to all enquirers, to publish *précis*, articles, and leaflets, to make arrangements for lectures, to send speakers, if required, to debates, and to assist all who desire to examine the arguments on behalf of experiments on animals. It hopes to establish branches in our chief cities, and thus to be in touch with all parts of the kingdom; and to be at the service of municipal bodies, Hospitals, and other public institutions."

The Inaugural Meeting of the Society was held on June 19th, 1908, at the house of the Royal Society of Medicine. The President's Address on that occasion is included in the present edition of the Society's literature.

The pamphlets here published have been selected by the Committee, and care has been taken to exclude all purely controversial matter. Other pamphlets of the Society may be obtained from the Hon. Secretary, 70, Harley Street, London, W., to whom all communications relating to the Society should be addressed.





# RESEARCH DEFENCE SOCIETY

## ADDRESS

GIVEN BY

The Rt. Hon. THE EARL OF CROMER, G.C.B., G.C.M.G., O.M.

*At the Inaugural Meeting of the Research Defence Society, held at the  
House of the Royal Society of Medicine, June 19th, 1908.*

MY LORDS, LADIES and GENTLEMEN,—When I was first asked to become the President of the Research Defence Society, I confess to having experienced a feeling of some surprise. The greater part of my life has been spent in trying to steer a clear course through the bewildering shoals and quicksands of Oriental administration and diplomacy. This work, though it may, perhaps, under a somewhat strained interpretation of the word, be designated as an art, can scarcely be said to rise to the dignity of a science. I therefore suggested that it might be as well to choose as President someone who can lay claim to higher knowledge and scientific attainments than myself. I was then and there informed that the fact of my absence of scientific knowledge, which appeared to me to be a disqualification, was in reality my principal merit. And, on reflection, I came to understand that this view of the case was not altogether so paradoxical as might at first appear. The very eminent men of science engaged in this work



wished to show that they had the support of others who could not lay claim to special scientific attainments. And the humane men who have been so constantly accused of wanton cruelty to animals wished to show that they had the sympathy of those who had taken an active part in the prevention of that cruelty. From this latter point of view, Gentlemen, I could, I am proud to say, lay claim to a certain amount of qualification; for no part of my Egyptian work interested me more than the long, and, I may say, fairly successful campaign which was conducted against cruelty to animals in that country, by the Society of which I was, for many years, President.

Gentlemen, not only do I hold that there is nothing inconsistent, between something approaching absolute detestation of wanton cruelty to animals, and approval of experiments on living creatures in order to relieve human suffering as well as suffering in dumb animals: I go further than this. I maintain that the one attitude is almost the necessary consequence and corollary of the other. For if, as I hold, experiments may be justified by any good and sufficient grounds, it becomes both necessary and desirable that their execution shall be watched and controlled, as far as possible, by a body of men who would view with absolute detestation anything indicating indifference or callousness to the wanton infliction of pain. If I thought for a moment that the charge of indifference or callousness could be justified, the case would be very different, and I have no hesitation in saying that the Research Defence Society would then have to look out for another President. It is because I feel that the charge is baseless that I am here to-day. What, then, Gentlemen, are the main grounds on which these experiments can be justified? As far as I understand them, they are



twofold. In the first place, it has to be shown that they have already produced invaluable results, and that still further good results may be anticipated. In the second place, it has to be shown that the experiments are conducted in such a manner as to minimise, if not altogether to obviate, the infliction of pain. Now, I hold that both these propositions can be proved up to the hilt. I am, of course, aware that there is a certain small section of the community consisting of persons who hold that under no circumstances is it justifiable to destroy animal life. From those who hold this extreme view we must, I fear, agree to differ. I must say that if their views were carried out to their logical conclusions, they would lead us to very strange and practically impossible positions. However, I shall not attempt to argue this point, but will only say that this view has not been accepted by the civilised world in general. But there are others who do not hold these extreme views, and with them the case is different. Now, although I regret I am not always able to accept the accuracy of their facts, or to concur in their conclusions, I respect their motives, and I fully sympathise with the objects which they wish to attain. It is because I sympathise with them that I will not endeavour to reply in any unfriendly spirit to the somewhat numerous communications which I have received of late on this subject, many of them couched in somewhat unreasonable and, I may even go so far as to say, in violent language.

First, then, as to the utility of vivisection. I must, of course, leave to others of more special knowledge than myself the task of dealing with this question ; but it requires no special knowledge of any kind to arrive at the conclusion that since Harvey's great discovery of the circulation, which was an epoch-making discovery, well nigh every advance in medical science has been,



directly or indirectly, the result of experiments on living animals. Let me give you one or two cases in point.

Perhaps one of the greatest discoveries in modern times has been the fact that malaria is transmitted by means of mosquitoes: and a very eminent authority, quoted in one of the leaflets issued by Mr. Paget, says that this discovery is going "to make the Tropics habitable." I myself can bear some personal testimony to the value of this discovery. The town of Ismailia, on the Suez Canal, had almost become uninhabitable by reason of the amount of the fever there; but it has now almost entirely disappeared. It will be said, I know, that this discovery was not due to experiments on living animals; but that is a view which is entirely erroneous. I ask you to listen to what a very high authority says on this point. I refer to Professor Osler, the Regius Professor of Medicine at Oxford. He was asked before the Royal Commission on Vivisection whether the discovery would have been made, had it not been for previous experiments on living animals. "Never," was the reply. "The men," he said, "who made these investigations spent their lives in laboratories, and their whole work has been based on experimentation on animals." I think that evidence is of extraordinary interest to all parties. Then there is the somewhat analogous case, Malta fever, of which I need not give details. It was due to experiments made on animals, in this case monkeys, that the cause of that disease was discovered. As to the actual value in the direction of the saving of life, by experimentation on animals, the case can be proved to demonstration. Take the case of diphtheria, which has given rise to much discussion. These figures, if fairly used—which, I may be allowed to remark, is not always the case—are conclusive. I gather that in the hospitals under the Metropolitan Asylums Board the



percentage of fatal cases in this disease has sunk from 28 per cent. in the period previous to the introduction of the anti-toxin treatment, to about 8 per cent. Similar facts might be adduced as regards rabies. And need I answer the statement which has been brought against us that the scientific world has not yet discovered a cure for cancer? Scarcely, I think: I think a more inconclusive argument could scarcely have been used. So far as I am aware, it has never been held to be a reproach to Sir Charles Wheatstone, the father of modern telegraphy, that he failed to make the epoch-making discovery attached to the name of Marconi. Science, we must remember, goes slowly; it does not advance by leaps and bounds. It may be that at some future time a cure for cancer will be discovered, and if it is discovered I think it is quite safe to predict that it will be not by mere observation, but by the employment of the experimental method.

And now, Ladies and Gentlemen, let us turn again to the main point, to which I alluded at the beginning of my address, namely, the methods adopted in carrying out those experiments. Several causes have contributed to misapprehension on this subject. Firstly, it has been the practice to take one or two isolated cases and present them to the public with every sort of harrowing and revolting detail. Now, as regards these cases, I have to observe that, in the first place, the statements have to be accepted with very great reserve. It sometimes turns out on examination that the facts are greatly exaggerated, or, I think, in some cases, almost purely imaginary. In the second place, I want to say that it is an old and well-recognised maxim—and I feel sure that my friend, Mr. Sydney Holland, will bear me out in saying it—that hard cases make bad law. Of course, I fully admit that if even in a single case



wanton cruelty could be proved, it would be sufficient ground for careful enquiry, with a view to, if possible, preventing the occurrence of any such circumstance in the future. But I really must altogether demur to the conclusion that one or two cases of this kind, even if proved, are sufficient to condemn the whole system, which, as I have already stated, can be proved to be productive of invaluable aid to the human race, and, I must add, to dumb animals also. And I must allude to another point. So far as I am given to understand, many of the cases which are produced for the information of the public have occurred in the somewhat remote past, and it is possible that some cases of cruelty may have existed. But we are not concerned now with the history of vivisection: we are concerned with the working of the Act of 1876, and for my present argument, that work is satisfactory.

Then, a great deal of misapprehension exists in the public mind as to the number of operations which have been performed. According to the last figures I have seen, and which, I may say, I was only furnished with yesterday, so that I have not yet had time to go carefully into them, there were 73,000 experiments done last year under the Act. The public are inclined to conclude that there were 73,000 operations. That is not true. No less than  $96\frac{1}{2}$  per cent. of those were inoculations, hypodermic injections, and so on; that is to say, operations mostly of a wholly painless character; they were not really operations. In the small number of cases remaining out of the grand total, the animals were effectively anæsthetised. The testimony of Dr. Thane, the Government Inspector, is conclusive on this point. If anyone will take the trouble to read the evidence given by Dr. Thane before the Royal Commission, he will see that in all cases anæsthetisation



was effected, and in all cases was complete. I should like, while on this particular point, also to draw attention to the evidence of a very eminent man of science, Professor Starling, who is not only an eminent scientist, but also I am informed—I have not the pleasure of his acquaintance, but I do not doubt it is correct—that he is a man noted for his extreme sensitiveness as regards the infliction of pain on animals; that no one would be more sensitive than the learned Professor to any charge of cruelty to animals. This is what he said before the Royal Commission: “Though I have been engaged in the experimental pursuit of physiology for the last seventeen years, on no occasion have I ever seen pain inflicted in any experiment on a dog or cat, or, I might add, a rabbit, in a physiological laboratory in this country, and my testimony would be borne out by that of anyone engaged in experimental work in this country.” Here again, I think the testimony is almost conclusive.

Gentlemen, I could dwell further on these points, but I am sure you will be glad to hear those who are more qualified to speak on the subject than myself. Broadly speaking, I maintain that the small amount of pain and suffering which may be occasionally inflicted by experimentation is a price which may justifiably be paid, in view of the enormous amount of pain and suffering which is thereby prevented or relieved. Before many months are over, I trust that Lord Selby's Commission will have reported: but on that ground, that general ground, Gentlemen, I say that personally my opinion would not be shaken even if in some one or two isolated cases it had been found that a greater amount of pain had been inflicted. But such is the composition of that Commission, that I am sure its findings will carry weight with all of us. Possibly, of course, it may



impose further restrictions in the interests of humanity, or, on the other hand, it may allow some relaxation in the interests of science. But whatever they may report, they will give all of us who are interested in this subject an opportunity of revising our opinions by the light of the very careful enquiry which they have conducted, and it will also enable us to become acquainted with these new facts.

In the meanwhile, I may conclude by saying that I esteem it a privilege to be the President of this Society, and to be thus closely connected with a number of very distinguished and humane men, who in their zeal for science, and in their persistent endeavours to relieve the sufferings of humanity, have incurred a large amount of unjust and unmerited obloquy.



## EXPERIMENTS ON ANIMALS DURING 1907 IN GREAT BRITAIN AND IRELAND

### ENGLAND AND SCOTLAND

SEVEN new places were registered for the performance of experiments, and two places were removed from the register, during 1907. All licensees were restricted to the registered place or places specified on their licenses, with the exception of those who were permitted to perform inoculation experiments in places other than a "registered place," with the object of studying outbreaks of disease occurring in remote districts or in circumstances which rendered it impracticable to perform the experiment in a "registered place." In one instance, permission was granted, for a limited period, to perform inoculation experiments in a place that was not registered, on condition that the place should be open to inspection; and it was inspected while the experiments were in progress.

The total number of licensees was 423. Reports were furnished by (or, in a few exceptional cases, on behalf of) these licensees, in the form required by the Secretary of State. The reports show that 118 licensees performed no experiments. These numbers include 26 licensees whose licenses expired on February 28th, 1907.



The total number of experiments is divided into :  
(1) those in which anæsthetics were used ; (2) those which were performed without anæsthetics.

# I.

The total number of experiments in which anæsthetics were used was 2,580, being 206 less than in 1906. These 2,580 experiments were performed as follows :—

Under License alone	...	...	...	1,214
„ Certificate C	...	...	...	167
„ „ B	...	...	...	983
„ „ B+EE...	...	...	...	215
„ „ B+F	...	...	...	1

In all experiments made under license alone, the animal must during the whole of the experiment be under the influence of some anæsthetic of sufficient power to prevent the animal from feeling pain ; and the animal must, if the pain is likely to continue after the effect of the anæsthetic has ceased, or if any serious injury has been inflicted on the animal, be killed before it recovers from the influence of the anæsthetic which has been administered.

Certificate C allows experiments to be performed, under the foregoing provisions as to the use of anæsthetics, in illustration of lectures.

Certificate B exempts the person performing the experiment from the obligation to cause the animal on which the experiment is performed to be killed before it recovers from the influence of the anæsthetic. If the animal be a dog or a cat, certificate EE is necessary in addition to certificate B.

Certificate F is required in all cases of experiments on a horse, ass, or mule.

In the experiments performed under certificate B (or



B + EE, or B + F) the operations are required to be performed antiseptically, so that the healing of the wounds shall, as far as possible, take place without pain. If the antiseptic precautions fail, and suppuration occurs, the animal is required to be killed. After the healing of the wounds the animals are not necessarily, or even generally, in pain. Experiments involving the removal of important organs—including portions of the brain—may be performed without giving rise to pain after the recovery from the operation; and, after the section of a part of the nervous system, the resulting degenerative changes are painless. In the event of a subsequent operation being necessary in an experiment performed under certificate B (or B + EE, or B + F) a condition is attached to the licence requiring all operative procedures to be carried out under anæsthetics of sufficient power to prevent the animal from feeling pain; and no observations or stimulations of a character to cause pain are allowed to be made without the animal being anæsthetised.

In no case has a cutting operation more severe than a superficial venesection (the lancing of a vein just under the skin) been allowed to be performed without anæsthetics.

## II.

The vast majority of the experiments, no less than 96·5 *per cent.*, were inoculations, with a few feeding experiments, or administration of various substances by the mouth or by inhalation, or abstraction of a minute quantity of blood for examination. These experiments were all made without anæsthetics, as follows:—

Under Certificate A	...	...	...	70,137
" " A + E	...	...	...	462
" " A + F	...	...	...	195

It will be seen that the operative procedures, in ex-



periments performed under Certificate A, without anæsthetics, are only such as are attended by no considerable, if appreciable, pain. The certificate is, in fact, not required to cover these proceedings, but to allow of the subsequent course of the experiment. The experiment lasts during the whole time, from the administration of the drug or injection, until the animal recovers from the effects, if any, or dies, or is killed, a period possibly extending over several days or even weeks. The Act provides that, unless a special Certificate be obtained, the animal must be kept under an anæsthetic during the whole of an experiment; and it is to allow the animal to be kept without an anæsthetic during the time required for the development of the results of the inoculation that Certificate A is given and allowed in these cases. If the animal be a dog or a cat, Certificate E also is necessary: or Certificate F, if the animal be a horse, ass, or mule. It must not be assumed that the animal is in pain during the whole of the time. In cases of prolonged action of an injected substance, even when ending fatally, the animal is generally apparently well, and takes its food as usual, until a short time before death. The state of illness may last only a very few hours, and in some cases it is not observed at all.

In a very large number of these experiments, the results are negative, and the animals suffer no inconvenience whatever from the inoculation. In the event of pain ensuing as the result of an inoculation, a condition attached to the license requires that the animal shall be killed under anæsthetics as soon as the main result of the experiment has been attained.

A large number of experiments, almost wholly simple inoculations and similar proceedings, were performed either on behalf of official bodies with a view to the



preservation of the public health, or directly for the diagnosis and treatment of disease. Several County Councils and Municipal Corporations have their own laboratories, in which bacteriological investigations are carried on, including the necessary tests on living animals; and many others have arrangements by which similar observations are made on their behalf in the laboratories of Universities, Colleges, and other institutions. A sewage farm is registered as a place in which experiments on living animals may be performed in order that the character of the effluent may be tested by its effects on the health of fish. The Board of Agriculture has two laboratories, which are registered for the performance of experiments having for their object the detection and study of the diseases of animals. In other places experiments have been made on behalf of the Home Office, the War Office, the Local Government Board, the Board of Agriculture and Fisheries, the Metropolitan Asylums Board, the Royal Commission on Sewage Disposal, the Royal Commission on Tuberculosis, and the Sleeping Sickness Committee of the Royal Society. Fifty-one licensees return over 8,000 experiments which were performed for Government Departments, County Councils, Municipal Corporations or other Public Health Authorities; 2,825 experiments were performed by two licensees for the Royal Commission on Tuberculosis; and twelve licensees performed nearly 4,600 experiments for the preparation and testing of antitoxic sera and vaccines, and for the testing and standardising of drugs.

The total number of these experiments was much greater in 1907 than in 1906. This increase was almost wholly due to the experiments performed in the course of cancer investigations, almost all of them inoculations made on mice.



The irregularities which occurred during the year were not of a serious character, and all arose from misunderstanding or inadvertence with regard to the extent or application of certificates. They were as follows:—

One licensee performed three inoculation experiments in excess of the number for which the certificate had been given.

In two instances the licensee performed experiments on animals (not cats or dogs) other than those for which the certificate had been given.

Two licensees holding certificates given for inoculations made use of other procedures, in one case feeding, in the other, exposure to noxious vapours, which were not indicated in their certificates.

One licensee holding Certificate A, which dispenses entirely with the use of anæsthetics, performed inoculations on anæsthetised animals. For this the licensee should have obtained Certificate B, which is necessary when an animal under experiment is to be allowed to recover from the anæsthetic which has been administered.

By direction of the Secretary of State, an appropriate caution was addressed to each of these licensees.

### IRELAND

During 1907 there were 9 registered places in Ireland. The number of licensees was 14, of whom 4 performed no experiments in 1907. The total number of experiments during the year was 158. These were performed as follows:—

Under License alone...	...	...	...	4
„ Certificate C ...	...	...	...	11
„ „ A ...	...	...	...	133
„ „ B ...	...	...	...	10



The animals were as follows :—

Mice	...	...	...	...	...	57
Guinea-pigs	...	...	...	...	...	50
Rabbits	...	...	...	...	...	45
Dogs	...	...	...	...	...	3
Goats	...	...	...	...	...	2
Cat	...	...	...	...	...	1

No abuses of the Act, or irregularities in its application, were found in Ireland during 1907.

### SUMMARY

Of the total number of experiments made during 1907 in Great Britain and Ireland, the vast majority were simple inoculations. No less than 96·5 *per cent.* of the animals used for experiment were subjected either to inoculation or to some similar treatment not involving any cutting operation. Many of them suffered no pain at all ; the result was negative. The chief purpose of these inoculations was for the study of cancer, and for that research the animals used were mice.

Of the remaining experiments, which are only 3·5 *per cent.* of the total number, the majority were made under a license alone, or under a license *plus* Certificate C. In all of them the animal was anæsthetised throughout the whole of the experiment.

There remain only the experiments made under a license *plus* Certificate B, or B+EE, or B+F. These are only 1½ *per cent.* of the total number. In all of them the animal was anæsthetised throughout the whole of the experiment, and was allowed to recover and to be kept for observation. The licensee was required to use antiseptic precautions, and, if these failed and suppuration occurred, the animal was required to be killed ; and a condition was attached to the license forbidding further operation or painful stimulation except under an anæsthetic.

The history of the city of Boston is a subject of great interest and importance. It is a city of many centuries, and its history is a record of the growth and development of one of the most important cities in the world. The city has been the seat of many great events, and its history is a record of the progress of the human race. The city has been the home of many great men, and its history is a record of the achievements of the human mind. The city has been the center of many great movements, and its history is a record of the struggles of the human spirit. The city has been the birthplace of many great ideas, and its history is a record of the progress of the human race. The city has been the home of many great men, and its history is a record of the achievements of the human mind. The city has been the center of many great movements, and its history is a record of the struggles of the human spirit. The city has been the birthplace of many great ideas, and its history is a record of the progress of the human race.



## SOME FACTS AS TO THE ADMINISTRATION OF THE ACT

(EVIDENCE BEFORE THE ROYAL COMMISSION)

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BEFORE the Act of 1876 was passed, it is probable that some experiments were made, not in the laboratories of well-known institutions, but in private houses. Whether many experiments were thus made we do not know. On this point, Mr. Byrne, Principal Clerk in the Home Office, says: "If there were, which is a very doubtful point, any considerable number of experiments going on in private houses and other unknown places, I should think the effect of the Act has been to abolish them entirely. It is impossible to believe that in thirty years, if unlicensed experiments were taking place, the Home Office and the police would not have heard of it—not one instance of it. I wish to bring out that matter before the Commission; that, as we have never heard of any case, it is very fair proof that they do not occur, because somebody would be sure to denounce them if they did occur."

Mr. Thane, the Inspector under the Act, giving evidence on 7th November, 1906, says: "The only cases in which private premises are registered for the performance of experiments are the pharmaceutical laboratories of Messrs. Wellcome & Co. and of Messrs.



Brady and Martin, Limited, and the tract of heather at Frimley." These "private premises" are used for the standardising of antitoxins and for the study of grouse disease. Also, experiments in unregistered places are allowed for the immediate study of outbreaks of infective disease among flocks and herds: that is to say, a few licensees are given a sort of roving commission to study outbreaks of infection in the only way in which they can be studied. Also, in three cases, within the last few years, leave was given for the study of "caisson disease," divers' disease, at unregistered places, *viz.*, the premises of a firm of diving engineers, and the bridge works at Newcastle-on-Tyne.

With these exceptions, all experiments are made in places registered under the Act, and open to inspection. The list of registered places is of great interest, because it shows how much of the work is now a national service—a part of the Government's care for the national health. The Board of Agriculture has two laboratories; the Local Government Board makes experiments on animals; the Home Office, indirectly, has been the occasion of "a good many experiments in connection with dangerous trades." The Metropolitan Asylums Board has five laboratories; Aberdeen, Cardiff, Colchester, Glasgow, Hamilton, Manchester, Wakefield, Worcester, have municipal laboratories of their own; in Liverpool, the University gives assistance to the municipality. These municipal laboratories are mainly for diagnosis: they are permanently at work and occupied, and the work is done by officials of the corporation or public body concerned. From these State laboratories, we come to the Lister Institute, the Imperial Cancer Research Fund, and the Royal Commission on Tuberculosis, which, though they are not State institutions, are doing the work of the State; and,



since the work of the State is done wherever the subjects of the State are cared for, we come also to our Hospital laboratories: there is no break in the chain, whether the work is done by Hospital teachers or for the authorities at Whitehall.

Let us suppose that a man wants to obtain leave to make some experiments on animals. What steps must he take to that end? First, he will take advice how to proceed. Next, he will (1) procure the necessary form or forms of application; (2) get them signed by two members of that very small body of Presidents of learned Societies, and Professors of learned Sciences, who alone are qualified, under the Act, to sign such applications; (3) submit his application to the Home Office. The Home Office (4) sends it to the Association for the Advancement of Medicine by Research. The report from that Association is received and considered by the Home Office, and the application is then (5) submitted to the Inspector, who considers the same, and (6) advises the Secretary of State on it; "frequently having to make, and making, further inquiries with regard to the proposals made, before he finally advises." (Mr. Byrne's evidence, Q. 149-156).

We have plenty of evidence that applications are indeed examined and scrutinised before they are granted; and that many of them are subjected to very strict enquiry or revision or limitation. Nobody, who has ever had anything to do with the working of the Act, needs that evidence; still, there it is. "It very frequently happens," Mr. Byrne says, "that if the wording of the license, or the certificate, is somewhat indefinite and would allow of experiments being carried out which were not really necessary for the purpose of the investigation, the wording would be so altered as to confine it strictly to the enquiry. That often happens."



"Every license which is applied for has to pass not only through three sets of eyes, but four sets of authorities, before it is granted. And the same with a certificate. Every proposed investigation of a novel, important, or painful character is submitted to the Home Secretary personally by the Under Secretary." Again, the Home Office regularly exercises its power to annex conditions to a license. For instance, there is nothing in the Act about killing animals which are in pain after inoculation, or about antiseptic precautions, or about the use of anæsthetics for any subsequent operative procedure.

The idea that any medical student can get a license is utterly false. In 1888 one student was licensed, and in 1890 one; with a special arrangement that their work should be supervised. All "amateurs" are refused; for example, a clergyman, and a "gentleman of independent means who was pursuing bacteriology for the love of the thing," and the manager of a mine, who wished to test the effect of mine-gases on birds and small animals. In veterinary medicine, of course, licenses are granted to experts. The applicant must state clearly on his papers the character and the purpose of the proposed experiments; and, having obtained his license, he must record and report all his work, and must also send to the Home Office a copy of any published account of it. And, of course, he may be required to send an *interim* report; and his work is open to inspection.

Inspection, according to the opponents of all experiments on animals, is a farce. It is impossible, they say, for three men to inspect so many places and so much work. We have the evidence of the inspectors on this question, whether the amount of inspection is sufficient.



"I do not think you would get any advantage (by more inspectors and more inspection). I do not think that any abuses are going on that you would stop. It would be only a satisfaction to the public, perhaps—but that is the only advantage it would be. . . . But I should, of course, suggest that the Inspector's staff should grow with the increased work demanded of it. The subject is growing, and I think that additional inspection will soon be required. I have managed to keep abreast of it up to the present, but it is getting to be more than one man can manage."

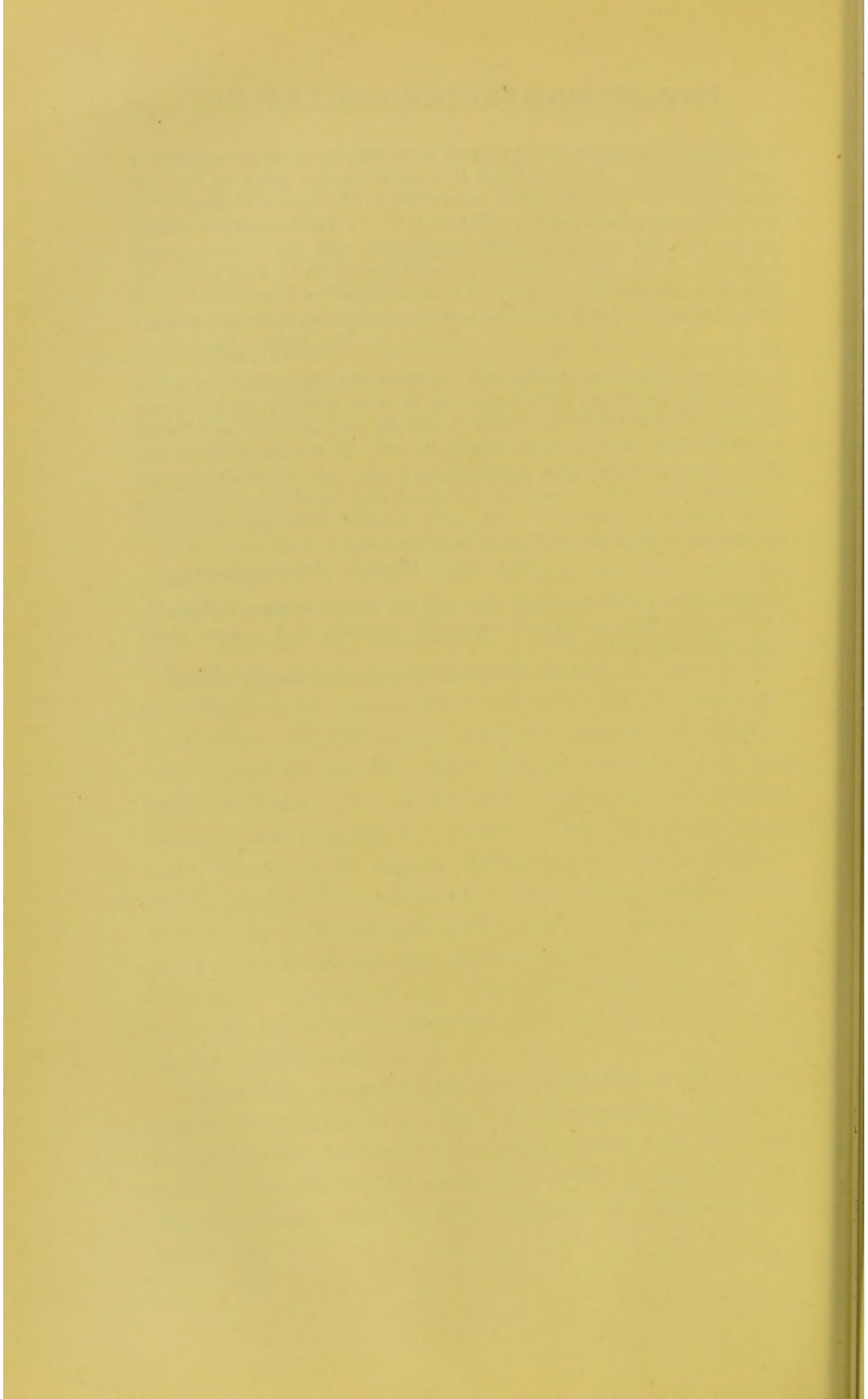
MR. THANE, *Inspector.*

"I think there is great safeguard. I think the inspection is essential to secure for the Home Office knowledge of what goes on; and it keeps licensees informed as to what they should do, and, as I have said, it has prevented their stupidly contravening the law. If the character of the people is not such that they would not do wrong, I do not think that any amount of inspection—even staying there all day—would secure that they would behave themselves. I am quite satisfied with the amount of inspection. I think it is about the right amount."

SIR JAMES RUSSELL, *Assistant Inspector.*

"I think so. I do not think there are any abuses existing in Ireland. I do not think there is any concealment, or anything that a dozen more inspectors could find out."

SIR W. THORNLEY STOKER, *Inspector for Ireland.*





## ON THE USE OF DOGS IN SCIENTIFIC EXPERIMENTS

BY ERNEST H. STARLING, M.D., F.R.S.

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FOR some thousands of years the dog has been bred and trained to help man in his avocations as hunter and herdsman, and has acquired, in the course of ages, a dependence on his master, and a consequent devotion to his interest, that well merit the affection with which the dog is regarded by the great majority of civilised men.

It is not surprising, therefore, that the ghastly accounts, which are sown broadcast throughout the country by the various Anti-vivisectionist Societies, of the cruelties alleged to be constantly perpetrated on dogs in the interests of Science, should excite opposition to the continued use of this animal for experiment, at any rate in the minds of those who give credence to such reports. Even those members of the community who realise that the knowledge and control of our bodily functions required for the successful treatment of disease can only be gained on living animals, are tempted to enquire whether results cannot be equally or at any rate sufficiently well attained by experiments on animals lower in grade of intelligence or less endeared to man by tractability and service.

The justification for the use of the dog must arise out



✓ of the indispensability of this animal for scientific purposes, and involves at the same time a responsibility to the animal of avoiding, so far as possible, the infliction of pain or even discomfort.

In order to arrive at a conclusion on these two points we must examine the conditions under which these animals are used for scientific purposes in this country. In the first place, the choice of animals which can be used in experimental research is for the most part strictly limited. The larger questions of Physiology and Pathology, those the solution of which must affect practice throughout the whole of its ramifications, are of necessity the subject of investigation chiefly in academic laboratories. Here only do we find the men the main ✓ object of whose life is the advance of Science. Here only is the investigator stimulated in his researches by the necessity of continually teaching the large truths of his science. Here only is it possible to obtain the brightest spirits among the students as co-workers, and train them as future leaders of Science. If, therefore, the investigations carried out in these scientific institutions involve the use of experiments on animals, the animals must be such as can be kept in a healthy and normal condition either in the laboratory itself or in buildings in close proximity to the laboratory, limited in their area and the nature of their surroundings by the fact that in most cases they have to be placed in the middle of populous centres.

Except, therefore, for isolated experiments, the ordinary animals of a farm, such as bullocks, sheep, pigs, and goats, are not available for our purposes. It is true that at the present time experiments are carried out on these animals, but these experiments take place only at agricultural stations, and have for their object the decision of practical questions bearing on the nutrition



and diseases of these animals. Only incidentally are the results of such experiments of wide-reaching importance on the science of life as a whole, or in the treatment of disease in man.

Let me here emphasise the point that the distinction commonly drawn between utilitarian and purely scientific experiments is entirely artificial. The whole aim of Science is the acquisition of control, either over the forces of Nature, or over the functions of our bodies, or over those of organisms in relation to man, and this control can only be obtained through knowledge. In the purely scientific laboratories it is the fundamental questions which are the chief objects of research. But an advance in such questions implies a far-reaching change in the relation of man to the science in question and every advance opens up at once a whole series of subsidiary questions relating to the immediate application of the science to man or man's pursuit. The purely academic investigations on animal electricity by Galvani, of the movements of a magnet when hung in the neighbourhood of an electric current by Oersted, of the relation of one current to another by Faraday, rendered possible the whole of the electrical industries at the present time. And it is not by purely utilitarian investigations, comparable with those into the most economical method of constructing some detail of a dynamo, that a similar revolution will be rendered possible in the relations of man to his environment.

All researches are utilitarian, *i.e.*, are for the benefit of man. We are, however, accustomed to restrict this term to those in which we can see the immediate benefit and in which, therefore, the advance can only be a small one of detail. The larger advances in Medicine must come from the Physiological and Pathological laboratories, and if animals are required for the advance of



these sciences they must be such as can be kept in health and comfort within the limits of the laboratory.

The following animals come within this category : the frog, mouse, rat, guinea-pig, rabbit, dog, cat, and monkey.

Of these the frog owes its value to the fact that, being a cold-blooded animal, its isolated tissues survive a considerable time after removal from the body, and can therefore be used for the study of fundamental phenomena common to all animals, such as muscular contraction, the function of nerves, etc.

The guinea-pig, rat, and mouse are of chief value for inoculation experiments, such as those of diphtheria and tubercle, where large numbers of experiments have to be made, and the operation in each case is relatively simple, the answer required being generally given by the survival or the death of the animal.

The rabbit takes an intermediate place between this class and that including the dog and cat. It can be used for certain more complicated experiments, but for many its organs are too small or too delicate. Moreover, the great differences between its diet and digestive system and those of man, and the low organisation of its nervous system, and, indeed, the greater simplicity of its organisation, limit its capabilities as a means of physiological analysis of higher functions, and, in particular, render it impossible to apply results obtained on it directly to the elucidation of the functions of man.

The only animals left, therefore, are the cat, dog, and monkey. The latter animal is useful especially for experiments on the brain and central nervous system. In a sense, it has the most highly developed nervous system, and is in this respect nearest to man. For this very reason we should be loath to use it for experiments where animals lower in the scale would suffice. Moreover, the



limited supplies of these animals, and the difficulties of keeping them in a healthy condition in confinement, will always prevent their use for any experiments which can be equally well carried out on other animals.

The cat and the dog are both carnivorous, and both have digestive systems presenting marked analogies to that of man. The dog, moreover, can thrive on a diet as omnivorous as that of man himself. Which of these two animals can be utilised depends in most cases on the size of the organs which it is desired to investigate. A number of experiments can only be performed on dogs, because the corresponding organs in the cat, though larger than those of the rabbit, are still too small to permit of experimental interference.

Though it is impossible to give a full list of such experiments, which must vary with the progress of Science, the following examples may serve to show the indispensability of the dog for a large number of important researches.

(1) Practically the whole of our knowledge of the production of lymph in the body is derived from experiments on dogs. This is owing to the fact that the main lymphatic ducts are too small and delicate in the rabbit and cat to permit of a tube being placed in them so as to measure the lymph produced under any given circumstances. The choice of this animal, therefore, has not been simply a matter of convenience, but is necessitated by the nature of the problems involved.

(2) Although some of the earliest experiments on the heart, *e.g.*, the causation of the heart sounds, and the interpretation of these sounds, which are utilised by every medical man when he listens to the chest of a patient, were made on a calf, the further analysis of these sounds and of their changes with different conditions of the heart was carried out in physiological laboratories, where



the only animal of sufficient size to be obtained was the dog. In the same manner the investigation of the pulse, of the work of the heart, and of the relations between the blood pressures in the heart and the blood vessels respectively, has been carried out on the dog, and further extension of our knowledge of these matters can only be looked for by continuing the experiments on dogs.

(3) The laws governing intestinal movements have been studied in many different kinds of animals. The clue to their interpretation was, however, obtained in the dog, and it would have been impossible to have arrived at these laws from experiments on the cat or rabbit, although, when once ascertained on the dog, it was possible, by altering the conditions of experiments, to show their applicability also to other animals. Observations on the dog furnished the key to the interpretation of the extremely complex movements observed in the intestines of other animals.

(4) In a series of important experiments made lately by Professor Schäfer, on the best methods of carrying on artificial respiration for the resuscitation of partly drowned persons, it was only possible to make use of the dog, since this was the only one of the laboratory animals in which the bony cage of the chest can be compared in any way to that of a man.

(5) The recent researches by Professor Pawlow, of St. Petersburg, on the physiology of digestion, have revolutionised our conceptions of this process, and must determine the whole of our treatment of disorders of digestion. These investigations involve the establishment of artificial openings into different parts of the alimentary canal (*fistulæ*, as they are called). Through these openings the different digestive juices can be collected at different stages in digestion, without



interfering in any way with the comfort or well-being of the animal. The cat would have been much too small, and would have yielded too minute quantities of juice to permit of their proper investigation. In this case the farm animals would have given results of far less service, owing to the wide divergence between the anatomy of their alimentary canal and that of man, whereas the results obtained on the dog can be transferred almost without alteration to the phenomena presented by digestion in man.

It would be possible to extend considerably this list, but the examples I have adduced may be sufficient to show that our present knowledge has been obtained by certain classes of experiments, involving some of the most important functions of the animal body, and of the utmost interest to the physician in the treatment of disease, which were made on dogs, and could only have been made on dogs. We may conclude that the use of these animals would still be necessary even if it were possible to utilise largely the herbivorous farm animals for the purposes of research.

It is probable, however, that many of these subjects would remain uninvestigated, and the advance of our knowledge would not have taken place, if the experiments that I have detailed involved the infliction of pain, or at least of pain at all severe. Fortunately for Science, this is not the case. The introduction of anæsthetics and new narcotics and of the aseptic method of operation into Physiology has well-nigh abolished pain from our Physiological laboratories, as it has from the surgical wards of our hospitals, and has advanced the science of physiology no less than the practice of surgery. I do not think that the absolutely painless character of the vast majority of physiological experiments is sufficiently appreciated. Records of classical experiments, performed before anæsthetics were invented or had come into



general use in laboratories, are too apt to be taken as typical of those of the present day, when the use of anæsthetics is invariable in all experiments more extensive than a simple inoculation.

Though I have been engaged in the experimental pursuit of physiology for the last seventeen years, I can say that on no occasion have I ever seen pain inflicted on a dog or cat in a Physiological Laboratory in this country, and my testimony would be borne out by anyone engaged in experimental work in this country.

Moreover, it is not merely the normal humanity of the operator that should deter the infliction of useless pain in a physiological experiment. It is the object of the experimenter to limit the field of his experiment so far as possible, so that when he is, so to speak, putting a question to any function of the body, this function shall be unaffected by any factor other than that which is being controlled by the experimenter. Of all possible disturbing factors in the body, none can be greater than that of pain. It is a common experience that a slight toothache will upset the processes of digestion, and a storm of pain playing on the different functions of the body might make it impossible to judge how far any result obtained was due to our experimental interference, how much to the irregular actions of the pain inflicted. It is true that the anæsthetised condition may be regarded as more or less abnormal. We are able, however, by using different anæsthetics, to vary this abnormality from one experiment to another, and thus to allow for it in interpreting the results of our experiments. We should not be able to allow for the effects of such an indeterminate factor as pain, and a physiological experiment which is painful is thereby a bad experiment.

The very small total amount of pain inflicted in physiological experiments will be rendered clearer if we



consider the conditions under which experiments are carried out. Since from the character of the lines of research pursued, more dogs are probably used in my laboratory than in any other laboratory in this country, we may take one year's record of experiments as an example. In the year 1902, 155 experiments were performed on dogs in the Physiological Laboratory at University College. Of these, 151 were performed under license alone. What does this mean? In experiments performed under license alone, the animal must during the whole of the experiment "be under the influence of some anæsthetic of sufficient power to prevent the animal feeling pain, and the animal must, if the pain is likely to continue after the effect of the anæsthetic has ceased, or if any serious injury has been inflicted on the animal, be killed before it recovers from the influence of the anæsthetic which has been administered." In all these experiments, therefore, the dog was first chloroformed; the experiment was then performed while it was fully anæsthetised, and at the conclusion of the experiment the animal was killed without ever recovering consciousness. With common care it is easy to keep animals for hours under the influence either of chloroform or ether, or of a mixture of these two drugs, in a state of complete insensibility, and the same result may be attained by the use of large doses of narcotics, such as morphia or urethane. In none of these experiments could the animal have felt anything at all of the operations.

No one has yet been denied our moral right to take animal life in the interests of man. Millions of animals are slaughtered every year for food. Nor are the lives of dogs in any way regarded as sacred. At the Battersea Dogs' Home over 20,000 dogs are suffocated annually in the lethal chamber in order to diminish the danger of stray dogs in the London streets. This



institution is mainly kept up by funds contributed by the charitable. In the vast majority of our physiological experiments euthanasia is attained even more completely than is the case in the Dogs' Home, but in the laboratory the death of the animal is utilised for increasing our knowledge of the animal body, and therefore in the service of man.

In 1902, four experiments were performed in my laboratory, under Certificates B. and E.E. Such certificates would be necessary for an operation such as the establishment of a gastric fistula. The animal being fully chloroformed, an opening into the stomach is made, with exactly the same precautions as are used when the operation is carried out on man in cases of irremediable stricture of the gullet. The wound is dressed with all aseptic precautions, and the animal is then allowed to recover from the anæsthetic. Experience on man shows that the healing of a wound made in healthy tissues is practically painless, and we have no reason to suppose that dogs are more sensitive to pain than man himself. In a week's time the wound is healed, and we have a dog normal in every respect, except that there is a direct opening between the exterior of the body and the interior of the stomach.

The earliest case of gastric fistula, which was the subject of detailed observation, was that of Alexis St. Martin, a Canadian, in whom a gastric fistula had been established as the result of a gunshot wound. Dr. Beaumont took St. Martin into his employ, and for many years carried out careful observations on the secretion of gastric juices, and on the movements of the stomach walls. His experiences are sufficient to show that observations on a gastric fistula, which has first been established in an animal, are perfectly devoid of pain or even discomfort.

The painless condition of a wound depends on its



healing aseptically. Experience on man shows us that infection of a wound may be followed or attended by pain. By the terms of the certificates under which these experiments are made, if the antiseptic precautions fail and suppuration occurs, the animal is required to be killed under an anæsthetic. It is generally essential for the success of these experiments that the wound should heal cleanly, and that the surrounding parts remain in a healthy condition. We may conclude, therefore, that in the majority of physiological experiments no pain is inflicted.

In a certain small proportion of cases, although we cannot speak of actual pain, the effect of our operative measures may be to cause sickness followed by the death of the animal. In all such cases the animal must feel ill and miserable, as it does in distemper, but it is just these experiments which have the most immediate bearing on the causation and treatment of disease in man. A disease such as diabetes is produced in the animal in order that we may study the conditions on which it depends, and so learn to control them. Such experiments do not, however, form one per cent. of the total number of experiments on dogs.

Since, as I have shown, the use of the dog is indispensable for the furtherance of our knowledge on many functions of the body, any legal prohibition of the use of dogs for experimental purposes would deal an irremediable blow to the advance of Physiology and Medical Science in this country; while the only practical result to the dog would be that a few hundreds more would be killed in the lethal chamber at the Battersea Dogs' Home, instead of obtaining euthanasia at the hands of the physiologist.





## ANÆSTHETICS USED IN EXPERIMENTS ON ANIMALS

NINETY-SIX and a half per cent. of all experiments on animals in this country are inoculations, or of the nature of inoculations. For these inoculation-experiments, anæsthetics are not used. But no cutting of any kind, more severe than the lancing of a superficial vein, is allowed to be done, except on an animal under some anæsthetic of sufficient power to prevent it feeling pain.

There are three ways of preventing pain : (1) local anæsthesia, by the use of cocain or eucain ; (2) anæsthesia by the use of such drugs as morphia or chloral ; (3) anæsthesia by the use of chloroform, ether, or nitrous oxide. (1) Local anæsthesia is very seldom used in experiments on animals. Sir James Russell suggested to the Royal Commission that it might be used, under certificate A, before an inoculation : " More for the sake of the feelings of some experimenters than for the needs of the animals. There are several experimenters who shrink from even the use of the hypodermic needle, and these are the very men who are apt to transgress by using an anæsthetic." That is to say, there have been cases where a licensee, making inoculations under certificate A, which dispenses with the use of anæsthetics, has anæsthetised the animal to avoid the momentary pain of the introduction of the needle : for which purpose he ought to have held, not



certificate A, but certificate B. But local anæsthesia is not applicable to, and has never been employed in, experiments involving any sort of operation.

(2) Morphia and chloral and urethane and similar drugs, to produce anæsthesia, must be given, and are given, in large doses. "The question of complete anæsthesia," says Dr. Starling, Professor of Physiology at University College, "will in each case be a question of the dose, whether you are dealing with chloroform or whether you are dealing with morphia. Morphia is a complete anæsthetic if it is given in large enough doses." Not a month passes in this country without some person killing himself or herself with morphia or chloral. They die profoundly anæsthetised; they cannot be roused, or, if they outlast the morphia and recover, they remember nothing or next to nothing. "My experience in this matter," says Prof. Starling, "would show that, after opium poisoning, if the patients have been saved, they are not conscious of the very strong shocks they have been given in order to try and hurt them while in that state of poisoning." For the use of morphia and of chloral in experiments on animals, we have the following evidence given to the Commission:—

Mr. Thane (Government Inspector).—Q. May I ask whether morphia is sometimes used on dogs as an anæsthetic, without chloroform or ether? A. Morphia is very rarely used as an anæsthetic alone, that is quite certain. Q. You think that morphia could be administered so as to secure complete anæsthesia? A. Morphia can be administered so as to secure complete anæsthesia; there is no question about it, but you probably would have to give a fatal dose. Q. You think that chloral and urethane would be effective? A. I am quite sure



that urethane would be. I have seen experiments with it. And I have no reason to doubt that chloral would be effective; but I have not seen actual experiments under chloral.

Dr. Schäfer (Professor of Physiology at Edinburgh).—*Q.* Would you say that morphia only dulls pain, and does not remove it? *A.* Certainly not. A sufficient dose of morphia absolutely removes all signs of pain.

Sir T. Lauder Brunton.—*Q.* We have been told here repeatedly that morphia is not an anæsthetic; that depends, of course, upon the quantity. We have been told also that chloral is not an anæsthetic; that also depends upon the quantity. These animals receive poisonous doses in order to completely narcotise them? *A.* Yes; and as to the statements that chloral and opium or morphia are not narcotics, and do not remove pain, there is no other word for it, it is simply a lie; you may as well say that chloroform does not remove pain. If you give any animal a sufficiently large dose of chloral or opium, you so completely abolish sensibility that there is nothing you can do that will awaken its sensibility. The animal is as senseless as a piece of board.

Mr. Henry Morris.—*Q.* Do you think that an animal, a dog or a cat, which receives a poisonous dose of morphia or opium, is in a condition to feel pain up to the time that death occurs? *A.* No, I do not think so. They suffer no pain. *Q.* We have been told here by several witnesses that opium is not an anæsthetic, and therefore, even when a poisonous dose is given, the animal is probably suffering tortures until death occurs. *A.* That is not so.

Dr. Dixon (Professor of Materia Medica at King's



College). We do not use (or very rarely) morphin alone as an anæsthetic, not because it is not one, but because it leaves the motor cells active, and the animal is reflex. But it is quite commonly used for man now in Germany, when it is given with some drug which also paralyses the motor cells as well as the sensory; and so in Germany, and to a limited extent in England, it is given with hyoscin (the so-called morphia scopolamine narcosis) for operations where chloroform is deemed unsuitable.

Dr. Dudley Buxton.—*Q.* In your opinion is morphia a complete anæsthetic? *A.* Quite. *Q.* For severe operations? *A.* Certainly. *Q.* No pain would be present? *A.* Not if you had a sufficient dose of it.

As to the doses of morphia, chloral, and urethane, which are used in experiments on animals, we have Prof. Starling's evidence. "Urethane is used in man, as a simple narcotic, to produce sleep. A man weighing 50 kilos receives from one to five grammes; to an animal, we give  $1\frac{1}{2}$  grammes per kilo, that is, *about fifty times as much*. We give that intravenously. We first give what would induce anæsthesia in the ordinary way, namely, morphia and chloroform; then, if for some reason or other we do not want to go on with chloroform, we should inject into the veins this very large dose of urethane. Or (if the high blood-pressure with urethane were a disadvantage) we might use chloral hydrate. In man, we give from 5 to 20 grains of chloral hydrate, that is, about 0.02 gramme per kilo. In the animal, we give  $\frac{1}{2}$  gramme per kilo, that is *fifty times as much*, and then we get complete anæsthesia. Then, again (if the vaso-motor action of chloral were a disadvantage), we have morphia. Morphia is generally used as an adjunct to chloroform and ether. If the



animal has had a previous dose of morphia, it will then go on with a small dose of A.C.E. mixture, instead of having to have a large dose constantly administered to it. In some cases morphia can be used as an anæsthetic; this is a use which has been much criticised. When we give morphia as an adjunct to chloroform or ether, we give from one-sixth to a quarter of a grain (about the usual dose for a man). When we give it as an anæsthetic, we give *from one and a half up to fifteen grains*, according to the size of the animal: that is to say, *a dose that is practically fatal*. Sometimes, in one or two cases, dogs do recover from the average amount, if they are kept perfectly warm; but in nearly all cases they die of the dose. It is a fatal dose."

(3) With regard to the use of chloroform or of ether, or of a mixture containing chloroform and ether, the evidence before the Royal Commission proves that animals can be and are profoundly anæsthetised by this method, and can be kept absolutely unconscious to pain for many hours if necessary. This fact is proved, not only by evidence in physiology, but by evidence in the daily practice of veterinary surgery. (See Mr. Hobday's evidence, vol. iv., Q. 16284-16523.) We have, with much else to the same effect, the following evidence:—

Sir James Russell. "I do not think that the licensees would dare to do in a hospital what they do in laboratories in the way of giving anæsthesia. I have frequently seen animals they have killed before beginning the operation, owing to pushing the anæsthesia too far. . . . The result of my personal observation of experiments on dogs has been that they were very fully under. Q. You have said that they were as completely anæsthetised as a human being would be, and as carefully? A. Generally more so, those I have seen,



Q. Do you think it is perfectly possible to keep, for example, a dog under complete anæsthesia during the whole of that time (an hour and a half, or longer)? A. I do not see any difficulty in it. . . . What I have seen, as I have said already, is that experimenters nearly always push the anæsthesia more boldly than they would in human patients. . . . And, further, if it is an operation before a class, say, in the Edinburgh University, where the professor has 200 or 300 critics in front of him, I think he would be a very bold man, even if he had the heart to do such a thing, who would venture to show an experiment where the anæsthesia was not complete."

Prof. Schäfer. "In all experiments which come under license, complete anæsthesia is secured during the whole period of the experiment, however many hours it lasts. I do not mean to say that an animal will never make a movement when it is under anæsthetics; of course, an animal will as a man will. But the object of the experimenter is to keep the animal under anæsthesia; his objects are likely to be entirely frustrated if the animal moves; and although the condition of anæsthesia may be more or less complete, the amount of anæsthesia used in physiological laboratories is in almost every case vastly deeper than that which is used in the operating theatre. It does not matter very much to us whether the animal dies of anæsthesia or not. The suggestion that we knowingly, or even unknowingly, allow the animal to come out of the anæsthesia is, on the face of it, an absurd suggestion, because it would absolutely defeat the object of our experiment. . . . I have witnessed a great many operations, in Germany and other countries; and the statements which fly about regarding the callousness of foreign physiologists



to the sufferings of animals are wild, and quite unconfirmed by anything which I have seen. And I have seen at congresses of physiologists large numbers of operations performed, always under full anæsthesia. Q. But assuming that in this country an anæsthetic has always been applied, the suggestion rather is, that it has not been applied fully and carefully, and so as to ensure complete insensibility to pain? A. That suggestion has no grain of foundation."

Prof. Starling. "With common care, it is easy to keep animals for hours under the influence either of chloroform or ether, or of a mixture of these two drugs, in a state of complete insensibility. . . . The administration of anæsthetics is a routine practice, just as it would be in the operating theatre. Nobody ever thinks of doing any cutting operation without thorough anæsthesia. . . . I think it would be a good thing if some of the Commissioners who doubt as to the completeness of anæsthesia would come and see an actual experiment."

Dr. Cushny (Professor of Pharmacology at University College).—"Q. Is there no difficulty in putting a dog and keeping it for a long time during a severe operation under perfect anæsthesia? A. There is no difficulty whatever. I have had a dog for six hours under anæsthesia. Q. And under perfect anæsthesia? A. Under perfect anæsthesia."

Sir Lauder Brunton.—"Q. You have been connected with people who have been experimenting on living animals for many years? A. Yes. Q. Have you ever known of any case of inhumanity or want of consideration for causeless pain; I am speaking of England, of course? A. No; in England certainly not, and I



do not remember any case abroad, because, as I said before, most of my experiments were done in Prof. Ludwig's laboratory in Leipsic, and he was always most careful of the feelings of the animals that were experimented upon. Q. You have had experience of chloroform given to a vast number of dogs? A. Yes. Q. And you have entirely convinced yourself that they have been under anæsthesia? A. Yes, entirely. Q. And complete anæsthesia? A. Complete anæsthesia; as complete as any patient could possibly be under on the operating table."

With chloroform, ether, or the A.C.E. mixture (alcohol, chloroform, and ether) the anæsthetic is given on a mask, or on a fold of lint, or, in some cases, through a tracheotomy tube. This last method is used in surgical practice for many operations on the head and neck. For the more usual method of giving the anæsthetic, we have the evidence of Prof. Starling and of Dr. Dudley Buxton.

Prof. Starling. "The usual thing we do is to give the animal, half an hour before the experiment, a hypodermic injection of morphia, of about a quarter of a grain—from a quarter to a third. The effect of that is that the dog becomes sleepy and stupid, and then sometimes it will lie down quietly, and if it is very sleepy you can put a mask over its nose containing the chloroform, alcohol, and ether mixture, which it takes quite quietly. If, at the time one wants to begin the operation, the animal is not fully under the influence of morphia—if it still seems restless—it is put in a box, and there it has some wool saturated with the A.C.E. mixture put in the box. The air gradually gets saturated, the dog gets more and more sleepy, and finally subsides at the bottom of the box."



Dr. Dudley Buxton : " In physiological experiments on dogs, of which you have seen a great many, they are all strapped down, first of all, are they not, before the chloroform is administered ? *A.* No, certainly not. *Q.* Is there not some difficulty in administering it ? The dogs struggle against it ? *A.* They are in a box ; you can put them into a box. *Q.* The dog struggles, I presume, to get out of the box ? *A.* No, it generally lies down and goes to sleep. *Q.* Not at first. In the early stages does it not struggle or bite the box ? *A.* As a rule, my experience is that the dog turns round once or twice and goes to sleep. *Q.* And then is it strapped down ? *A.* Yes, when it is unconscious, and tied on a board. *Q.* That, you say, is to prevent reflex action ? *A.* No, I did not say anything of the sort."

### CURARE

Curare is not an anæsthetic under the Act ; it is illegal to use it as an anæsthetic. In this country it is seldom used at all, and is never used alone in any experiment involving any sort or kind of surgical operation. In every such case a recognised anæsthetic must be given, and is given.

It is the general opinion of physiologists that curare, though in small doses it only abolishes motion, in large doses also abolishes sensation. The evidences in favour of this opinion are : (1) the well-known case of arrow poisoning recorded by Mr. White, Q. 15920 ; (2) Schiff's experiments on the local exclusion of the poison from one limb of a curarised frog by ligature of the main artery of that limb ; (3) the relationship of curare to other drugs. It is thus described by Prof. Dixon in his evidence before the Royal Commission :—



“It is not an isolated drug, having this peculiar action all by itself. There are lots of other drugs having the same type of action. It is, perhaps, the one which has the most characteristic action on the motor nerve endings, but there would be no difficulty in picking out a whole host of others that do the same. All this group of drugs paralyses the nerve cells, the brain, and every one of them paralyses the motor nerve endings, and they may all cause convulsions by acting on the spinal cord. These three facts apply to all of them. Some members of the group have one action well defined, and others another. Thus, nicotine first paralyses the nerve cells and later the motor nerve endings, whilst hemlock (conium) paralyses the nerve cells and nerve endings almost together. Curare first paralyses the motor nerve endings and later the nerve cells, whilst hemlock (conium)—the poison that killed Socrates—paralyses the nerve cells and nerve endings, roughly, about the same time. I picked those three examples from a group to show the various stages, how one produces its action at one time, and another at another time. I mention this to show that even curare, given alone, is a complete anæsthetic, if enough is given, although we in England, conducting experiments, assume that curare has no action on the nerve cells, and always give enough of some other anæsthetic to completely paralyse the brain. Of course Claude Bernard really started this idea that curare acts on the motor nerve endings, and not on the sensory nerve endings or cells. But Claude Bernard’s experiments only apply to the spinal cord; he did not prove anything else at all; all that he showed was that the sensory cells in the spinal cord are not paralysed by curare. That was all his experiments meant. None of these other drugs paralyse the sensory cells in the spinal cord in moderate



doses. Chloroform, except in the largest doses, does not paralyse the sensory cells in the spinal cord. . . We believe that small doses of curare would paralyse the motor nerve endings before the brain cells were paralysed, but that large doses of curare will paralyse the whole of the brain like chloroform."

With regard to the general characters of curare, we have the evidence of Prof. Starling and Prof. Cushny. Prof. Starling is asked: "What is curare, is it a herb?" He answers: "It is an arrow poison, the South American arrow poison. It is used for poisoning arrows by the Indians, and is brought by them into commerce in gourds. It is now becoming extremely difficult to get curare, and it is getting more and more impure, more and more poisonous in its effects, so that it is being used as little as possible." Prof. Cushny says the same. He is asked whether curare is much used by experimenters in this country, and he answers: "I do not think it is much used anywhere; to tell the truth, it is very difficult to get, and the reason why I refuse to give any definite statement as to curare is that it is so indefinite. We have not the same curare that we could have got thirty or forty years ago. As a matter of fact, at the present time, much of the curare that we get fails to paralyse muscles or anything. I tried to get it in a number of places a few years ago, and I could not get any curare that would paralyse the muscles at all. What is called curare is very often quite inactive."

As to the infrequency of the use of curare, we have the evidence of several witnesses before the Royal Commission. Sir James Russell, Assistant Inspector in Scotland, says: "I have not seen it used for years. I did see it once used in a blood-pressure experiment about fifteen years ago. In that case the anæsthetic



used was a very heavy dose of urethane, administered before the experiment began, and the animals were heavily narcotised. I happened to see that experiment from beginning to end."

Dr. Gotch, Professor of Physiology at Oxford, says: "I have had very little experience of curare." Later he is asked: "Did I rightly understand you to say that in the course of your twenty years' experience you have not had occasion to use curare on your own responsibility?" and he answers: "I have not used curare. I do not use it for the blood-pressure experiments that I show. I have not used it for the research experiments that I have done upon the nervous system."

Sir Lauder Brunton says: "I have very rarely used it. I do not think I have used it at all since the passing of the Act, because I always had the feeling that curare alone might not completely destroy sensibility. I may, perhaps, mention that I was very anxious to find that out, and when I was in Leipsic in 1869, I proposed to Prof. Ludwig to give me curare, and then, perhaps, apply a hot iron or something to the back of my hand, and keep up artificial respiration till I came to life again; and then I would tell him whether it would hurt or not; but he said that the risk was too great, that the means of keeping up artificial respiration were not sufficiently good, and he thought it was not worth while to do it—and he did not do it."

Prof. Schäfer says: "I have not used curare at all for years. I have not been engaged in any experiments which require the use of curare."

It is plain, from the evidence before the Royal Commission, that curare is seldom used at all, and is never used without an anæsthetic in any experiment cal-



culated to give pain. Indeed, apart from all question of humanity, it is impossible to imagine an experimenter deliberately using curare instead of an anæsthetic. As Sir Richard Douglas Powell said to the Royal Commission, "Curare is very expensive, and very difficult to obtain—very difficult indeed—and I cannot conceive of any man using curare for any other purpose than to prevent reflex muscular movements which would interfere with his experiments under an anæsthetic. To substitute it for an anæsthetic would be a piece of clumsy extravagance which I cannot imagine any sensible man making use of."

It is to be noted that curare is only used in conjunction with an anæsthetic in those cases in which the animal is killed under the anæsthetic without recovering consciousness; thus, Prof. Starling is asked (*Q.* 4056), "Is curare ever given under certificate B in cases of animals that are to recover from the anæsthesia?" *A.* Never. *Q.* 4057. "Therefore every animal that has curare is, so to speak, bound to die under the anæsthetic?" *A.* Yes.

Prof. Starling explained to the Commission the circumstances which would require the use of curare. "A case in which one must use curare is where one is exciting, say, a nerve going to the arm.<sup>1</sup> We know that this nerve going to the arm contains fibres which will cause contraction of muscles, and which will also cause contraction of blood-vessels. If we want to get a contraction of blood-vessels, we cannot record these, or see whether they contract, if the muscles are contracting at the same time; so we should give curare, which would paralyse the nerves ending in the muscles, but would not paralyse

<sup>1</sup> It hardly needs to be pointed out that the stimulation of the efferent fibres of a nerve does not cause pain.



the nerves ending in the blood-vessels, so that, after curare, if we stimulate this nerve *here* (*describing the same*) the blood-vessels would contract alone. It is under that sort of condition that one has to give curare."

Further questions were put to Prof. Starling as to the use of curare, as follows:—

Q. 3620. It not being clear that it is an anæsthetic (you say it may possibly be one, and your own opinion, I rather understand, is that it is one), it must be assumed that it is not? A. Yes.

Q. 3621. And, of course, an anæsthetic must be given in such a case? A. Yes.

Q. 3622. And anyone who did not give an anæsthetic, but used curare, would clearly be doing wrong? A. Yes; he would be contravening the Act, for one thing.

Q. 3623. And might possibly be inflicting great pain on the animal? A. He might be, and, therefore, it would not be approved of in our laboratories at all while there is a shadow of a doubt that it is an anæsthetic.

Q. 3624. Have you yourself ever used curare in a painful experiment without adequate anæsthetisation? A. No; and I have never seen it used in this country without simultaneous and adequate anæsthetisation.

Q. 3625. Neither as a student nor as a professor? A. No.

Q. 3626. It paralyses the voice too, does it not? A. Yes; it would paralyse all the motor nerves, and, therefore, it would paralyse the voice as well as other movements.



Finally, many witnesses before the Royal Commission were asked as to the possibility of pain occurring from the passing off of the anæsthesia in an animal that had also received an injection of curare. Prof. Starling is asked: "Are there any means, other than the cries or struggles of the animal, by which you can tell whether the anæsthetic is passing off?" And he answers: "Yes, you can tell it by the blood pressure. Struggles have also what we call their visceral side. This activity of the muscles of the body is associated with activity of the centres which govern the blood-vessels, and when one is working without curare one notices that the pressure goes up, and then, if one does not attend to it, after that comes a little movement, and you give more anæsthetic."

Q. 4055. "So that the presence of curare does not prevent your knowing whether the anæsthesia is complete?" A. No, it would make it more difficult; but you have that clue. What one does, of course, is to ensure the complete anæsthesia, and continue that anæsthesia during the curare—continue the same amount.

Dr. Langley, Professor of Physiology at Cambridge, is questioned on this same point, and answers (Q. 15169): "I have had experience of the use of curare for particular experiments, and having obtained a knowledge of the way to administer anæsthetics, I am confident that there is no difficulty in keeping up the anæsthesia while curare is given. The operator must start with complete anæsthesia, and he must know from past experience the amount of the anæsthetic which it is necessary to give in order to maintain it. For instance, with chloroform, the chloroform is given at the intervals and in such doses as his previous experience has shown will maintain com-



plete anæsthesia. Pain would cause a rise of blood pressure, but I should myself always rely on the previous experience of the anæsthesia, how it is produced, and the depth of it, and see that it is maintained in just the same way as if the curare were not given."

Dr. Waller, Director of the Physiological Laboratory of the University of London, gives a similar answer: "I know, if you give the animal 2 per cent. of chloroform vapour, it is of necessity under the influence of the chloroform vapour. I know that I am on the safe side as regards pain to the animal."

Prof. Schäfer, *Q.* 10087, and Dr. Thane, *Q.* 1705, give evidence to the same effect.



EVIDENCE OF  
LORD JUSTICE FLETCHER MOULTON  
BEFORE THE ROYAL COMMISSION ON VIVISECTION

*Wednesday, 24th July, 1907*

The Right Hon. Sir JOHN FLETCHER MOULTON,  
called in; and examined.

12691. (*Chairman.*) You are a Member of the Privy Council, a Fellow of the Royal Society, and a Lord Justice of Appeal?—I am.

12692. For many years you have taken an interest in the progress of curative science?—Yes, I have taken a very keen interest in it both from the scientific side and also from what is called the ethical side. Having been a politician, and realising that the public take to themselves the right and the duty of controlling everything that goes on in the kingdom, I have realised for many years that the question which this Commission is directed to consider would come on in some form or other in the way of an enquiry; that, in other words, the justification for scientific research in connection with curative science would be examined. As I have in many other things observed, the advance



of science takes the workers in science more and more beyond the ken of the ordinary public, and their work grows to be a little understood, and much misunderstood; and I have felt that, as in many other cases, the need would come for interpreters between those who are carrying on scientific research and the public, in order to explain and justify their work. The consequence is that I have considered the subject very much from the very point of view from which this Commission has to consider it. I have come, many years ago, to a very deep conviction upon it, and therefore I am glad to have the opportunity of putting before this Commission the reason for the faith that is in me.

12693. You say you have taken great interest in the subject for a long time, and I believe you have very closely watched what has been going on with reference to it on both sides?—Yes, I have watched it very closely on both sides. Of course, you quite understand that so far as the scientific side is concerned, though I am qualified to judge of the scientific results and of the evidence for them, I am as an outsider immeasurably less qualified to speak with authority on the scientific points themselves than are some of those whom you have had before you; but, on the other hand, I think that with regard to the scientific methods, and with regard to the bearing and meaning of the results upon the subject of this Commission, I am, as a close observer from outside——

12694. A highly qualified observer, I may say for you?—I am qualified to give some assistance to the Commission.



12695. In your long experience at the Bar, before you went on to the Bench, you were specially interested and employed in matters that dealt with questions of scientific investigations of all kinds?—Yes; I have had, I think, unrivalled experience in being what I have described as an interpreter between those who are doing the pioneer work in science and the people who have to judge of the results of their work; and it is, perhaps, more from that standpoint than from any other that I desired to put my views before the Commission with regard to this question.

12696. In your view, I understand, the real issue raised by the agitation against experiments on animals is, whether or not curative science shall be studied experimentally or whether it shall become a purely observational science?—Yes. I think that in the controversy a great deal has been lost by looking at it in too narrow a light. It is not a question of vivisection—that is to say, the performing of cutting experiments on living animals; that is a mere nickname, a mere catch phrase, which was originally invented, I have not the slightest doubt, for purposes of prejudice. I am not saying that with a desire to find fault. One always likes to get a name which expresses one's own point of view without further explanation; but it is a most imperfect representative of the real issue. The real issue is whether curative science is to be an observational science or whether it is to be an experimental science, and, as I shall hope to show this Commission, the importance of the decision of that issue is impossible to be exaggerated. But I shall deal with that a little later on, after I have



dealt shortly with the grounds of the opposition to its being an experimental science.

12697. You have something to say, I think, on how far the opposition is based on humanitarian grounds?—Yes; the opposition purports to be based on the principle that we are bound to regard the sufferings of animals, and that the avoidance of the suffering of animals is a motive which ought to influence every man with a conscience. It is a consequence, no doubt, of a change which has come over the views of mankind decidedly in the right direction. Of old, cruelty was thought nothing of, whether it was to men or animals. You cannot read the history of the world down to, say, the seventeenth century, without feeling that there was an extraordinary callousness to suffering of every kind. A great change from that time has been passing over the world. First, there came the regard for the sufferings of men, and cruelty towards men gradually passed out of favour; and now the thought of human suffering and the desire to avoid it is one of the most unquestioned and influential motives that guide the action of mankind. Presently there followed the extension of the feeling to the sufferings of animals, and there is no doubt that now, with the best part of humanity, sympathy for the sufferings of animals and the desire to lessen those sufferings are most influential motives of action. Now that appears to me all in the right direction, and so far as my opinion goes it is not only not contested by either party to this controversy, but both of them would in words accept it as a duty to lessen so far as possible the sufferings of animals as well as of men. I do not wish to be misunderstood when I talk about the



sufferings of animals in the same breath, as it were, with the sufferings of men. I must therefore point out a very broad distinction between the two, which must be borne in mind if we are to come to right conclusions in this matter. The sufferings of animals are substantially physical only. The sufferings of men are not solely physical. Almost as important a factor in that suffering is mental suffering, arising partly from a man's relations to society—that is to say, that death or sickness will cause pain and suffering and trouble and misery to those who are intimately connected with the man—and partly in the individual himself. He is capable of feeling anxiety, regret, dread, and many other things which are of the most serious importance in measuring human suffering, but which are practically absent from animal suffering. I do not say this in any way to detract from what I have said about the importance of avoiding and preventing, so far as we can, animal suffering; it is only that we may keep true our ideas of what suffering is, and to do that, one must bear in mind the broad distinction I have just mentioned.

12698. You mean that if a man and an animal have each to be subjected to a serious operation under anæsthetics, the whole of the pain and suffering that the animal experiences after it is properly anæsthetised and dies under the anæsthetic is covered by the anæsthetic?—Yes.

12699. And it has not suffering before or after?—No.

12700. But in the case of a man, he has the suffering of anticipation, thinking of the future, of those who belong to him, and if he dies he has the



suffering of his family. If he survives, he has suffering from that again, which may amount also to disablement and loss of some of his functions?—Yes, that is a very striking example of the difference, and it brings out one other point which you must also bear in mind, and that is, our responsibility with regard to mankind as compared with our responsibility to animals. In the case of an animal, if the future is to be a future of pain, we unhesitatingly kill it. No matter how certainly the future must be a future of pain in a man, we must by universal acceptance keep him alive. Therefore, in deciding on our duty to men and animals, we have to realise that, no matter what be the consequences, we have no right to decide with regard to man as to whether it is better to terminate his sufferings or not. If you take the case of a man with some terrible disease over him which may perhaps be cured by an operation, he has the terror of the uncertainty of the cure. The operation is fortunately under anæsthetics, and he does not feel it, but afterwards there may come an only partial cure, and a painful life ahead of it. Not one of these elements exists in the case of the animal. The animal, if the pain is going to be greater than the value of life, is put out of the way painlessly. So that we must remember that distinction, because it is not permissible in a serious enquiry like this to shut our eyes to any truth. There is no safe side on which one may lean in the way of exaggeration in the examination of a question like this; and although you are going to be loyal to the duty of lessening the pain of animals, you must not mistake the relative position of pain with them and pain with us.

12701. You admit that there is a responsibility on



everyone who operates on animals to avoid unnecessary pain?—Oh, yes. In fact, I go further, and I think that one ought to admit as a fundamental principle that it is the duty of all men to work for diminishing pain. The diminution of the totality of pain in animals and in men ought, I think, to be a guiding motive and a prominent motive in the case of people in the position of those who are working in curative science, and also in the position of people in ordinary life; and in my opinion it is just as operative, and, if I might give my private opinion, it is far more operative in those who are connected with the curative sciences than in the people who attack them so bitterly. And it is for this reason: Because those who are dealing with the curative sciences are perpetually brought in face of pain, and it is a point of honour with them to conquer that pain and relieve it, till that aim becomes to them a kind of second nature—a kind of all-pervading motive.

12702. You are speaking rather, are you not, of the practising physician or surgeon than of one who devotes himself entirely to research?—I am; but the reason why I cite that is this, that there is an almost unanimous opinion, among those who are engaged in the practical work of the curative sciences, in favour of experimental research in connection with them. That support has been discounted by people saying: ‘Oh, those who are engaged in curative science get callous to pain.’ Now, in my opinion, they are more sensitive to pain, because it is perpetually appealing to them, and, if I might say so, it is the lifelong foe which they are engaged in fighting. I mentioned therefore the extent to which the desire to diminish



pain was present to those who are engaged in it, not so much as dealing, as you say, with those who are engaged in research, as with those who, with a full knowledge of the matter, give them their support, in order to point out that that support has the very high sanction of coming from people who all their lives are fighting pain, and fighting it often at very great personal discomfort and self-sacrifice, till it has become to them, as I say, an almost all-dominant motive. The difference between the two schools is this: Those with whom I range myself, who are desirous of extending and supporting experimental research in the curative sciences, consider not only the pain that is inflicted, but they consider the pain that might be prevented, and they hold themselves responsible for permitting pain which they could stop, just as much as for inflicting pain deliberately—they look at the two together. The other school consider only inflicted pain. They think it their duty to prevent pain being inflicted, even though the infliction of pain may lead to the prevention of many times that much pain in the future.

12703. Of course, your argument, if carried out—I am not disputing it, or offering any opinion about it—would lead to this, that if anæsthetics had never been invented, you would still be justified in carrying out experiments on living animals, and inflicting the necessary pain upon them, for the sake of the knowledge that would be acquired in the saving of pain in the future?—It would; but if you will allow me I will put my practical conclusions latest. I want first of all to lay down the foundation of the decision. I want to get before the Commission the fundamental principles as I view them, and to establish them, and



then I propose to take the practical conclusions, when I will deal with such a matter as you have referred to.

12704. But, of course, the actual fact that anæsthetics and their use have been discovered now does not render the argument I was putting a very practical one. It is rather a logical consequence than a practical one?—Certainly; I quite understand that. Now I want the Commission to allow me to take what I may call a simile or an illustration. I am going to take a case which in my opinion exactly represents the attitude of the two rival schools; it is not connected with experiments on animals at all, and that is one of the reasons why I have chosen it. I want the Commission to understand that I take it as explaining my views, and I shall trust to bring the question which is before this Commission up to the level of this illustration. I will suppose that a ship which is plague-stricken, and has got rats on board, arrives at a port. A man with a sense of his responsibility, knowing that there is a high probability that rats convey the plague, would unhesitatingly extirpate those rats, even though his only method of doing so was by putting them to a painful death, whether it was by poisoning them with phosphorus or by stifling them, or by even more painful methods. He would not hesitate; he would feel it his duty to extirpate them. Now, supposing that a person were to come and say, "I could not bear to see those poor creatures running for their lives and in danger, trying to save themselves from their relentless pursuers, and so I let as many as I could escape," I have no doubt that the person who did that would think that he acted from humane motives. But what would be the consequence? It might communicate plague not only to a town, but to



a whole nation. It might bring positively measureless misery. The first man would be right, because he would look at the inflicted pain which would be to the bad side of the ledger. No one would have a right to inflict that suffering merely capriciously. But he would see beyond that pain he was inflicting—that in acting thus he was preventing an amount of pain which was beyond all measure greater than that which he was inflicting; and if he was a man to whom pain appealed, who had a heart which felt keenly suffering whether in men or animals, he would do it all the more unhesitatingly. The other man would think only of the inflicted pain, and say, “I am too tender-hearted to inflict it.” He would not consider that by not doing it he was causing preventible pain on such an enormous scale. That is typical of the struggle between the two parties. I have chosen that example, not because it is an exaggerated one, or because it is an unfair one. I have chosen it because in that case there is no veil between the act and its consequences. One can see plainly that the letting free of those infected rats might produce those consequences. But now just let me take a hypothesis. I will suppose that, instead of bringing a plague, the killing of those rats would lead to the discovery of the antiseptic treatment. That antiseptic treatment put an end—substantially, of course, I mean—to an amount of human misery that we can scarcely realise. The suppuration of wounds, accidents leading to months of painful sickness and a recovery which was only partial and left the people maimed, the horrors of war doubled, the deaths in war enormously increased, were all consequences of sepsis—it was just as bad as a plague. Now if, instead of it being a question of “either you extirpate the rats or you have the plague,” it had been “either you extirpate the rats



or the antiseptic method will not be discovered, and the suppuration of wounds and all the horrors which follow from that must remain in the world," you see at once that to the thoughtful man the argument in the two cases is precisely the same—"If I do not inflict this pain I permit an unmeasured amount of pain which I could prevent." In my opinion, when you once see clearly the causal connection between the pain you inflict and the diminution of pain which follows from it, it makes no difference in what way it follows. Your duty is to take that line which produces the minimum total pain, and whether the pain is inflicted pain, or whether it is preventible pain which is not prevented, is in my opinion one and the same thing.

12705. Supposing that you have not got an immediate prospect of preventing pain or of preventing septic conditions, but are pursuing these experiments for the purpose of acquiring knowledge that you do not possess, with the hope and belief that it will lead to some good, how do you deal with that?—You have anticipated the very next step which, in my opinion, we have to take in the examination of the subject. The reason why I gave this illustration was that I wanted to put before you by an example the criterion which I say every humane man ought to follow. It is that he ought to take that line which before his conscience he thinks will lead to the diminution of total pain, and if he is satisfied that the infliction of a certain amount of pain is the right way to diminish the total pain he is bound, from his very feelings of humanity, to take it. And now you say—and, if I might respectfully say so, quite rightly—if that is going to guide you in a matter of this kind, you must be satisfied that a man ought to realise that the practice of the experimental



method is the wisest way to work for the diminution of the totality of pain. If I have brought the question to this point, it is all I want to bring out of the example which I have taken. I admit that those who claim that they should inflict pain are bound to show that it is the wisest thing to do with the view to reduce the totality of pain. But I want to point out one other thing, and that is this—that a man would be bound to take the same course with regard to the rats if there was not a certainty, but a reasonable ground for thinking, that plague would follow. He would have no right to say, "It is not demonstrated; I will risk it."

12706. There is a case, of course, beyond that, where a man is making experiments upon a living animal with a view to ascertain precisely what the action of certain parts of the body is—what their functions are?—Yes.

12707. Not that he can point to any particular saving of pain or good that can be done by it, but he is doing it to acquire knowledge which he does not possess, with a philosophic belief that it will lead to the good of reducing pain?—It is a real pleasure to me to have such points put to me, for this reason—it convinces me, as indeed I knew before, that I have the honour of speaking before those who have thought very seriously over this matter, and realise the various points which arise. You will find that I shall take that point up in its proper place; because, in my opinion, it is of the greatest importance that we should face specific questions of that kind. You cannot, in this matter, come to a wise conclusion by simply dealing in vague generalities. But if you will allow me, I will take it up later, and you will find, I think, that I have put it in its logical position. Now, I said that I took that



example of the plague-stricken ship, not because it was exaggerated, but because there was an obvious connection between the act and its consequences, and then I pointed out that if you could get an equally obvious connection between pain inflicted and a great discovery it would be the same thing. I said that the parallel I have taken was not unfair to either of the two parties, and I want to digress for a moment to show that I am justified in saying so. I think if you were to ask a man who had given thought to the matter, who, of all living men, had been privileged to do most to reduce pain, the answer would, almost without exception, be "Lord Lister," who introduced the antiseptic method, which has been followed now by the various aseptic and antiseptic methods which obtain all over the world. Yet I saw the other day in a paper that at an anti-vivisection meeting Lord Lister's name was mentioned, and it was greeted with shouts of "Brute." They called a "brute" the man who had done most of all living men to lessen pain. And that was, if I might say so, perfectly consistent. They knew that he had voluntarily inflicted pain in his experiments, and that was all that they looked to; and they did not realise that if their real motive, the thing which was the real spring of their action, was the desire to lessen pain, Lord Lister's name should have been the most highly honoured of all. Now, I am not speaking bitterly at all of these people, though I oppose their action so much; I only want to point out that they are acting according to the effect on their emotions of the contemplation of pain; not according to the pain itself. The prevented pain, which has made Lord Lister's name so esteemed, is not present to their minds. The inflicted pain strikes their imagination, and the consequence is that they, with the best of motives, denounce him



because he is willing to inflict pain, without realising that he, who is the most capable, at any rate one of the most capable, of all men to know the ultimate result of his actions, has been doing it for the purposes of reducing suffering, and has succeeded beyond all hope. So that I am not treating those who oppose me unfairly in pointing out that they do not regard the more distant consequences of their action—they only regard the question of the immediately inflicted pain.

Now, I want to go on to what the Chairman has put to me, viz., that I must establish that experimental research is the wise mode of action if we wish to diminish pain. I start from the following fundamental facts. I say that if you look round the world, the only way in which we can diminish pain is by human action. Animals go on regardless of the pain they cause to one another. In fact, the universe is built on pain. Whole races of animals live simply by killing other races, and killing them without the slightest regard to suffering. So that we must look to human action alone to diminish pain. Now, what is it that prevents our diminishing pain in the world? One feels at once that it is not the absence of desire to do it. I believe that desire is very prominently present. It is because we do not know how to do it; it is our ignorance. Take the case of doctors. Doctors are as desirous as they can possibly be of lessening suffering in the world, and yet how often they stand by the bedside and the patient goes on suffering and they can do nothing. Now, the absence of our power of diminishing pain is due to ignorance, to our not understanding two things. First, not understanding the causes which excite pain; and, secondly, not understanding the action of those causes on the organism—that is to say, how it is that those morbid causes, if I might use the phrase,



produce pain. I call the first one (simply to distinguish it) the pathological factor—that is to say, what are the springs of disease; and the other is the physiological factor—that is to say, how those springs of disease cause pain in the organism; that is just a division, for convenience, of the knowledge which we must possess in order to be able to lessen and control pain. Let me give an example of the way in which lack of knowledge increases suffering. The discovery that the organism could, by means of anæsthetics, pass into unconsciousness without passing into death, and that all the living operations could go on equally vigorously while consciousness—that is to say, the possibility of pain—was entirely suppressed, led to the use of anæsthetics, and, as a consequence, to the diminution of suffering, both directly during operations, and indirectly in increasing the possibilities of surgery. Without the knowledge obtained from that discovery men were obliged to perform operations in the brutal method of the old surgeons, because there was no other alternative. This is only an example of the way in which our power is limited by our knowledge. And I wish to point out with regard to this point, that here again we have no difference of opinion. Not only the whole medical profession, but the whole public agree that doctors ought to be armed with all the knowledge of the time. There is no difference of view as to this. Every attempt is made to increase the efficiency of the education of the doctor; because we feel that by arming the doctor with the knowledge of the time we arm him as best we can with the means of diminishing pain. That, of course, is true with regard to the knowledge that has been attained during the last, let me take it, forty years—the only years as to which I can speak; and that knowledge has been mainly due to experi-



mental research. Therefore all must feel that this knowledge which has been obtained by experimental research is useful for the purpose of lessening pain, because we try our very best to make all those who are engaged in practical curative work masters of it. I do not think I need point out to this Commission further how all-important knowledge is where you are dealing with organisms, and you want to stop suffering.

There is one other thing I want to say, and that is this. That our inability to stop suffering, owing to absence of knowledge, is not only to be found in the case of obscure diseases. They afford striking instances of it, no doubt, and are by no means rare. I should think there are very few of us who have not seen those near to them suffer from diseases which have baffled the doctors, and whether or not they could be eased or saved was decided by whether or not the doctors could read what was the cause of the trouble. A friend of mine has just died, apparently of a painful disease which the doctors could not touch. A *post-mortem* showed that it was only because they did not realise what the true cause of the disease was; it was one which might almost with certainty have been relieved. Such diseases may have marked symptoms, but the doctors are unable to read from those symptoms what is the cause, and therefore they cannot fight the cause. But, although these cases are striking instances of the principle, they are nothing like the most important; the most important are diseases which are quite common, of which we cannot yet find the cause, and not finding the cause all we can do is to deal with the symptoms.

12708. I think we all agree that there is a very vast field of medical knowledge yet; I think every medical



man would agree to that, as well as ourselves. But really, the question is how far the knowledge can only be found in experiments upon animals?—Precisely. That, I think you will find from the *précis*, is the next point I want to mention. But I wished to put in the forefront that it is want of knowledge which prevents our diminishing suffering, because I shall trust to show to this Commission that the polestar by which we steer is knowledge. It is ignorance that hampers us. I am using the term ignorance in a sense that will not, I trust, be misunderstood. I am aware of the gigantic amount of knowledge that the present and past members of the medical profession, and those who have been engaged in research, have already accumulated, but what I mean by ignorance is the vast field of what yet may be known, but is not at present known. I desire to impress upon the Commission that that is the real cause of our impotence. Now, let me take the question of how we are to get rid of this ignorance—and here we are on firm ground. No man who knows anything of science has any doubt whatever that the right way to advance knowledge is by experiment. You can take the whole range of the sciences, and I would challenge an opponent to name one in which advance, if it has been rapid and striking, has not been through experiment. Where we are reduced to observation science crawls. Where and in proportion as you can use experiment, the science advances rapidly. I could take any science to show that; it is much easier to show that experiment has led to advance than to find a case in which advance has been made purely by observation; because a scientific man rushes at once to experiment if he can do so. He adds, of course, the testimony of observation—that is extremely valuable for the



purpose of guiding and starting his experiment; but everybody knows that each observation becomes only the nucleus, or, rather, the basis, from which you start your experiment. I was puzzling to think of some branch of science where there was only observation, and the only thing I could think of was the case of volcanoes. Now, there is not anything that has attracted human attention more, or fascinated it more, or has been on a bigger scale or more open to observation, than volcanoes; and yet we are almost in the same state of ignorance of the origin and the *modus operandi* of volcanoes as Pliny was.

12709. The difficulty is just as great now as then for anybody to go down a volcano when it is in eruption?—Precisely. In no way can you bring experiment to bear upon it. As soon as you can bring experiment to bear upon a subject you are free; but as long as you can merely observe, your progress is very slow. The reason is that experiment is like cross-examination. You can put the question you want, and Nature always answers it. She does not answer the question you meant to put; she answers the question you actually did put. She swears by the card in the most shocking manner. She does not care in the least what you meant to ask, but she does care what you asked, and she answers it with perfect truthfulness. And the consequence is, that when you adopt experiment, the great experimenter can put a question, the answer to which lets the whole secret out. I am going to give an example that I remember impressed me very deeply. I cannot tell how many years ago, but it was just about the time when it was first discovered that guinea-pigs were susceptible to tuberculosis. I heard from a friend that a doctor of his acquaintance,



a practising physician, I suppose, had been troubled as to whether consumption was a communicable disease or not: I should say that the vast preponderance of opinion at that date was that it was hereditary. I remember, as all of us remember when we were young, the way in which consumption would, as it was called, go through a family, and it was thought that this was because it was in the strain. Then some bold people suggested that it was possible it might be due to its being communicable, although probably to the ideas of that time it looked about as likely to be communicable as spinal disease. What that doctor did was this: he took a dozen guinea-pigs, divided them into two sixes, and he let one six have the run of the wards of a consumption hospital, and the other six have the run of the wards of another hospital, just about in the same conditions of temperature; he left them there for the requisite number of weeks, whatever it was, and then he killed the whole dozen, and he found that the six which had been running in the consumption hospital had tuberculosis, and that the six that had been running in the other hospital had no trace of it.

12710. (*Chairman.*) The other was not a consumption hospital?—No, it was not.

12711. (*Sir William Collins.*) Whose experiments were those?—I cannot tell you the name of the doctor, because it was not given me, but I heard it long ago, in the early days of research upon tuberculosis, and I believe it to be true. But if it was not actually performed, it would still serve as a typical example of experiment. I have no reason to doubt that this experiment was actually performed, because the man who told me was a most intelligent man, and he told



it to me at the time as having been done quite privately, by a doctor whom he knew, in order that the doctor might settle the doubt in his own mind.

12712. (*Chairman.*) You would say that it is rather an illustration than a typical example, if it is not given us at first hand in some way?—You may take it simply as an illustration, although the very thing has been done, I know, by other people. Klein did it. If you remember, Klein put guinea-pigs into an air shaft which led from the wards of a consumption hospital, and found that they developed tuberculosis. But we will take it merely as an illustration. I am not basing anything on the fact. What I want to point out is this, that such an experiment would settle the question more than would twenty years of observation,—I might say a century of observation—for this reason, that you had placed these similar animals under entirely similar circumstances, with the exception that in the one case, but not in the other, there were present in the immediate neighbourhood persons who were sick of the disease, and you will find as a result that in the one case they become sick, and in the other they do not. There is no question of heredity, and there is no question of the acquired disease being the consequence of different circumstances of living, of different circumstances of nutrition, or anything of that kind. The only thing that is present as a cause is the neighbourhood of the sick people in one case and not in the other. In the result, the difference is disease in the one and not in the other.

12713. What was the fact that it was wanted to discover there—whether guinea-pigs could take the complaint?—No, whether the disease was communicable from one person to another.



12714. But there are plenty of examples of people who have not tuberculosis daily frequenting hospitals and not acquiring it, are there not?—Oh, yes; but the point of the experiment was not under what circumstances was the disease communicable, but whether it was communicable at all. Just take the case of persons who are ill of spinal disease.

12715. I follow you.—Their relatives go freely ✓ among them, attend to them, and try to make their sickness as easily borne as possible. And so it undoubtedly used to be when members of a family were sick of tuberculosis. Everyone thought it was only kindness that the brothers and sisters should attend to their sick sister, and nobody thought that there was danger. But when you had found that this was a communicable disease, your duty with regard to children and other people in the presence of the disease became very different, and it was only to find out this that the experiment was tried. The experiment showed affirmatively it was communicable. That was only, of course, the first of a necessary series of experiments to show how it was communicable; but from that moment the doctor knew how great was the responsibility of allowing people to attend or be in intimate contact with one who was affected by consumption. Just try and see how you could get an equal degree of certainty from observation. You take a case where it has run through a family. Yes; but it might be that it was hereditary in the family. Then you find that in a particular place it is very largely prevalent. Yes; but that may be because, as compared with other places, the climate or soil of that place produces a predisposition to it. Neither group of cases points necessarily to communicability. Some people will be struck in one way with a series of these cases, others



will be struck in another way, and there will be a perpetual conflict as to which is the true explanation. But when you take such an experiment, there is not a doubt; you cannot explain it, except that the disease is communicable. And the consequence is that you commence your further examination with the consciousness that it has been demonstrated that it can pass from the sick to the well. Now I was very much struck—as illustrating the impossibility of arriving at these things by observation—by a piece of cross-examination by Sir William Collins of one of the witnesses before the Commission; it illustrated it in the most striking way. He was dealing with the result of the serum treatment of diphtheria. An appeal was made to the statistics of diphtheria hospitals in London, and the witness said: “Oh, the serum treatment is being demonstrated as being a great success, because you have here the same hospital in the same place dealing for a consecutive number of years with the same population, and the statistics show a great diminution of the percentage of deaths after the introduction of the serum treatment.” Sir William Collins, if I might say so, quite justifiably cross-examined on that. He will know whether I am fairly representing him, but, as I remember it, he asked, Are we now getting the cases earlier; is it not true that we have made such advances in the diagnosis that we know better what is diphtheria and what is not? And he went on pointing to differences in the circumstances of the earlier years and the later years as taking away from the conclusiveness of the statistics.

12716. (*Sir William Collins.*) As an element that required consideration.—Exactly, as an element that required consideration. That is perfectly fair. Statistics that are got in that way must be rightly open to



that criticism. And this is the reason: You dare not let the children wait in the later years so as to make the time at which they are taken up for the purpose of treatment comparable with what it was in the earlier years, because you are bound to do for every child the best thing that you can, and the consequence is that you dare not make your experiment scientifically more perfect, because there is the paramount duty towards human life. Now, you could not have had a stronger case, *i.e.*, one in which the observational method was working under greater advantages. You had hospitals devoted to this disease alone, dealing, as I have said, with the same population, in the same place, under, as far as possible, the same circumstances; but you could not, and you dare not, and you ought not to, make the circumstances identical, because of your duty to the individual. Compare that with the case I was putting forward of the guinea-pigs; I could give another and more striking example, which is the classical experiment in connection with anthrax, in which, after Pasteur had worked out the treatment by inoculation against anthrax, he took 50 sheep for his experiment; 25 of them were inoculated and 25 were left uninoculated. Then the whole of the 50 were inoculated with virulent anthrax, and within four or five days every one of the 25 that had not been inoculated died, while of the others 24 were alive, and one was shown to have died from things unconnected with anthrax. You see by these examples how in experimental research you can make the circumstances identical, and one experiment of that kind (properly repeated, so as to eliminate error) gives you a certainty that years of observation could not give. And all those years of observation have paid their toll in suffering. It is no use saying, Well, we shall learn in a few years hence, instead of learning it



now. All that time there has been preventible pain, which has not been prevented because you have not known how.

What, therefore, I want to point out is that we know that the way to acquire knowledge with certainty is by experiment; it follows from its very nature, and from our universal experience in all sciences, that this is the way in which you best acquire knowledge, because you can make each experiment answer some critical question. You can arrange matters so that you have two cases precisely similar in all respects, save that one is without that cause present, and the other is with that cause present, and the contrast gives you a light which you could not get from observing instances where you cannot eliminate other causes. The more complex the subject is, the more factors there are at work, the more essential the experimental method is; and the most complex of all phenomena are those that relate to living beings. I am sure there are those here who have made experiments in connection with life, and know from experience the truth of what I say. The number of factors at work is so large, the difficulty of isolating them is so great, that it often takes very much longer to realise how you can put the question to Nature than it does to put it, and to draw your conclusions from it when you get the answer. But the more complex the subject is, I say the more are you driven away from observation, which only gives you the total result of many causes which are varyingly present in all cases, to something which will enable you to isolate several of the causes and determine separately their effects.

12717. (*Chairman.*) That brings you, I think, to the question I was putting to you about pure experimentation, and the justification of experiments on



animals where you have no specific disease in view?—Yes. Many will think me a heretic on this point, but I have a strong view that, when you have once realised that experiment is the right way to acquire the necessary knowledge, it is a bad thing to work too directly and too consciously for practical results.

12718. When you call that a heresy, of whom are you speaking as the orthodox?—Most people say that you should only make such experiments with the direct view of some practical application for the benefit of mankind.

12719. We have had a good many witnesses before us who take what you call the heretical view.—I am delighted to find that I am not alone.

12720. As well as those who take the other view; and others who would say that you do not go far enough.—I am glad to find that I have got my comrades. You must not misunderstand me. I think that the object and the reward and the ultimate justification of research is the benefit it confers. But what I wish to urge is, that it is unwholesome to keep that before your mind when you are working, at all events in the earlier stages. May I give a parallel which I think explains and justifies this view? I take the history of alchemy. For centuries men of the highest intellectual attainments—for there can be no doubt of the ability of the men who worked at these subjects—worked hard at the transmutation of metals, and the result of those centuries has only been snippets of knowledge, if I might use such a phrase. I do not undervalue them; they gave us, I believe, some very valuable reagents, but that is practically all. And the reason was that they did not commence by working so as to get to



know the nature and properties of the things on which they were working; they worked straight for a result.

12721. For an impossible result, was it not?—It may have been an impossible result. But whether it was impossible or possible would have made very little difference if they had commenced by laying the foundation in knowledge, because, although we should not have obtained the transmutation of metals, we should have had modern chemistry some three centuries earlier than we did. But they only worked for a result.

12722. They did not care about chemistry. Their researches were not chemical researches?—Well, transmutation of metals was intended to be a chemical triumph. If I might take a parallel in curative science, this work was like the shots at specific cures for cancer—violet leaves and all that sort of thing—made by people working straight for a nostrum that will cure a disease like that, the nature of which is shrouded in such mystery.

12723. I only meant those people were fighting a particular disease which they had before them, and which was evident under their eyes, and they were seeking remedies blindly?—Yes.

12724. The other people were seeking something in the clouds altogether; they were not pursuing what you would call chemical research, although they used certain chemical experiments?—But if they had only laid a basis; if they had only worked at it as you try to reduce a fortress, by parallels, where each parallel brings you nearer to the fortress. If you attempt to take it by a rush and fail, you are no further than you were before; but if you make your parallels you are so much nearer, and that is a permanent advance. Just



in the same way I think that if I were to ask any scientific man of position in the medical profession, "Where do you look for the solution of the great problem of cancer?" he would say, "I look to a gradual acquisition of knowledge about it, and the breaking up of the obstinate silence of the disease which will tell us nothing, neither its preferences nor the things it dislikes, nor its origin, nor anything." Such men do not give much heed to the investigations aimed directly at its cure, because they do not believe they will succeed. They believe that we shall have to know a great deal more about the disease itself before we know in what direction success can come. But what they do think is this, that by gradually acquiring knowledge of it, knowledge acquired quite independently of whether it is a thing we could use or not, the disease will gradually cease to be a mystery, and when it has ceased to be a mystery we shall find some weak point in its armour. Therefore I am satisfied that the wisest thing to do is to realise broadly that our ignorance of the springs of disease and the nature of the organism that suffers are the cause of our powerlessness, and that all research which is intended to lessen our ignorance is in the right direction, and that it is in vain for us beforehand to say which will soonest lead to a beneficial result. I feel, therefore, strongly that this is the principle which, with proper regulations and restrictions, we ought to accept; and that we ought to fix our eyes on knowledge and not on immediate promise—immediate promise is likely to be delusive—and when I come to the instances by which I trust to justify the serviceability of experimental research, I think I shall be able to show that those things have sometimes reaped the richest harvest in which the promise came quite late.



12725. You think, to sum up that part of your evidence, that the experimental method is justifiable even though you have no immediate practical object in view beyond the acquiring knowledge and the hope and belief that it will lead to some ultimate useful purpose? —Yes, you have the hope and belief that it will, and you have the certainty that it is the right way to work for it. Where you are ignorant of the evil and ignorant of how it operates, you are like a hunter who is not yet on the trail of the fox. He has to cast about in order to come upon it. Similarly, it takes a very great deal of experiment to know in which direction practical success may be looked for.

✓ I want to say one more thing before I go to the examination of whether, as a matter of fact, the experimental method has shown itself to be of this great practical value, has thus justified its use. So strongly do I hold that what we ought to fix our eyes upon is the acquisition of knowledge and the removal of ignorance, that if I was here without being able to show a single practical result of experimental research in curative science I should give evidence in the same direction, and so far as I personally am concerned with the same confidence, for this reason: Supposing I was to go back, say, 40 years (I am not suggesting for a moment that prior to 40 years ago there was not a great deal done in research, but I take that period as including the great outburst of experimental research, beginning with the early sixties and since then), I should have all my data. I should have the fact that ignorance was vast, vaster even than now, that ignorance paralysed our power of preventing suffering, and that the right way to get rid of that ignorance was by the experimental method; and therefore, even though I could not show that we had obtained any practical



results. I should say to this Commission, if it were sitting in the early sixties, that it was their duty to take care that experimental research was not hindered. The idea that you do not justify experimental research unless you can show that it has already produced practical results would make it never justifiable to commence it, and, in my eyes, it would be just about as ridiculous as to revile winter sowing because in April there were no crops. The moment when the practical results come depends upon the nature of the subject. You cannot foresee it; they may come at a burst. After long investigation which apparently leads to nothing you may suddenly find your reward.

12726. It might not have been unreasonable in Adam, but since his day there has been a very long experience of winter-sown crops?—There has been a long experience of winter crops, but what I mean is, that a man has got no business to say that because the crop has not yet come last winter's sowing has failed.

12727. It would have been an unreasonable thing in Adam?—I agree with you; but, if I may say so, I should use that in my favour; because I should say that if you look at any science you will find that theoretical investigation has always led ultimately to practical power. I could give examples in industries, but they will occur to most of those present. Investigations which have been purely scientific have almost always led to practical results, because the knowledge has been able to be used, and it has produced great results. So that, just as since Adam we have had great experience in winter sowing, so I should say that since the days of Bacon or Newton we have had great experience in this—that you never can



have an increase of knowledge in any subject bearing on practical life without its leading to increased practical power.

I want now to deal with the justification of the use of the experimental method by what it has actually performed, and I am going to ask you to allow me to confine myself to the work of the last 40 years, because that is the period which has fallen under my direct notice. I shall group it in the way I group it in my own mind in order to make out this justification. As I have said, to my mind this direct appeal to practical results is not necessary, though it is immensely helpful, to enable one to make up one's mind as to what is the right course to pursue; but it is all-important in dealing with the many well-meaning persons who do not go along with me in their views with regard to it. The difference is not, I think, because there is a difference of fundamental principle—they are as loyal, probably, according to their lights, to the doctrine that we ought to do our best to lessen suffering, as I am; but they have to learn that which scientific training easily teaches those who have had much to do with it, that the right way to do so is to make full use of the experimental method. I wish, therefore, to take the results of experimental work in the last 40 years, and point out how it has removed ignorance—that is to say, how it has given us knowledge, and how that knowledge has become of practical value in reducing suffering.

12728. If you please.—Of course the first example which one must take is that of sepsis and the antiseptic method. If you look at the books of 40 years ago you will find that the idea that sepsis in the case of open wounds was due to organisms derived from outside was rarely held; I doubt whether it was held



by any; it was certainly held by very few, and it was not put into practice in any way. And the work of those who demonstrated that sepsis was in all cases due to organisms, and where access was possible, it was almost always due to organisms coming from outside the animal attacked, gave rise to the antiseptic treatment, the value of which it is quite unnecessary to dwell upon. It was purely the result of experimental research, and it is a triumph the practical value of which puts it at the head of all the changes in the last 40 years. But I am not going to deal with that any further than just to refer to it, because I am sure that its value and its origin are present to the mind of everyone here.

I wish chiefly to deal with the case of microbic diseases, which, for reasons that will appear, I shall divide into infectious diseases and diseases communicable otherwise than by what is ordinarily called infection. If you go back 40 years you will find that these diseases were complete mysteries; they were, alas! recognised as facts, because they could not be otherwise; they were ever present with us. They were known as things which ran through a certain course, their symptoms were studied, and the doctors of that time did their best to alleviate them, no doubt, by nursing and treatment. A great number, no doubt, tried to do so also by drugs, which, I think, most authorities to-day would say were practically of little use. But the diseases themselves were, so far as their causation is concerned, perfect mysteries. Now experiment has changed that from top to bottom. The bulk of these diseases are known now to be the result of an invasion of the system by specific organisms which multiply in the system, and the disease is due to the presence and action of these foreign organisms. In fact, I do not think that I should be giving an



incorrect idea of the result of the work of these 40 years, if I was to say that it has revealed the fact that we live not as isolated living organisms, but that we are surrounded by and penetrated by infinitely small living things of very varied descriptions—that we are, as it were, bathed within and without in a sea of microbic life; I am using the word microbic in its broadest sense. Within us we have them permanently and probably normally; in fact, if you include the organisms which live in the blood, certainly normally. We are surrounded by them, and instead of diseases of this kind having to be looked at as due to defects or failure in normal action in the organism itself, we have grown to realise that they are the result of attacks upon the organism by external foes.

12729. Do you regard all this state of things which you have been describing as wholly due to experiments on animals?—Absolutely. It is absolutely due to them.

12730. We have had a good deal of evidence from other witnesses on the subject, and we need not trouble you to describe the instances.—Quite so. It is difficult for me to say which is the earliest case in which this was established; but I will take one of them, because I wish to show how baseless is the idea that the work which has been done in this respect is work which has only led to doubtful or hypothetical results. I wish to show the actual and certain advance of knowledge. Then I wish to show next the way in which that is due to experimental methods. Then I wish to show the practical methods to which it has led. I will take a single example—any one will do—but I will take the example of anthrax. When Pasteur took up anthrax, it was only known as a terrible disease among cattle, leading to a vast proportion of deaths. He ascertained



that it was due to an invasion of a particular microbe, which is known as the microbe of anthrax, which multiplied with infinite rapidity, and which ultimately led to the death of the animal. He then found out a method of inoculation (I am not going to deal with the details of his method for a moment) against it, and in the classical experiment to which I have referred he exposed to anthrax the 25 sheep which were inoculated and the 25 which were not inoculated. He might have done it by putting them in company with diseased animals. As a matter of fact, he took the severer test of deliberately inoculating them with the disease. The result was that those which were treated with his process did not die, and the others did. Now, that is a scientific result as certain as the action of nitric acid would be on iron; I mean that it was a definite experiment, capable of being repeated, and showing conclusively that there was a way of defeating this disease, a way which might, or might not, be availed of by mankind, according as the importance of warding off the disease was great or was not. There was nothing hypothetical in it; it was a fact which was just as much demonstrated as any fact that has been demonstrated in chemistry or in any other science. I have there taken a case which relates solely to animals. I have not approached the question of the applicability of the process to mankind, because, fortunately, anthrax is very rare among mankind. But if you confine yourself to the consideration of it as a disease of animals, you see the advance that has been made. First of all, there is the knowledge of the cause—that is to say, that it is due to the presence of microbes. Then (as I shall presently point out) the fact that it was due to the presence of microbes led to the discovery of the method of combating it; and that led to the



practical application of that method, and, if you choose to avail yourself of that method, the disease is conquered. The whole is based upon the discovery of the origin of the disease. It was the knowledge that it was due to microbes which led to the whole of that discovery. Persons might say: "What good does it do to mankind to know that this which they call a disease is really a consequence of a particular type of small life which has got into the organism and multiplies there? It does not alter the nature of the disease; people die of it all the same." And you would think that the pure theoretical knowledge, that it was due to this particular cause, left the practical problem where it was. May I point out how that piece of knowledge did not leave the problem where it was, but put it in a totally different position, and necessarily led to its solution? You can see it in this way. It instantly put the phenomenon of recovery in a new position. When an animal was healthy, and there were only a few microbes put in it, when you would say it was best calculated to repel invasion, they multiplied furiously. At the moment when it was weakest, when the microbes were strongest, most numerous, and the animal was most exhausted (if it was a case of recovery), the tide turned, and the enfeebled organism was able to fight the strengthened assailants successfully. That necessarily led to the conclusion that there must have been a change in the organism during that period, which entirely altered the relative strength of the two forces; and that was the beginning of the realisation that in these diseases there comes some protective change in the organism that is attacked, which brings recovery at the time when you would least expect it. This led to the enquiry: What is that change? It must be something that survives the disease, because we



know that when a man is recovering from an infectious disease he can give it to other people. Yet although he is more exposed to infection from himself than any other person could possibly be, he is not infected. Therefore it must be something that survives the disease. Then the question came: If it survives the disease, is it possible to produce it under circumstances so that it may be present in the organism independently of the disease? In fact, men came to realise that recovery in a case of microbic disease means the "turn of the tide" in a process where, on the one hand, the invading microbes are multiplying, and on the other hand these protective forces are multiplying, and recovery or death means whether the turn of the tide comes too late or not. The moment you see that that is so, the whole question becomes—Can you antedate this turn of the tide? Can you contrive that this protective condition shall be produced earlier, before the mischief is done? It is no use putting a fire out when all that is valuable in the house is burnt. From these ideas there sprang almost immediately the two main methods of treatment. The one seeks to produce this protective state during the period of the disease, and it is a treatment of this type which succeeded in rabies; the other seeks to produce the protective state before the disease comes, and is the method that was illustrated in anthrax. Finally, they led to the third line of discovery. Is it possible to get the protective substance from somewhere else, and introduce it during the disease, in order to antedate the time when the system will become strong enough to repel the attacks of these foreign invaders? Now, if you think of all those three lines of discovery, which have respectively led up to the treatment of rabies, to the prophylactic methods which are used in the case of anthrax, pneu-



monia, and other diseases, and to the serum treatment of diphtheria, you will find that they all came from the knowledge that the cause of the disease was a foreign organism, capable of multiplication, and that Nature defeated it by a change in the organism which made it more capable of resisting. These practical applications were the direct outcome of those two facts, which were pure pieces of scientific knowledge. So long as the disease was considered merely as a disease which ran its course, which was due to an unknown cause, whose consequences were only known by its symptoms, no one of those things could possibly be discovered. Their discovery was solely due to the experimental examination of natural processes. I was much amused by some evidence given by one of the lady witnesses who have given evidence before you. She seemed to be very much disgusted with the consequences of all this knowledge, and, if I might paraphrase what she said, it was: "Nature has made such nice drugs and put them in the plants all around us. Why should we not use these, and not go to such messy things as serum?" Those are not her words, but they express the effect of them. Nature has put all kinds of useful drugs in plants, but she never dreams of using them for curative purposes. Her method of curing is entirely by means of the messy things with which the researches of the last 40 years have led us to work. We are now, thanks to the theoretical knowledge that we have acquired of the cause of these diseases, working to help Nature along the very lines which she has from the foundation of the world herself taken in fighting these diseases; and therefore, in my opinion, if we are to be guided in our action by our respect for what Nature has so kindly done for us, our course would be to pay very little attention to drugs,



and to pay very much attention to those lines of treatment which are based on the study of the two closely analogous phenomena of recovery and immunity.

12731. Assisting our natural friends in fighting our natural enemies inside us?—Yes, fighting our natural enemies by those means which, in the cases in which we do beat them, are the weapons which we use.

12732. (*Chairman.*) I think you were going to deal with the question of the influence of experiment on communicable disease?—I have been pointing out that the whole modern conception of the nature of these diseases, and the mode of their cure, arise from discoveries which have been arrived at purely by experimental methods, including necessarily experiments on living animals, namely, the discovery that they were due to foreign organisms that entered and multiplied in the system, and the discovery that the changes in the system which unquestionably produce recovery are closely allied to those which also produce immunity after recovery. So far I have only spoken of our attempts to effect a cure by introducing those protective substances which Nature, when there is need, produces in some strange manner. But it looks at this present moment as if we were going to combat some microbic diseases still more successfully by stimulating other agencies by which she effects her cure. I do not know whether Sir Almroth Wright is to give evidence before this Commission, but if so he will point out how he has devised a method of stimulating the action whereby the white blood corpuscles actually destroy physically the organisms themselves, so that we are gradually utilising both of Nature's methods of cure (and utilising them exactly as Nature does) for the purpose of antedating what I have called the turn



of the tide, that is, strengthening the resistance of the organism that is attacked more than Nature would do merely by her methods of reaction. I now want to pass from these to another class of diseases in which equally we have been studying during the last forty years the cause of the disease and its action on the organism, but where research has led to a totally different method of fighting them—I refer to the communicable diseases which cannot be called infectious. Take the case of malaria, the tsetse in animals, and Malta fever.

12733. And rabies?—Rabies belongs to the first set, because we fight it by generating in the body a protective substance. The way in which we fight it is, we have got a method of giving an attack of rabies which is very quick but very slight, and the consequence is that it produces very swiftly a small amount of protective substances. We then give another one which is also quick, but is stronger, but which can be borne by reason of the presence of the protective substance, and continue doing so while the main body of the attack is moving up. We have thus gradually accumulated a body of protective material, which, when the main attack comes, which would have been inevitably fatal, enables the system to resist it.

12734. I merely thought that the gnat was serving the same purpose and function that the mad dog was; therefore I thought it was really in the same class of disease?—May I apologise? You are quite right. It is not infectious, but is communicable in a different way, and ought to be in the second class. The reason I already mentioned it with the first class was, because we there use the method of cure of which I have spoken—that is to say, we attempt to produce a



protective substance. It was I that was wrong. I want now to pass to cases where we cannot imitate the method of cure, but because we know the cause of the disease and its method of communication we are able to intercept it. Take the case of malaria. I do not know that our methods of curing malaria have advanced substantially, but we now know the cause of malaria, and we are destroying the possibility of communication. The work that has been done at Ismailia is an example of this. They have got rid almost entirely of the mosquito, which communicates the disease by its bite, and have thus almost got rid of the disease.

12735. Would you say that that was discovered by experiments on animals?—Certainly. They had first to discover in what way this disease was communicated. As soon as they had discovered in what way it was communicated, the destruction of the communicating animal presented itself at once as a method of preventing the disease. A similar case is that of the tsetse, which is absolutely fatal to cows in districts where the tsetse fly is found. They find that it inoculates an organism which produces death. I do not think they have made any advances in fighting the disease when the disease is once communicated; but knowing that it is communicated in that way, our attention is at once turned to discovering how one can fight the tsetse fly, or how one can prevent the tsetse fly itself getting the organism into it which it passes into the animal that it bites. In certain places in England, where there used to be ague, ague is now stopped. It is quite possible that that ague was communicated by the bite of an insect that derived the organism which is the cause of ague from biting some affected animal. We



have drained the country; the insect probably exists, but in far smaller numbers, and there are fewer people there, if any, who are affected with ague from whom it can get the infection. The consequence is that the insect is harmless, because it cannot communicate the poison, or rather the poisoning organism, because it cannot get it. And, similarly, we can, when we know the cause of the disease, set to work to prevent the occurrence of those circumstances which enable it to be communicated. This is now being done with yellow fever and many other diseases. It may be that the disease is so bad that the only method we have of fighting its spread is to kill the animal. Take the case of glanders. Now that we thoroughly understand what glanders are, when we thoroughly understand the method of testing whether an animal is suffering from glanders, the animal may be killed at once and that stops the propagation of the disease. Without that knowledge we could not ascertain so soon what animals we ought to kill, and they would be left as centres of contagion. So that it may be equally effective from the point of practical utility whether we find out the means of communication and stop it, or whether we attack the disease when it is communicated. In both cases it is the knowledge of the cause of the disease, and the knowledge of the way that that cause comes to operate on the organism, which enable us to devise these practical methods. And all that knowledge has been derived entirely from research work, conducted for the purpose of acquiring knowledge, and from the knowledge has come the power. I do not suppose the investigation of the cause of these diseases was carried on upon the lines of any direct idea of a protective method, but the object was to find out the real nature and operation of that against which protection was



necessary. When this is done, the step to practical utility always comes sooner or later.

I have been dealing thus far with the causes of disease. I will now turn to another matter which I see has formed the subject of a great deal of evidence, and that is the study of the organism on which these diseases operate. A vast amount of experimental work of the last 40 years has been directed to discover the physiological actions which are going on in man. Mere anatomy, mere structure, will not tell you physiological action; the knowledge of physiological actions must be obtained by experiment from a living creature, because, as a rule, as soon as death comes they cease. The importance of this work is just as great as is the importance of the investigation of the causes of disease. Take, as an example, that which I see has been the subject of evidence before this Commission—the localisation of function in the brain—the discovery from the symptoms of paralysis, or epilepsy, of the place where the interference with the nervous system is taking place. It would be quite impossible to ascertain the laws which govern this excepting by experiments on a working animal—that is to say, a living animal. In many cases it need not be a sentient animal; the experiments may be done when consciousness has ceased; but it is absolutely impossible to ascertain them unless you make experiments on an animal that is still living. But there are similarly important experiments which go to blood pressure, to digestion, to the function of the great organs, such as the liver, or the pancreas, or the kidney, or the suprarenal capsules, in which it may be necessary to trace out consequences which do not occur immediately. In that case you must perform them on animals which are not only living at the time of the experiment but which are allowed to live afterwards. The examples



which have been given you, I submit, show how all-important such investigations are for several reasons. One of the reasons is that without the knowledge so acquired you cannot read causes from symptoms. I should define the great change between curative science, as it exists now, and curative science as it used to exist many years ago, as being that now we try to fight causes, and then they only tried, or mainly tried, to fight symptoms. Fighting symptoms may be an extremely dangerous thing. A man who, not knowing anything about an engine and finding an over-driven boiler blow off, should fight the symptoms by screwing down the safety valve, would come to serious trouble. And in the same way, if in the case of a symptom—say the symptom of the rise of temperature going up—you say, “The disease makes the temperature go up; very well, then, we will help the organism by putting it down,” you may get into serious trouble supposing it should turn out that the rise of temperature, by lessening the resistance to the circulation, eases the heart and makes its work less onerous; it may be that the fast-beating heart has been able to do its work without injury only because the temperature has risen and its work is lighter. If, now, you put the temperature down without removing the cause of fast-beating, it may be that you overstrain the heart—do mischief just as the man who screws down the safety valve. I am not saying that this is so. That is not a matter on which I can speak. All I want to point out is that it is only by intimate knowledge of the organism that we know how far it is safe to fight symptoms. But, more than that, it is only by such intimate knowledge that we are able to diagnose causes. You get a headache; it is a mere symptom which may come from many different causes. Unless we have perfect knowledge of the organism we may imagine that



a thing which has been successful for one headache is useful for another, whereas it may positively aggravate it instead of doing it good. The aim of all this investigation into physiological action, which is so varied in its character, and relates to every different part of the organism, is to put the medical man of to-day in the position of a man who knows the construction and operation of the engine he is working, who knows what is the meaning of every symptom of irregular action; and the increase of his power of alleviating suffering and staving off death is enormously increased by this increase of his knowledge and power of diagnosing, which has arisen from these experimental researches. As I have said, these experiments must be experiments carried on upon living animals, because their object is to ascertain what is the mode of working of each particular organ, and what is the effect of any particular interference with that organ. Sometimes these experiments have resulted in curative methods. You could not have a better example than that which was put before the Commission, namely, the relation of the thyroid gland to myxœdema and cretinism, where, I think, to the surprise of everybody, it was discovered that we have glands within us which are producing protective substances for the normal life, just as Nature will, when there is an attack of a microbic disease, produce *pro hac vice* a protective substance against the foreign invader. When you take away the thyroid gland, and there is not this protective substance, which is no longer formed, then you find the body gets out of order because that is no longer present which was necessary in order to keep down the inherent forces of dissolution. Then it was discovered that, if you supplied artificially that which this gland produced, you could keep down this form of disease just in the same way as you can stop the effects of



diphtheria, if you put in from another animal that which Nature would produce in order to repel the microbic attack. Just as in diphtheria you get recovery, so you find in myxœdema that when you supply this substance which the body has ceased to have the power of producing, you get this remarkable recovery. And this appears to be only the commencement of a series of analogous successes. But, apart from the question of direct curative methods so arrived at, the power of diminishing suffering that is given through increased knowledge of the organism is so great that it is difficult to over-estimate it. I do not think it is necessary to give further instances to this Commission. I only want to put those forward to show that there is abundant justification for saying that knowledge which, from its very nature, must be obtained by experiment has already been of the very widest benefit to mankind. I will go on to the question whether experiment is permissible for the purpose of acquiring such knowledge. Here I must go back for one moment to the example which I gave, as a typical one, of preventing plague getting into a town by killing all the animals which could convey it. In my view, we are just as much bound to prevent suffering due to ignorance, and just as much justified in inflicting such pain as is necessary for the purpose of doing so, as we should be in killing noxious animals. I have pointed out that this necessary knowledge has in the past been and must be obtained by experiment. It must be done by experiment, it can only be done by experiment on men or by experiment on animals. I unhesitatingly say that our right to experiment on men is extremely limited. In the first place, we have no right, voluntarily, to allow death to occur, even though the man would be willing to permit it. Nor do I think we have any right, voluntarily, to allow serious damage



to occur, unless it perhaps may be where it is directly for the purpose of saving life. So I do not think, in view of mankind's power of anticipation, of memory, and the possibility of future suffering, we ought to take the responsibility of allowing experiments which might produce serious consequences to be made on man. Let me give an example. I do not think that we should have the right for experimental purposes to allow a man to infect himself under special circumstances, even though they would assist science, with a disease like syphilis, in order to add to knowledge. It is too serious a responsibility to take to allow that to be done, considering that that man will live for years afterwards, and cannot divest himself from social relations.

12736. Supposing he was sacrificing himself in that way, and by his sacrifice he could make probable the saving of a great many lives in future, why should you prevent him on the principle that you have to look forward to ultimate results of torture or sacrifice?— Well, it should be the last resource. But I will tell you what, in my opinion, I think constitutes the real difference. I do not think that you ought to lessen in any way the feeling of sanctity of human life, because the consequences are so very widespread. To let a man, in a moment of enthusiasm, do a thing which might, or perhaps must, have permanent evil effects throughout all his life, approaches in my mind very close to an infringement of the great principles which make us refuse to consider whether it would be a benefit that one man's life should be taken. Everyone of us knows men whom it would be a blessing to mankind to remove, whose lives are a curse to those around them, but, however much we feel that this is the case, we do not allow ourselves to act upon it, because if we



were once to commence to act in that way towards men, the consequences that would follow would be so far-reaching that we have found it best to lay it down as a rule that it has been, except in special cases prescribed by law, not permissible under any circumstances for an individual to take human life or to permit a man to die if he can prevent it; and you will find that doctors will not only work as hard for a bad man as they would for a good man, but they will actually bring a man back from the doors of death, although they know that he is going to be hanged for what he has done; because we find it is absolutely necessary to take as an unchallengeable principle that human life is sacred. Therefore I think that, although in small matters you may use experiment on man, and for the very last stage of experiment you probably must do so, you ought to stop there.

12737. (*Sir Mackenzie Chalmers.*) You mean with the consent of the man himself?—Yes, even with the consent of the man himself. Where you have established a well-founded scientific probability that the thing is safe, then I think you are justified, but before you attempt to experiment on man, you must have done everything to prepare for it, and you must know with fair scientific certainty what will happen. And that is the reason why I do not think that experiments on man are to be considered at all when you are thinking of the enormous amount of work that has to be done in scientific research. The necessary work must be done otherwise. Now, I turn to the question of whether we should use animals for the purpose of research. In my opinion, unquestionably, it is not only permitted to us, but it is our duty to try to remove ignorance by, if necessary, experiments on



animals ; and I want to give the Commission the principal reasons which make me have such a confident opinion on this point. The first reason is the overwhelming preponderance of the prevention of suffering by this method. The great bulk of the necessary experiments, as you know, can be made without any pain to the animals at all, because the animal never need be conscious, and therefore no pain is caused at all. But taking the others, the amount of experiment, if properly done, which causes pain is incredibly small compared with the results of the knowledge obtained, even if they be measured by what has already been achieved. Just look at the complete change that there is in our knowledge of all those great groups of diseases which I have called infectious or communicable. We are no longer fighting them blindly ; we are no longer striking in the dark ; we know what they are. This very knowledge enables us to avail ourselves of experiments which are not painful for the purpose of assisting us in the task, and every man who feels his responsibility does all he can without occasioning pain. But what is done, is done with a knowledge of the enemy we are fighting, so that the experiments grow more telling. The number of painful experiments, as is shown by looking at the actual experiments which have been made, is quite infinitesimal. I read the description of the experiments done under license in England, where excellent research work is done, and most carefully done too ; I read through the list of those which were thus done in a year, and I very much doubt whether the total amount of suffering caused by those experiments would be much greater than would be caused in a single fairly large shooting party, where there were one or two bad shots. If you consider the amount of suffering that is caused in the world, not



only thoughtlessly, but even deliberately done by people who are ordinary normal men, and may be able to show a reasonable defence for what they do, it dwarfs so utterly the amount that is requisite to produce this useful knowledge, that if the matter was not so serious it would be almost ludicrous to think that there was this organised opposition to the pain caused in scientific research in proper hands. Why, what is attacked here is the only bit of fruitful pain in the world. The greater part of pain had better not be. A man suffers and dies, or suffers and gets well, and all the pain he has suffered has benefited nobody. And in the case of animals there is all this vast mass of pain which is inflicted or permitted, and people tolerate it and say nothing about it, and look upon it as an ordinary thing; but there is one little bit which brings return in lessening the sufferings of the world, and the people are to be found to organise themselves against it, and throw the whole of their strength into denouncing and preventing it. In my opinion, if you look at the medical science of to-day and the medical science of 40 years ago, and realise that the advance has been caused by physiological research, which is largely carried on under the very Acts which restrict, which regulate, but which distinctly permit painful experiments, and then consider on the one hand how much pain that has caused and how completely it has changed our power of dealing with disease and of alleviating suffering, it is really incomprehensible that anybody who sees the totality of misery in the world should think that the small amount of pain that has produced that gigantic result is the first that ought to be stopped. That brings me to the next point, and that is this. Mankind not only claims, but perpetually exercises and properly exercises the right to cause or



permit suffering in animals when needful or desirable. It requires considerable thought to realise the extent to which that is admitted by all, and is, indeed, unchallengeable. Take the case which I gave of the rats on board the ship. I pointed out that it was right to kill those rats in order to prevent the possibility of their spreading the plague, but no such serious reason is necessary to justify killing them. I do not suppose there is anyone who would challenge the right of the captain to do it if they would injure the cargo, if they would produce a small pecuniary loss; under these circumstances it would be considered that it was perfectly right for him to do it. We unhesitatingly kill vermin—we kill things that do pecuniary harm, and no one dreams that it is a thing which a man of high principle will not do. So that nobody ever dreams of questioning the right of causing pain for the purpose of a useful result, when that useful result is merely pecuniary. But when instead of the result being pecuniary, it means diminishing the suffering of the world for all time and for all the world, forsooth, it is challenged. Take the case, for instance, of a herd of cattle attacked by some painful disease, from which, we will say, 50 per cent. of those attacked survive. A man would be considered perfectly justified in allowing them all to go through the disease. The 50 per cent. that would die would die, the rest would have the pain of the disease and get better; and he would say, "Well, but I could not afford to sacrifice the 50 per cent. that would survive—it would be too big a loss to me." For the £10 apiece that they were worth he would have permitted them to be killed on the spot; but he considers that he has a just and perfect right to allow them to suffer all that pain in order to save



himself from the loss of the 50 per cent. that survive. And I do not say he is wrong, because the comfort of his family and other things of importance to him may depend upon the question of how great is the loss inflicted on him pecuniarily by this attack. But if it is allowable to permit the whole of that suffering in order to avoid a pecuniary loss, the question as to whether it is right to increase by a little the suffering by well-designed scientific experiment to secure a return, not in money, but in the power of stopping suffering, seems to me literally to permit of only one answer. No man could consider the matter without realising that such infliction of pain was justified, if he would do what I hold he ought to do: add inflicted and preventible pain together. The moment you take as your guiding principle that you are responsible for pain which you could prevent, and that this and the pain which you inflict must be taken together in order to guide your action, it appears to me that there is no painful treatment of animals which is nearly so completely justified as that which leads to knowledge. Nobody, so far as I know, would hesitate to overdrive a horse in order to save a life or to bring assistance to a life that was in danger, and yet that would be suffering inflicted for the purpose of benefit to a single individual. The people that are engaged in scientific research are working for something which will benefit not one single individual, but will benefit the race for all time.

I feel myself that the justification for the necessary use of even painful experiments, where they are required for the purpose of obtaining knowledge, can only be questioned by shutting the eyes to the further consequences of our action—putting a veil between our action and what it ultimately leads to. And



I cannot help thinking that the people who lead the movement on the other side must be aware of this, because they deal so persistently in misrepresentation. It is very easy to misrepresent the work of those who are a long distance in advance from the ordinary man. I have known this illustrated again and again in manufacture. Processes have been stigmatised as adulteration, as falsification, and everything that was bad, whereas if people had followed out the advance of science they would have known that they were simply better methods for doing the same thing as earlier processes, and doing it with greater certainty and with greater cheapness. But they had not followed it out, and, because the new processes were different, a contrast to the old ways, and people thought that therefore they were something to be stigmatised, so it is here. If we could get people to learn what science is and what it has done, they would never attack those who are at work on it. And it is to keep them from learning, that there is this frightful misrepresentation. I remember, and I think the Chairman of the Commission probably remembers, how in the seventies the walls of London were placarded with a poster representing a rabbit in the process of being roasted alive.

12738. (*Chairman.*) I do not remember it, but we have been reminded of it; we have heard about the roasted rabbit.—I remember it well, because I wrote about it to the late Sir Michael Foster, and I asked him, What is the lethal temperature? because I recognised at once that the experiment which was thus misrepresented must have been one to find out when temperature alone would suffice to occasion death.

12739. You may take it for granted that we know all about it; we have had it explained by Sir Lauder



Brunton.—Very well. It turned out that the temperature was something like 109 or 111 degrees.

12740. (*Sir Mackenzie Chalmers.*) 114 to be exact.—It differs very much, of course, in different animals.

12741. (*Chairman.*) That was the outside temperature, not the blood temperature.—I was giving the temperature of the blood. Anyone would realise, of course, that the object was to do it under such circumstances that no reaction should be set up—that there was simply an increase of temperature, and that therefore there must be no disturbance of the organism, and that the poster was absolutely false. Yet that placard was all over London. It is not surprising that a great number of people join this organisation, because they get their ideas from these very serious misrepresentations. They believe themselves to be humane, but when one realises the evil that ignorance does, and that the only way in which ignorance can be removed is by the experimental method, and the enormous advantages in the way of saving pain that these results have produced, one must feel that the truly humane men are the people who are defending scientific research.

Now I should like to turn to the practical conclusions to which I have come with regard to this subject. You see that the good basis of all these movements is the desire of saving pain in animals and men. Now if that is so, the whole motive ceases with the conscious life of the animal. As soon as it has finally passed out of the conscious life the whole *ratio agendi* ceases. It is as absurd to object to an experiment on an animal that has ceased to be conscious and will never again be conscious as it would be to object to the dissection of a dead animal. The only motive is the desire to save suffering, and suffering then is as impossible as if death had



actually occurred. Now what is the consequence of that? Hence there ought to be no interference with experiments on animals which are in anæsthesia, except that they should be permitted only to persons who can and will take care that the anæsthesia is complete, and that the animal is killed before it comes out. There is no other principle on which any interference could justifiably take place. There must be somebody in charge of or superintending the experiment who, from his character and position, can be trusted with the responsibility of seeing that there is what I may call permanent and effective anæsthesia. Therefore, with regard to such experiments, it is not only not necessary to interfere with their being used for educational purposes, but if the Commission may trust my experience they will indicate that in their opinion it is most important that they should be so used. For there is no comparison between the living effect of an experiment that you have seen and one that you have merely read of. May I give my own experience? I have many and many a time read over carefully-described processes, and have imagined that I understood them; but I knew of old what that meant, and used generally, in cases of any difficulty, to insist on what we call "having a view." I used to go down and insist on being taken, not necessarily by an educated person—I much preferred a workman—right through the whole process, and seeing it done before my eyes. I went back with a knowledge of the case, with a power of handling it, and with a power of drawing conclusions as to the processes, which were quite new-born. So it is with the man whom you are educating for this serious duty of fighting disease. If he has actually seen an experiment, it lives in his memory. But that is not the only thing—it remains in his memory as a living thing, and when he acquires



new experience or new knowledge connected with it, he will find that it will make the old experiment mean more than it did to him even at the moment when he saw it; because he sees the whole thing before his mind's eye, and not only reads a description which, after all, only states certain results. And, as there is no ground, therefore, from the side of humanity to interfere with these experiments which cause no pain, I think they should be largely used educationally. Medical education is of prime importance to the community. The greatest difficulty in the way of giving to the world the full benefit of all the accumulated knowledge of this last 40 years is that you have to educate your practical men up to the level of it. Just as in war it is of no use having medical appliances at the base if you cannot get them up to the front of the army, so it is of no use to have this accumulated knowledge unless the power of using it to prevent suffering is in the hands of those whom you train. Therefore the efficacy of our methods of tuition ought not to be looked upon as a matter of little importance—it is a matter of the very gravest importance; and I should put no restrictions upon the use of painless experiments in connection with it, excepting that the experiments must be under the supervision of someone possessing a certificate such as I have indicated, which should be a certificate granted to persons who could be trusted with regard to anæsthesia. And whether you have reports of those experiments or not I do not think is of the slightest importance, provided it is thoroughly understood that it is the duty of those possessing the certificates to see that the anæsthesia never ceases, and they are held responsible for so doing.

I turn now to the more difficult question, a question which requires more careful examination—namely, that



of experiments that are in themselves painful. There, I think, you should divide the certificates into two classes. Certain men of acknowledged capacity in research, who have shown that they are not only capable of serious research, but have already done it, should have general certificates entitling them to perform such experiments, subject only to one thing, and that is that they should report fully every experiment. They are immeasurably better able to judge what is worth doing than any body of men that you could put over them. They are the people who are working at the subject itself, and they are, as a rule, men of such high position and high character in England that there can be no ground for being afraid of trusting them with this power. But I am satisfied that, both for the satisfaction of those who desire to proceed cautiously and for the good of mankind, and also to prevent any possible abuse, they ought to report all that they have done. I do not think that a painful experiment should be allowed to pass into oblivion. It is made, in my opinion, for the benefit of the race and for the increase of knowledge; therefore I think such reports should be made, and I do not think that anybody concerned would really object to that being done.

12742. Do you mean that that report should be made by the inspector or by the operator?—By the operator.

12743. Sent into the Home Office?—Sent into the Home Office. I think he ought to do that. I would put him under no restriction as to the character of his experiments; I would not put him under any restriction as to the place in which they are done; but I would have a full report sent into the Home Office. Of course, a certificate of that kind would be given only in recognition of an acquired position and high



worth in research. You can only do harm by interfering with men of that class. There is no danger of such men developing recklessness. I have not examined anything excepting the experiments that have been done in England, and I am therefore speaking only with regard to them. I have never, in the years that I have followed the matter, found anything which from this point of view I call recklessness of suffering in any experiment made for research.

12744. Have you found levity? We have heard accusations of levity on the part of those who see experiments.—I feel very strongly that such an accusation is unfair even in the case of students. I do not find that the medical student of to-day is a man of the Bob Sawyer type. I think they work extremely hard. Those who see them in their classes can give you better information on this point, but certainly those I have come across are hard workers and are not guilty of any levity.

12745. (*Mr. Ram.*) Would you have any inspection of these experiments?—I would have no inspection of the first-class certificates.

12746. (*Chairman.*) You do not mean the first-class certificates described in the Act?—No; I mean my first class. Just let me give an example. Supposing it was a question of giving a general certificate to Sir Lauder Brunton. The idea of controlling what he should do with it would, in my opinion, be nothing but a blunder. But he would have to report all that he did; and if, by some accident, a mistake was made in any case, if a person developed levity, or even recklessness or cruelty, his reports would show it, and his certificate might be withdrawn by reason of it. He



might then be relegated to the second class, which I am going to describe.

12747. (*Sir Mackenzie Chalmers.*) How do you suggest that a man should get into the first class? You are imposing a new duty upon the Home Office.—I know it.

12748. (*Chairman.*) You begin by supposing that he is a first-class man?—Yes. I am quite prepared to say how I think the Home Office ought to decide. I think it ought to decide by the opinion of the leaders of the medical sciences, because I am satisfied that they possess, to an equal degree with any other body of men in the world, the moral qualities necessary to enable them to advise; and beyond question they possess, better than anybody else, the intellectual qualities and the qualities of knowledge which would enable them to do so efficiently; and a certificate of this kind should only be given where there was a consensus among the advisory body that the person held such a position in medical science that he might have this general certificate. I now pass to those who have not attained to that position—which, as I have said, would be an exceptional position, although I am happy to say that there are many men in England who would merit it. I think that in the case of younger men, or men who had not yet attained to the commanding position of those to whom I would give this general certificate, the lines of the present Act are the right lines. I think it is reasonable to expect them to accept specific limitation of the type of experiment, of the scope of the research, and of the place where the experiment is to be performed, in order that there might be the security of the supervision of those who are over the laboratory, if there be any such persons,



and also the security of inspection. Limitation of this kind, which the people would be bound to respect, and I believe would respect, should prevent all danger of abuse, which, though I think it would rarely become a reality, is more possible to occur than it would be in the case of the exceptional men to whom I have before referred. I see no reason why those restrictions should not be put on; and, as before, full and complete reports should always be made, so that a record of all these experiments and their results should be preserved. The line, then, that I should advise, would be as follows:—Certificates with regard to non-painful experiments—that is to say, experiments where the animal was kept under anæsthetics and not allowed to survive—should be quite general, but should only be issued to persons who would perform or supervise those experiments, and could be trusted to see that the anæsthesia was complete and permanent. For painful experiments there should be a small but select class who should have general certificates. The other class should have special certificates, specifying the nature of the research, the nature of the experiment, and the place where it was to be done; and there should be full and adequate inspection of those places while the experiments were going on.

12749. Strangers you would not have present, I understand?—I would not have strangers present, first of all, because, in my opinion, it would not assist the experiment, and, secondly, I do not think it would be a good thing for unqualified persons to see these things. They are the serious work of research, and persons who are not trained by medical or physiological study would gain no good from witnessing them. But I would encourage students being associated with this research. It is the



finest training that they can have. So far as it can be done without interfering with research work, it is a mistake to keep people out who are capable of learning from it; but that the public should be admitted would, I think, be a still greater mistake. In my opinion, they have no business there, and it is much better to exclude them wholly.

12750. (*Sir Mackenzie Chalmers.*) You mean that the public would go there in the same spirit that the public used to go to an execution?—Exactly. Now I hope that I shall be forgiven if I say one or two words about the two restrictions which have been recently suggested to the Home Office.

12751. (*Chairman.*) Yes, we should like to hear your suggestion about that.—I thoroughly disapprove of them. The first relates to foreign savants who are not naturalised Englishmen. There is no possible reason why they should be put at a disadvantage as compared with British subjects. Of course, for the first class of certificates under the system recommended, they must have a recommendation from English people of the proper position, to show that they deserved the privilege; but I am not talking about that for the moment. I am talking about the existing system. Foreign universities and foreign men of science have been extremely good to our students. They permit them to take part in their courses; they permit them to use their laboratories, and without good reason I would not show any want of reciprocal kindness towards foreigners. No reason is put forward for thus placing them at a disadvantage, if they possess the qualifications which would justify the certificate being granted to an Englishman, excepting that it is suggested that you cannot enforce



the performance of the conditions. That is quite a mistake. The only difficulty in the way of enforcing the performance of the conditions is that they are capable of changing their residence; but an Englishman who wants to break the conditions is equally capable of changing his residence. The true remedy in both those cases is to have a responsible head of the laboratory, who has to see that the conditions are duly performed, step by step as the work goes on, and, in my opinion, there would be no greater difficulty in assuring this being done in the case of a foreigner than there would be in the case of an Englishman.

12752. That would be so in the case of a foreign doctor working in an English laboratory; but supposing that he wanted a laboratory of his own, and hired a laboratory of his own, and started it for the work for a year in England, would you have a supervisor over him then?—I think that you might quite fairly require that there should be some person, resident in England, responsible for the observance of the conditions—that there should be somebody, such as the head of the laboratory, to whom Government can look to see that the conditions are performed, not in a lump, but *pari passu* with the work done. You are justified in recognising a difference in the case of foreigners to that extent, but no further.

12753. Do you not think that if he took a laboratory by the year, we will say, the country has got just as much hold upon him as upon any Englishman who took it?—Yes. There are a great many foreigners in England who should be trusted to the same extent as an English person who is well known in England. But



if there is any question about it, you must have somebody in England responsible.

12754. (*Sir Mackenzie Chalmers.*) The difficulty is that they may be well known to scientific men in England, but not known to the public?—Yes; but I think the action of the Home Office should be regulated by the knowledge of scientific men. These public reputations are apt to be misleading in both directions. You will find, if you take the public estimate of men, that the best lecturer is considered to be the greatest man in research. My experience is by no means so. There are men with a magnificent power of exposition, who are thereby so well known to the public that they are supposed to be the leaders of science, whereas in truth they are merely bearers of good news from the front, and are in no sense the leading workers. May I pass to the second restriction recently suggested to the Home Office?

12755. (*Chairman.*) If you please.—The second is that a medical diploma should be required. In my opinion, specialisation has gone so far that the distinction between people who actually work practically at the curative sciences, and those who devote their lives to research in those sciences, is becoming marked. A man who is actively employed in practice, as a first-rate man ought to be has not usually the time for consecutive research; he has to get his time in fragments just when he can. On the other hand there are many men who are so devoted to research that they give up medical practice as a method of earning their livelihood, and devote themselves entirely to research. The wide diffusion of wealth in this country facilitates this. England has always been noted in science for the numbers of its first-class amateurs. Cavendish was



an amateur, and I could mention many other great names of men who have had the wherewithal to devote themselves to research, and have made it their life's work without seeking any remuneration for their labour. What should guide the Home Office entirely is, whether or not the applicants for certificates or licenses are suitable for research. Whether or not they have taken out a medical diploma which gives them the nominal right to practise, when they have no intention to do so, but mean to devote their whole time to research, is a matter which should be quite immaterial. I am quite satisfied that there are now, and there will be yet more such in the future, men in the very first rank of research work, who do nothing in the way of the practice of medicine, and deliberately abstain from it, because it would interfere with their scientific research by taking their time and their attention. Those people ought to be encouraged rather than discouraged. Therefore this proposed restriction would, in my opinion, be a retrograde step. So that I should strongly advise that neither of those two things should be adopted as a principle.

12756. Have you studied the Act with a view to suggesting amendments?—You see, I agree with a great deal of it, excepting that I think there are a certain class of men who should have these unrestricted powers of experiment, and that the practice of the Home Office with regard to non-painful experiments should not have regard to the nature of the experiment, but simply to the reliability of the person on whom is placed the responsibility of the anæsthesia. With these modifications I do not quarrel with the Act, because I do not think that the real worker, if he is not really hampered in his research, chafes against these restric-



tions, which are, after all, only a recognition of what I might call the fundamental principle of his action. He is working that pain may be lessened. He is a person whom I have always found extremely sensitive to the cry of suffering, and he has no wish to protest against this Act, which does homage to that principle, provided that it does not hamper him. I have not specially considered the provisions of the Act, because I thought it had been dealt with so much by people who knew its working, and are so much more qualified to deal with it than I am ; but I doubt whether my conclusions clash very much with the Act as it at present stands.

12757. (*Sir William Church.*) I should like to ask one question with regard to those to whom you would grant these first-class certificates. Of course, you consider that any person who is placed in the position of head of a laboratory connected with a University or a public institution approaching in importance to a University would necessarily be a person of sufficiently good repute ?—May I put it another way ? I should hope that a University would never choose a man for the position who did not deserve it.

12758. Then, besides persons in charge of laboratories, you would grant these what you call first-class certificates to such men of repute ; and in their case I understood you to say they should not be necessarily restricted to working in licensed laboratories ?—No ; I should leave them perfectly free, subject to report.

12759. So that they might work either in their own rooms or wherever was most convenient for their work to be done ?—Yes, certainly.

12760. Then, with regard to all others who hold



licenses, I presume that you look forward to their all working in licensed laboratories?—Certainly. Of course, I should trust that the best of those who commenced with a license would pass in time to the higher degree; but, as long as they only had a license, they would work in proper laboratories subject to inspection.

12761. So that, even as you propose, it would not be possible for a research student, whether holding a medical diploma or not, to perform experiments on living animals even in a licensed laboratory, excepting if he held a license himself?—No; not painful experiments. He could not perform painful experiments.

12762. And, of course, all those who held what you call first-class licenses would be enabled to perform the experiments which are now performed under Certificate B without having to get anything further than their license?—Yes, certainly.

12763. (*Sir Mackenzie Chalmers.*) I should like to take first the two points that you have raised about the Home Office practice. I suppose you agree that, apart from the wording of the Act, the Home Secretary is bound to have regard to public opinion to some extent—that there is a real danger of the powers being lost if suddenly public excitement were got up against them?—He is bound to have regard, I should say, to the Act. I think that he has no need to regard public feeling beyond the extent to which it is expressed in the Act.

12764. You think that his sole duty is to administer the Act, without regard to whether he is imperilling the existence of the Act or not?—I think that the safest way to maintain the Act is to administer it in the way in which it is best for research. The real defence of



research will come from the good that it has done ; and I think it would be an unwise thing to administer the Act in a niggardly way, in the hope that it would lessen the possibility of a popular storm. I do not myself fear very much of the popular storm. I know perfectly well the power of a certain small number of determined people to prejudice the minds of the public, and I appreciate that it is considerable ; but the more that the public has experience of the good results of research, the safer it is in the hands of the public.

12765. Of course, as regards the foreigner himself, the man who is temporarily over here, he is to some extent free from the law. He performs certain experiments, and the results of those experiments are not published, probably, until he has returned ; and then the Home Secretary may be blamed for allowing the law to be broken by a man over whom he had not effective control. You recognise that difficulty, do you not ?—He ought to have effective control, and I think that this would be best obtained by requiring that the reports should be sent in from time to time, and that there should be some responsible person to see this is done.

12766. Would you go so far as this, that supposing a foreigner were authorised to experiment, say, at University College, you would make the head of the laboratory there surety for him ?—Yes ; I would make him see that the thing is done. And if the man is not performing his duty, it is the duty of the head of the laboratory to report to the Home Office that the experiments are being carried out without due observation of the conditions.

12767. But what practical power of enforcing it have we ? Would you withdraw the license of the head



of the laboratory if there were any contravention of the conditions by a foreigner working in his laboratory?—Not unless he connived at it. But, in my opinion, the report of an experiment should be written out as nearly as possible at the time; and if he neglects to see that this is done, it appears to me that he is responsible for the breach.

12768. Now, coming to medical diplomas, is there not this difficulty: that when once you get away from the medical diploma, you have no guarantee whatever as to a man? If he belongs to the medical profession, he has been trained up in a profession whose sole object is, as you say, to diminish pain. When once you get outside that, where are you to get your information from as to the qualifications, moral and scientific, of a person who is to have this licence?—Would you say that we had no knowledge of the qualifications of Frank Balfour, before he was killed so unfortunately, years ago? You will remember that he started a biological school at Cambridge which was full of the greatest promise? Do you think that the addition of a medical diploma would have made Frank Balfour a more reliable man?

12769. Personally I do not. But then, you must take the case of a good many persons who are not known to the public, and you must remember that public opinion is nervous on the question.—I should require the most exceptional testimony in the case of a man who had not done scientific study at a university and under proper training; but that it should have taken the form of medical study seems to me unnecessary. You must understand that the scientific degrees, though they are often taken by medical men, and ought to be taken by them are in themselves in-



dependent. They may not qualify for a diploma, but they connote an amount of knowledge which would quite warrant your recognising the bearers as fit men, if they were duly recommended by those who advise the Home Office. Of course, you will occasionally meet with a man who without any scientific study in a recognised university is a man of pre-eminent value. Michael Faraday had had, I think, no university training at all. But those cases are extraordinarily rare, and would only be dealt with when vouched for in a way which was quite unexceptionable. So that, generally, you would have the security of university recognition that the applicant was properly qualified.

12770. Do you think that the existing certifying authorities, which are mainly medical authorities, under the Act, would be able to deal with the case of the people you refer to without medical qualification?—I think so.

12771. Or ought the advising body to be enlarged?—Those who examine up at the Universities usually possess medical degrees, and a great many of them possess also science degrees. I do not know whether Sir Michael Foster had a medical degree.

12772. (*Dr. Gaskell.*) Yes, he had, and practised.—I did not know that. But you can easily imagine that there may be some who have not.

12773. (*Dr. Wilson.*) Pasteur had not; he was a chemist.—No, Pasteur had not; that is a good example.

12774. And Metchnikoff was a chemist?—Yes.

12775. (*Sir Mackenzie Chalmers.*) Then I should like to ask your opinion upon this. It has been sug-



gested to us by Mr. Coleridge, whose evidence, perhaps, you have not seen?—I have not.

12776. It has been suggested that a certificate of humaneness should be required before a license was given. What is your opinion on that? He suggested, I think, that a certificate should be given by one Justice of the Peace and one minister of religion. Perhaps you would rather not express an opinion?—It is not enough to say that it is unnecessary. It would be an absolute insult to the people whom you would be consulting. The suggestion that the heads of the medical profession are not judges of humanity, of humaneness, I ought to say, is a piece of the most intolerable insolence. It is shocking when you consider the way in which, as a rule, medical men disregard their own comfort, and put themselves to any amount of trouble and discomfort for the purpose of helping people who are sick, very often when it does not bring to them the slightest *kudos* or the slightest pecuniary return. To suggest that such people do not know what humaneness is and are not moved by suffering is intolerable.

12777. I think the suggestion rather was, from the evidence that we have had, that the present certifying authorities regard only scientific ends and qualifications and do not consider as within their province the question of humanity.—So far as Englishmen are concerned (of whom I can alone speak from personal experience) the question as to whether they are likely to use power properly from the point of view of regard for suffering is from my knowledge of the people who are likely to take out licenses practically settled before the application is made. But the certifying authorities have to advise that licenses should be



granted to the applicants, and if they think that *par exception* they are people who have not got any care for suffering, and will make a recklessly painful use of their powers, they are bound to say that they are not fit persons to receive licences.

12778. Do you think that ought to be expressed in the Act or the rules in any way?—I should say “fit and proper.”

12779. You think that would cover it?—I think that would cover it.

12780. Now, coming to the ethical side of the question; may I rightly sum up your statement in this way—I want to know if I have understood it—that all pain is an evil, perhaps the supreme evil?—Yes.

12781. And that we are justified in the present infliction of a lesser evil when there is a reasonable prospect in the future of avoiding a very much greater evil?—Yes, quite so.

12782. That would be the test and the touchstone which we should apply to all animal experiments?—Yes, that is the touchstone. And in applying that touchstone we must conscientiously use the whole of the teaching that the history of science and the history of medicine have given us. The particulars I have given were in order to show that where there is serious research there is an overwhelming probability that the answer will be in the affirmative.

12783. Of course, as you know, by other ethical witnesses, we have had other tests suggested. For instance, one of the witnesses suggested to us that the test would be the conscience of a progressive people. I must say it did not convey very much information to



my mind.—It conveys none to my mind. I feel satisfied that that is an extremely bad definition. "Conscience" is too often used where the true expression should be "emotion." Emotion may be a good motive power, but it is a bad guide, and, in my opinion, there is a very great deal of force in the phrase which somebody has used: "If you want to do good in a particular way, and want to know how you can do it effectively, give your heart a rest and your brains a chance." The only thing that can safely guide you is your reason. Your emotions may give you a motive just as I say that the motive which should dominate the whole of this question is the desire for the suppression of pain. When you have got that motive and desire to obey it, it is your reasoning power which ought to tell what you ought to do.

12784. What is pressed upon us continually is this: Admitted that pain is an evil, you have no right to inflict a definite voluntary amount of pain when the future saving of pain is absolutely problematical. What do you say to that argument?—It is simply because the people have not studied the question that they talk about its being absolutely problematical. What you have to do in life is to act on probabilities. It is quite impossible to prophesy exactly what will happen in the future, but when you see from the teaching which the past has given us that there is an overwhelming probability in favour of a thing happening you are bound to act upon that probability. Would a person refuse to take a medicine because it had not always cured people? It would be a doctor's duty to give it if there was a probability that it would do so.

12785. Then passing from what I call first principles



to the secondary principles, if I have understood your evidence, you say that at any rate we have no right to prevent experiment for the purpose of increasing knowledge and controlling pain and disease while we allow the infliction of death and pain in sport for the purpose of providing food for mankind, and for a mere commercial purpose, such as spaying sows and castrating horses?—Yes, and in infinitely more cases than those—cases in which, as I have said, you inflict pain for the purpose of preventing pecuniary loss. If you have a valuable dog you see it through the distemper. If it is not valuable you kill it to begin with. Yet you might be perfectly willing to sell that dog in any case. That is simply permitting suffering for the purpose of avoiding pecuniary loss. Otherwise, I really do not understand why people consider it right to kill beetles. Beetles will only destroy a certain amount of their food, and yet they extirpate them, just as they extirpate mice and they extirpate rats, and consider that they are justified in doing so, because they say that such animals do harm. That harm is really pecuniary harm.

12786. Perhaps the fairest way of putting some of these ethical points that have been put before us is to call your attention to a little publication I have just received from Mr. John Page Hopps, who has given evidence here. May I ask you to look at the second paragraph on page 3, beginning with the word "But"? May I divide it into paragraphs and ask you whether you have any comments to make upon it? May I read the first words that I want to ask you about: "But when all is said on the score of results and the artist in vivisection has done his best to convince us that he is the apostle of mercy, many grave considerations



'give us pause.' For instance, what law of God or Nature justifies this treatment of our poor relations? Who gave to this amazing enthusiast the right to say off-hand that he was at liberty to exploit 'the lower animals' for experiments?"—May I point out what it is that gives the whole force of that to the people he is talking to? It is the use of the word "experiments." They do not know what it means: they do not know its importance. Supposing I was to put, instead of "experiments," "saving life or stopping suffering," the whole appeal would fall to the ground. "Experiment" to an uneducated person does not connote what it does to persons who are acquainted with the nature and results of research. If you read it in that way: "Who gave to this amazing enthusiast the right to say off-hand that he was at liberty to exploit 'the lower animals' for saving human life?" the answer would be "Why not?"

12787. As regards that expression of his, "What law of God or Nature justifies this treatment of our poor relations?" what is your comment?—It is all based on this want of appreciation of the meaning and effect of scientific research. Supposing I was to put it, for instance, "What law of God or Nature justifies our killing things, or permitting them to suffer, in order to save us from pecuniary loss?" Yet we do this, and must do it, every day. A beetle is a poor relation, or a mouse is a poor relation, just in the same way as a guinea-pig is; and yet we treat our poor relations in the shape of mice and beetles with phosphorus, and let them die in pain, because we say we must keep them down.

12788. If his argument was right, as a logical conclusion we should have no right to keep a cat who



destroys mice by a cruel and lingering death?—  
 Certainly not. We should first kill all the birds of  
 prey, and then kill the birds they prey on, because they  
 prey on insects; and then we should kill the greater  
 part of those insects because they live, many of them,  
 on still smaller things. You get back to the state of  
 the Hindoo. Nobody ever dreams of doing that. It is  
 only when it is applied to scientific research, the ad-  
 vantage of which they do not know, that these qualms  
 come in.

12789. They do not believe in scientific research and  
 its results. They honestly do not believe in it?—They  
 do not believe in it; but that is entirely due to their not  
having studied and mastered the subject; otherwise  
 language such as that would not have any effect.

12790. And Nature herself nearly always provides a  
 cruel and lingering death for every wild animal?—Yes,  
 it is terrible. I think it is Seton Thompson who says:  
 "The end of every wild animal's life is a tragedy." And  
 it is perfectly true.

12791. Now may I take you to the next sentence:  
 "For laboratory purposes, his spectacles would not be  
 safe in the streets; and if he put his proposal into  
 effect, and got his babies on the dissecting table, the  
 very costermongers would raid his laboratory, and even  
 medical students might help them. Why? The  
 cutting-up of one baby might save the lives of thou-  
 sands of other babies; and the torture of one for an  
 hour might save thousands from suffering for years.  
 Why object?"—I object because you ought to get that  
 knowledge in other ways. Everybody who has studied  
 the subject realises that the knowledge can be ob-  
 tained in other ways. The analogy between living



creatures is so marvellously close that you can, without any experiments on mankind (excepting that you ultimately apply to them the methods which you have worked out scientifically), acquire all the knowledge that is necessary.

12792. It has been suggested to us that if we encourage experiments on living animals, it *per se* will tend to encourage experiments on human beings. What do you say to that argument?—It is the alternative of it. I remember a discussion in society on the subject of these experiments, and a lady at last put this question to the anti-vivisector: “Would you prefer an experiment to be tried on a cat or a baby?” And the person replied, “I would have no experiment tried at all,” not seeing that when you have not got knowledge, when you are working blindly, all you do is one long series of experiments on mankind. You are just as really trying experiments; you are not trying experiments under such circumstances that they enlighten you, and the consequence is that the result of what you do is to add very little to our knowledge.

12793. You mean that as long as you are treating disease empirically in mankind, you are experimenting?—Purely experimenting. You are either just sticking to ignorance, or, if you are trying anything new, you are experimenting on mankind.

12794. Pressing Mr. Hopps’ argument to its logical conclusion, it would come to this, I suppose: If experiments on animals lead to experiments on babies, the eating of animals for food would lead to eating human beings for food?—You are honouring his argument by attempting to follow it out. That is what it would naturally lead to. But, in the case of experi-



ments, it is because we will not try the experiments on babies that we do them on animals.

12795. Would you kindly look at the last paragraph on page 35, and the first paragraph on page 36? I think you have really dealt with that question. Mr. Page Hopps says, talking of voluntarily incurred experiments: "There is a splendid opportunity here for the suicide. Instead of a coward in retreat, let him be a hero as an offering. 'The world,' he says, 'is full of misery—sordid, diseased and despairing. I will get out of it.' He is full of pity for mankind, and is disgusted at its lot; so he decides to give it no help, but to go. What a lame and impotent conclusion! What an opportunity for heroism lost!" Does that strike you as somewhat unpractical?—I have dealt with that. It is not only impossible, but to my mind it is immoral in the highest degree, and it shows an absolutely crass ignorance of the nature of scientific research, to think that by a few suicides you could replace the experiments on animals which, in a complicated matter like this, must be numerous, but need rarely be painful, and which, if they are painful, can, in the great majority of cases, be stopped by inflicting death.

12796. I suppose another difficulty would be that you would not get any scientific man to experiment on the would-be suicide?—If he did, he would probably be saved the trouble of suicide himself.

12797. Then Mr. Page Hopps, at page 36, makes another suggestion as regards minor experiments, as he calls them: "Or might it not be possible to connect some minor forms of vivisection with crime? Here is a criminal who has earned his fourteen years of penal servitude. Let him commute it for six months in the



hands of a reliable vivisectionist, within limits. And so throughout the whole scale of penalties?"—I think that is loathsome levity; that is all I can say.

12798. Then, leaving that and coming to what you have said yourself, you thought that a man is not justified in experimenting on himself when there is any prospect of real danger?—Yes, I think so, unless he is obliged to do it—and I think he rarely is.

12799. Take a well-known instance. Haffkine invented a prophylactic serum, or injection rather, for plague, as you know?—Yes.

12800. The first person he tried it on was himself. Was he justified or not?—Certainly he was justified if he had scientifically worked it out till he had a well-grounded right to expect that it would not lead to evil consequences. At that stage a man may justifiably, and to the great benefit of the human race, experiment upon himself.

12801. Either on himself or any other person who thoroughly knows what he is doing and consents?—Yes.

12802. (*Chairman.*) It is very like Columbus taking out his ship to discover America?—Yes, except that Columbus ought to have made a few more observations before he did it.

12803. He had good reason for believing that there was land out there?—No doubt.

12804. (*Sir Mackenzie Chalmers.*) Would you justify the course of experiments of Dr. Leonard Hill and his assistant experimenting on themselves in the way of



testing how many atmospheres they could subject themselves to?—Yes. That is a most interesting instance. He had worked at the subject until he felt clear that he had got, if I might use the phrase, the rule of danger, and having worked it out he had the confidence to submit himself to it, and in that way he enormously assisted the acceptance of his methods. I think he was right. But he would have been perfectly wrong to go trying one method after another upon himself before he had worked his method out to that high degree of scientific probability.

12805. I think the only difficulty that I feel is this: where do you draw the distinction between the man who, for a scientific purpose, submits himself to a dangerous experiment, and a doctor who goes into a hospital reeking with typhus at the imminent risk of his life to carry on the ordinary work of his profession?—I said that I made an exception when it was necessary to save human life. You see, if a doctor knows that if he does not do that, many lives in that hospital will certainly be lost, I think then that he is perfectly right to say, Well, I will risk my life in order to save those lives. But in the other case, I think that he is a bad scientific man if he does not find a way of working it out, without exposing his life, up to a point when he is justified in doing so. That is my feeling. In giving this evidence, I have in my mind all the time what science is. Science is not the bungling, haphazard sort of thing that the world outside believes it to be. It is organised common sense enlightened by appeals to actual fact, which are framed for the express purpose of giving you the information which is necessary for your common sense to act upon. And when you realise this, you feel that the man who is



content to follow scientific methods is not driven to these heroic steps; he can, with the minimum of suffering to animals and without endangering human life, work out the problems which are before him. If he is impatient he would like, perhaps, to experiment upon himself or on men, but if he is patient he need not do so. And I want the scientific man to be patient in that way.

12806. There is only one other question that I want to ask you. You urge the importance of painless experiments before students?—Yes.

12807. On the old principle *Segnius irritant animos demissa per aures*?—Yes.

12808. But what we have been told is that the performance of these experiments tends to demoralise students, tends to create a morbid curiosity as to pain in their minds. What is your opinion as to that?—My opinion is that that fear is entirely bred in the minds of the people who express it. I do not believe there is the slightest justification for it. We compel students to be present at operations on living men and living women because we feel that we must do so, and no one would listen to the suggestion that they ought not to be present there. How in the world can it have a bad effect when they see operations on animals if it does not when they see them performed on man? I do not believe that there is the slightest justification for the fear, and, as a rule, I do not like or attach any importance to suspicions as to impurity in other people without adequate evidence.

12809. (*Mr. Tomkinson.*) All your evidence, I think, is pretty well based upon the assumption that practic-



ally perfect anæsthesia can be and is maintained in these physiological experiments?—Yes.

12810. And you have no qualms about it as to the possibility of perfect and continued anæsthesia in operations?—I have no doubt whatever about it. Some one expressed it to you in a way which I think exactly represents the truth, viz., that consciousness is the first thing to go and the last thing to come back.

12811. (*Dr. Gaskell.*) Consciousness of pain?—Yes; consciousness of pain, I mean, is the first thing to go and the last thing to come back. We have the experience of people who have had the most serious and long-continued operations performed upon them, and have come back to consciousness, and their universal testimony is to absolute unconsciousness of pain.

12812. (*Mr. Tomkinson.*) Then that being the case, and anæsthetics being an established fact, there is no reason for me to ask you how far you would press your theory of the justifiableness of inflicting pain, even intense pain, upon individual creatures in order to prevent a much larger amount of suffering spread over a vast number of individuals; in other words, the infliction of vicarious sacrifices?—You ought only to do that where it is necessary for you to get the knowledge which will enable you to prevent pain in future, just in the same way as in my simile of the plague-stricken ship. I think the man ought to take the most painless method that is applicable to kill those rats, but he must kill them even though it should be painful.

12813. But then that is to avoid and prevent a gigantic danger?—Yes.



12814. That would hardly be on all fours with a very painful experiment—an awfully painful experiment, say—upon an animal for a possibility of discovery?—That is just the point. There have been many painful experiments in discovering the true nature of disease which, as I say, makes us think so differently about all these microbic diseases that we cannot put ourselves back into the ignorance of fifty years ago; but they have been for the purpose of ascertaining the nature of these diseases in order that we might fight them. The number of very painful experiments is very few—extremely few. The greater number of the experiments have been inoculations, and as soon as the disease has developed itself the animal is killed, because what the experimenters have wanted to find out was aye or no, would the disease be taken under such circumstances? The number of cases in which you have to allow really painful experiments is confined to these—that is, the cases where you are examining the distant effects of certain lesions of the nerves, of interference with the digestive organs, in order that when you see symptoms which are so produced you may know where the evil is. They are never, I think, performed casually; the very painful ones would almost always, I should think, in the history of English research in physiology, be performed for some very definite object, in order to give us this very essential knowledge.

12815. And as a matter of fact, with regard to the destruction of dangerous or destructive animals, the common way of trapping them is about as cruel as can be adopted?—Quite so.

12816. And yet it is recognised?—Quite so.



12817. You probably would agree with me that some more stringent law in the direction of prevention of cruelty to animals would be very desirable in those regards?—Yes, I agree. That is just what I feel. I feel that this infliction of pain for the purpose of knowledge is the last thing you ought to touch. I should be very strongly in favour of legislation for lessening pain, if such a thing were possible; but I am happy to say that the need grows less. I think that there is a growing of increased sensitiveness towards suffering which would help legislation of the kind that you speak of, and which is even rendering such legislation unnecessary. I see it everywhere.

12818. Another instance: that entirely misleading statement of baking rabbits prompts the question of the boiling of lobsters?—Yes. There may be much ✓ that one might advantageously inquire into there.







## THE EXPERIMENTAL STUDY OF THE ACTION OF DRUGS

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IT is difficult to explain the influence which the experimental method in pharmacology has exercised on therapeutics in the course of the last half century, because one is unable now to appreciate the standpoint of the physicians of earlier times, without prolonged and exhaustive study of their writings. Drugs influencing the more obvious processes of the body have been long understood and appreciated, *e.g.*, the emetics and purgatives; accordingly, experimental enquiry has modified the therapeutic use of these drugs in only a minor degree, although in some instances it has been proved that other systems than the alimentary tract are involved in the action, and these secondary effects are sometimes those to which the drug owes its present applications. And the method of action, and consequently the sphere of usefulness of all of them, have been rendered more precise.

But the greatest advance has been made in regard to drugs which affect functions which are less open to observation than those mentioned. For drugs can act only by changing the activity of various organs, and



their effects can be determined only when the normal function of the organs is known and can be measured.

I have no desire to minimise the value of the results of clinical research, but there can be no question that it failed in many cases to explain the direction in which drugs unfolded their action, and the result was often reflected in erroneous treatment. I may cite in this relation the account of digitalis given by a writer<sup>(1)</sup> on Therapeutics in 1860, with the premise that digitalis was not a new drug, but had been introduced by an English physician, Withering, seventy-five years before, and had since been in general use. Digitalis is said, in 1860, to slow and weaken the heart, and the conclusion is drawn that it is useful in aneurism and other similar vascular enlargements, in apoplexy, and in acute fevers. This was the result of seventy-five years of clinical observation. Within a few years Traube and Brunton showed by experimental methods that one effect of digitalis is to raise the blood-pressure to a marked extent, exactly the worst treatment possible in aneurism and apoplexy, and no one would dream of using digitalis in such conditions at the present time. Acute fevers, and especially pneumonia, were still treated with digitalis, however, until the exact seat of action of digitalis was determined, by experiments performed on animals, by Brunton, Schmiedeberg and others, to be the heart muscle. This gave definition to the use of digitalis which was absent before; it is useful in pneumonia only when the heart is affected, while in other forms it may do more harm than good. This example of the influence of experimental research on therapeutics might be repeated in regard to dozens of drugs, were it necessary. It may serve better than a general statement to show how the discovery of the

<sup>1</sup> Clarus, Handbuch der speciellen Arzneimittellehre, 1860.



action of a drug reacts on its therapeutic use by lending it greater precision. Instead of using such a drug as digitalis as a routine treatment in all cases of pneumonia, it defines the conditions under which it is likely to be of benefit, and excludes others in which it is not necessary. Doubtless, it may be objected that clinical observation alone would have led to the same result in time, and that, as a matter of fact, experimental results can only suggest a clinical examination of the truth of a theory based on them. But two generations had passed since the drug was introduced without any material advance in its therapeutic use. And the danger of trusting exclusively to clinical examination for therapeutic advance may be exemplified by the same drug. It is undoubtedly of value in certain forms of pneumonia, and is useless or deleterious in others. If it were adopted in all cases, the mortality statistics would probably be scarcely different from those of cases not treated with it, and the result would be the rejection of the drug. The heart action discovered by experimental methods, however, directs the clinician's attention to this phase of pneumonia in relation to digitalis, and he finds that the statistics of cases of pneumonia in which the heart is involved are improved by digitalis.

Another result of experimental enquiry is that the physician demands more certain evidence of curative action before accepting a drug. For many years ergot has been used to arrest hæmorrhage from the lungs, presumably because it is of value in hæmorrhage from the uterus. And it is extremely difficult to estimate the value of a drug in pulmonary hæmorrhage, owing to the fact that the bleeding often stops spontaneously. Now, however, Dale has shown, by experiments on animals, that ergot does not affect the vessels in the



lungs in the same way as those of the uterus, and, the analogy on which its use was based having failed, more definite evidence is required of its effect in pulmonary hæmorrhage, and unless this is forthcoming the use of ergot in these lung cases will be abandoned.

Numberless examples of this increased accuracy in the therapeutic use of drugs might be cited as the results of the minute examination of their effects in animals. Many old drugs have been discarded as the result of these enquiries, while others have proved to have properties which were previously unsuspected. The physician now has a much clearer view of what his remedies can do, and prescribes with a definite purpose, while formerly he could apply them only on the general knowledge that they were followed by favourable symptoms in some cases resembling more or less closely the one in hand. Until the exact method of action of a drug is known, it cannot be realised what condition it is likely to benefit, and the tendency is to treat diseases as a whole, rather than to ascertain the exact phase of the disease which is to be attacked.

#### THE INTRODUCTION OF NEW DRUGS AS THE RESULT OF EXPERIMENTAL METHODS.

An immense expansion of the resources of the therapist has occurred as the direct result of experimental enquiry. I shall give a number of groups of drugs which have been discovered in this way. A feature that strikes one in following the recent history of therapeutics is that most of these remedies have been discovered quite accidentally in the course of investigations which had no direct therapeutic object in view.



## I. SOPORIFICS.

(a) *Chloral*.

Up to 1868 the drugs used to produce sleep and allay restlessness and nervous excitement were opium and its derivatives, hyoscyamus and Indian hemp, and potassium bromide, but of these opium and bromide alone were in common use. In 1868 Liebreich, of Berlin, took up a problem of purely scientific interest, namely, whether "a substance is broken up into its constituent parts before it is oxidised."<sup>1</sup> And for this purpose he injected chloral into frogs and rabbits. This body was formed by Liebig in 1832, and thus had been available for use for 36 years, but had never before been employed either in therapeutics or experimentally, and nothing was known of its effects on the organism. Liebreich observed that it caused sleep in animals, and abandoning the primary object of his research, devoted his attention to a long series of experiments on its soporific action in animals. For it was necessary to determine whether chloral could be used without injury to such organs as the heart before it could be recommended as a remedy in man. He states, at the end of an account of these, that "the foregoing experiments on animals give us such a precise knowledge of the method of action of chloral, that it did not seem rash to commence with its use in man."<sup>2</sup> He accordingly tried it in a number of cases in order to combat sleeplessness, with success, and since the publication of his results chloral has assumed its present position as an invaluable hypnotic. It has been included in all the pharmacopœias.

<sup>1</sup> See *Liebreich*, *Das Chloral, ein neues Hypnoticum*, Berlin, 1868.

<sup>2</sup> I have translated the original as literally as possible.



(b) *Sulphonal*.

While Baumann and Kast<sup>1</sup> were examining the changes in organic sulphur compounds in the body (a research in physiological chemistry of purely scientific interest), their attention was attracted to the action of a group of bodies, the disulphones, on a dog, which fell asleep and only regained its normal condition a number of hours afterwards. Kast examined this phenomenon in a series of experiments on different animals, and then took occasion to test the effect on man. The successful results induced him to introduce into therapeutics the very valuable hypnotic sulphonal, which he found the best of the disulphones.

(c) *Trional and Tetronal*.

Later, comparisons of the effects on animals led him to prefer the analogous compounds *trional* and *tetronal*.

(d) *Paraldehyde*.

In 1881, Cervello<sup>2</sup> examined the effects of a number of bodies on animals, among them *paraldehyde*, which had been formed by chemists since 1848. He was much surprised to find it cause sleep, and advised its use in medicine; it is now included in most pharmacopœias, including the B.P.

(e) *Other Hypnotics*.

Crum-Brown and Fraser were the first to point out as the result of animal experiments that bodies resembling each other in chemical composition often

<sup>1</sup> *Kast*. Berlin Klin. Woch., 1888, p. 309.

<sup>2</sup> *Arch. f. exp. Path. u. Pharm.*, xvi., p. 265, 1881.



induce somewhat similar effects in the animal body, and the discovery of these sleep-compelling compounds suggested the view that all bodies similar to them in chemical composition would act as useful hypnotics. As a matter of fact this is only partially true. Each body has to be tested on animals to find whether it has hypnotic properties which can be utilised in practice, and comparatively few have stood the test. Liebreich's chloral has, however, proved to be the first of a very considerable group, all introduced into medicine by the same way of animal experimentation. These are amylene hydrate, urethane, hedonal, neuronal, chloretone, isopral, chloralamide, chloralose, bromoform, and last of all, perhaps the best of the series, veronal and propanal.

*No soporific has been introduced in the last forty years, except by means of animal experiment.*

## II. LOCAL ANÆSTHETICS.

### (a) Cocaine.

Over thirty years had passed since the introduction of the general anæsthetics, ether and chloroform, when von Anrep<sup>1</sup> examined the effects on animals of an alkaloid, cocaine, which had been isolated by Niemann from the coca plant in 1860. There was no idea of its anæsthetising effect. On the contrary, all that was known of the coca plant was its traditional power of preventing fatigue and hunger. Von Anrep noted in the course of his experiments that cocaine induced local insensibility to pain, and states at the end of his paper that he had "intended after the examination of the physiological action of cocaine on animals, to investigate its effects on man; other occupations have

<sup>1</sup> Pflüger's Arch. f. d. ges. Physiol., xxi., p. 38, 1880.



made that impossible for me as yet. But I would recommend cocaine as a local anæsthetic." But the idea of local anæsthesia was so new that his words passed unheeded, and I believe that he died shortly after writing his paper, and without realising the importance of his discovery. In 1884, however, Koller,<sup>1</sup> an ophthalmologist of Vienna, took up the question again, and tested the anæsthetising properties of cocaine on the eyes of guinea pigs, rabbits and dogs. He found that a few drops of a 2 per cent. solution applied to the eye removed sensibility to pain in the organ, while inducing no general effects. The eye could be touched or scratched without the least symptom of pain. "After animal experiments, which were so remarkably successful, I did not hesitate to use cocaine in human eyes." He used the same solution and the same method as, he had learned, was successful in animals, and the result was the introduction into medicine of a new method of relieving pain and permitting of operations, whose value is recognised by every surgeon and practitioner of medicine. The sphere of usefulness of cocaine has been very much extended of recent years, so that most of the major operations of surgery have now been performed under it.

(b) *Eucaïne and other local anæsthetics.*

But while cocaine caused a revolution in many departments of surgery, its use was soon found to be attended with certain drawbacks; it could not be sterilised very easily, and a number of grave cases of poisoning occurred. Substitutes for cocaine were therefore sought for which should combine its anæsthetising properties with a less poisonous action. Their toxicity

<sup>1</sup> Wiener Medizin. Wochenschrift, 25th Oct., 1884.



had of course to be tested on animals of all kinds. As a result of these experiments, eucaine was introduced by Vinci,<sup>1</sup> and has since been followed by anæsthesin, novocaine, acoine, stovaine, alypin, and others, which appear to be less toxic, but are still capable of much improvement.

(c) *Orthoforms*.

In the search for new substitutes for cocaine, some other bodies—the orthoforms—were found, which, while not available for the same purposes as cocaine, have a valuable effect in relieving pain in gastric cancer, and some other conditions.

*No local anæsthetic has been discovered except by means of experiments on animals.*

### III. ANTIPYRETICS AND ANALGESICS.

(a) *Antipyrine*.

Another large group of remedies which were introduced by means of experiments on animals is formed by the antipyretics, such as antipyrine, antifebrine, and phenacetine.

Until 1870, the only reliable drug used to combat fever temperature was quinine. A fall in fever temperature in animals and man was observed soon afterwards from the use of several drugs such as salicylic acid and kairine, but these tended to induce unpleasant symptoms, and the first antipyretic which has succeeded in maintaining its foothold in therapeutics was antipyrine, which was recommended by Filehne<sup>2</sup> on the

<sup>1</sup> Virchow's Archiv. 145, p. 78, 1896.

<sup>2</sup> Zeitschr. f. Kl. Med. VII., p. 641, 1884.



ground that it reduced the temperature in animals in fever by artificial infection.

(b) *Antifebrine.*

Antipyrine was soon followed by Antifebrine or Acetanilide, which was recommended by Cahn and Hepp, from their results in animal experiments. They state that "we convinced ourselves, by repeated and varied experiments on dogs, that antifebrine, in contrast to the nearly related aniline, can be given in relatively large doses, without any poisonous action." Examination of the changes undergone by antifebrine in the tissues of animals suggested that bodies of a certain chemical composition (paramidophenols) would also elicit this action, and phenacetine was soon introduced, to be followed by a large number of similar bodies. Each of these had to be tested in animals before being used in therapeutics, as it was found that though many paramidophenols are antipyretics, some of them are inactive, and others elicit undesirable symptoms. Among those available may be named phenacetine, analgine, thermifugine, antitherime, salipyrine, exalgine, lactophenine, malakine, saliphen, salophen, apolysine, citrophen, kryofine, phenocoll, salocoll, euphorine, thermordine. These bodies were introduced as substitutes for the earlier members of the series on the ground that they were less poisonous, as was demonstrated in a series of animal experiments. There is no question that all the antipyretics were used to an unnecessary extent fifteen years ago. But there is equally no question that they have a great sphere of usefulness in relieving pain and discomfort and fever.

*All the modern antipyretics were introduced by means of animal experiments.*



## IV. PHYSOSTIGMINE OR ESERINE.

The experiments of Fraser<sup>1</sup> on animals first demonstrated the action of physostigmine or eserine in contracting the pupil, and led to his examining whether the same results could be obtained in man.

This effect of physostigmine has led to its use in the treatment of glaucoma, a disease in which the tension in the eyeball is abnormally high, but may be reduced by remedies which contract the pupil and thus permit of the escape of the fluids of the eye.

## V. CARDIAC TONICS.

(a) *Strophanthus*.

An African arrow-poison was sent to Sir Thomas Fraser<sup>2</sup> as an object of toxicological interest, and the examination of its effects in animals led him to the discovery of a valuable new heart remedy, strophanthus, which has since been used widely, and is contained in most pharmacopœias.

(b) *Other Cardiac Tonics*.

Several other cardiac tonics have been introduced into therapeutics, and have had more or less vogue, helleborein, convallamarin, etc.

## VI. VASCULAR DILATORS.

(a) *Amyl Nitrite*.

Amyl nitrite was first formed by Balard in 1844, but its therapeutic value was not realised until 1867, when Sir Lauder Brunton,<sup>3</sup> having been present at some experiments made by Gamgee on animals with it and

<sup>1</sup> Edinburgh Med. Journal, 1863, pp. 123 and 235.

<sup>2</sup> British Medical Journal, 1885, p. 904.

<sup>3</sup> The Lancet, 27th July, 1867; Journal of Anat. and Phys. v., p. 92.



seeing the marked reduction of the blood pressure from its use, was induced to try it as a remedy in angina pectoris, in which he had observed a very high tension. The immediate relief given by nitrite of amyl in angina pectoris has been testified to by thousands of patients and physicians, and amyl nitrite is now recognised by all the pharmacopœias.

(b) *Nitro-glycerine*. (c) *Sodium Nitrite*. (d) *Erythrol Tetranitrate*.

Soon afterwards, nitroglycerine and nitrite of sodium were introduced on the ground of their similarity to amyl nitrite, each having been tested on animals, and more lately erythrol tetranitrate and other nitrites and nitrates have similarly been advocated in therapeutics.

*No vascular dilator has been discovered except by means of animal experiment.*

## VII. VASCULAR CONTRACTORS.

(a) *Suprarenal Capsules*. (b) *Adrenalin*.

Oliver and Schäfer<sup>1</sup> and Szymonowicz<sup>2</sup> discovered simultaneously in the course of some experiments on animals that the extract of suprarenal gland exerts an extraordinary action on the vessel walls. This observation was followed almost immediately by the introduction of the extract into therapeutics to induce local constriction of the vessels in inflammatory conditions and in hæmorrhage. Soon the active constituent, adrenalin, was isolated, and a solution of this body has since been used throughout the civilised world. New uses to which it may be put are still being developed, and the importance of the discovery cannot be over-estimated.

<sup>1</sup> *Journal of Physiol.*, xviii., p. 230, 1895.

<sup>2</sup> *Pfluger's Archiv.*, lxiv., p. 97, 1896.



*(c) Other Vascular Contractors.*

Some nearly related chemical compounds have recently been examined by Meyer, and prove to have a similar action.

*All the Vascular Contractors have been discovered by animal experiments.*

## VIII. DIURETICS.

*(a) Caffeine. (b) Theobromine (diuretine).*

Caffeine has been used occasionally in medicine, but its action and usefulness were misunderstood, as it was generally supposed to be a cardiac tonic. Von Schroeder first vindicated for it a position in therapeutics as a pure diuretic by his researches on animals,<sup>1</sup> and its use has since been much extended. Von Schroeder found out that caffeine was somewhat uncertain in its action, owing to a secondary effect it exerts on the circulation, and advocated in its stead the use of the nearly related substance, theobromine, as a more powerful and more certain diuretic. Theobromine had not been investigated before, either in animals or in man. Since von Schroeder's experiments it has been used very extensively in therapeutics, either as theobromine or in diuretine and similar bodies.

## IX. URINARY DISINFECTANTS AND SOLVENTS.

Nicolaier, in 1894,<sup>2</sup> introduced urotropin into therapeutics, stating that "on the basis of experiments with urotropin, which indicated that only very large doses induce symptoms, and that these disappear as soon as the treatment is stopped, I thought it safe to try its effect

<sup>1</sup> Arch. f. Exp. Path. u. Pharm. xxii., p. 39, xxiv., p. 85, 1887, 1888.

<sup>2</sup> Centralbl. f. Klin. Med, 1894. He states explicitly in a later paper (Ztschr. f. Klin. Med. 38, p. 357) that these experiments were performed on animals.



on man." This drug was followed by a number of other remedies of similar constitution, which have been used more or less for their effect in gravel and other conditions.

#### X. MODIFICATIONS OF OLDER REMEDIES.

Some of the older remedies have been modified by chemical manipulations, and the products have been advocated in medicine after preliminary trials on animals. As examples may be cited heroine and dionine from morphine, euquinine from quinine, aspirin from salicylic acid, etc.

#### XI. ANTISEPTICS AND DISINFECTANTS.

##### (a) *Carbolic Acid, Corrosive Sublimate, Cresols, etc.*

The whole of antiseptic surgery is based on the experiments of Lister, and the use of carbolic acid, corrosive sublimate, etc., thus arises from these. Their relative antiseptic action could not be tested in animals, but only on living microbes. But as soon as it was realised that in addition to their local action they might prove poisonous by absorption into the general system, they became the subject of animal experiment. And new antiseptics were soon advocated on the ground that they were less poisonous to the higher animals and therefore to man. Examples are the cresols (lysol), thymol, and many substitutes for iodoform.

##### (b) *Formaldehyde.*

The most powerful disinfectant introduced of recent years is formaldehyde, and Aronson, before advocating its use, tested whether it could be safely applied by exposing animals to its vapour for several hours, and also by injecting it hypodermically.



## XII. GENERAL ANÆSTHETICS.

A number of new anæsthetics have been examined in experiments on animals, and though none of them have ousted ether and chloroform from their positions, they have enjoyed a certain limited popularity—pental, ethyl chloride, ethyl bromide.

## XIII. EMETICS.

In 1869, Matthiesson and Wright formed apomorphine from morphine, and Wickham Legg<sup>1</sup> found from experiments on animals that it possessed powerful emetic properties when injected hypodermically. It soon found a place in the pharmacopœias, and has retained it as the most reliable and most convenient method of causing vomiting and evacuating the stomach in cases of poisoning.

## XIV. THYROID EXTRACT.

Sir Victor Horsley first showed beyond further question by animal experiment that the removal of the thyroid gland was followed by certain symptoms, and suggested that when these symptoms occur spontaneously in human beings, they should be treated by engrafting a healthy gland. This was done with success, but Murray showed later that the same results could be attained by the injection of the juice of the gland, and this led finally to the administration of the gland by the mouth. The successful treatment of myœdema and cretinism by thyroid gland medication is now universally recognised, and preparations of this gland are included in the British Pharmacopœia and in those of most other countries. It may be added that these symptoms had been recognised and described long

<sup>1</sup> St. Bartholomew's Hospital Reports, Vol. vi., p. 97, 1870.



before Horsley, but no suggestion had been made for their treatment that bore the slightest promise of success.

This list by no means exhausts the new drugs introduced by means of the experimental method in the last forty years, during which it has been systematically practised with a view to investigating the action of remedies. And I have no desire to minimise the importance of other methods of investigation, but when one contrasts the number of valuable drugs introduced into therapeutics without the aid of experiments on animals, one finds it disappointingly meagre. In the last forty years, during which the experimental method has been so fruitful in valuable remedies, the only drug of even mediocre importance introduced by other methods is pilocarpine, a sudorific which is occasionally employed in dropsy, and which was introduced (1874) from its being used by the South Americans as a sudorific.

A doubt is still sometimes expressed whether the experimental method has been of real service to medicine, but such a position only indicates ignorance of the history of therapeutics in the last half-century. No medical man of the present day can afford to reject such remedies as chloral, cocaine, amyl nitrite, eserine, adrenaline, caffeine, strophanthus and their allies. And no medical man pretends to reject them.

It is, of course, possible that the usefulness of these drugs would have been ascertained by other methods in course of time, but there is no indication that medicine was trending in that direction when they were introduced by means of the experimental method. And it is to be noted that many of them were available for investigators along other lines for many years. For instance, chloral lay unused for 36 years, paraldehyde



for 33, cocaine for 20, amyl nitrite for 23 years, although the introduction of any one of these into therapeutics would have relieved many a sufferer.

Another service which the method of animal experiment has done therapeutics is in the sifting out of valueless drugs. A large number of old vegetable and animal bodies, which used to cumber the pharmacopœias, are slowly disappearing as the medical profession learns that they are inactive, and as the theory on which they were introduced is shown to be erroneous. A much larger number of new bodies, the result of the activity of the chemical industry, have to be examined and accepted or rejected as they prove to be useful or poisonous. And among those accepted, comparisons of their virtues have to be continuously made. So highly does the chemical industry value the aid given it in this way that its leaders are no longer willing to wait for the dictum of the University pharmacologists, as formerly, but have appointed pharmacologists and erected laboratories for animal experiment at the cost of many thousands of pounds per annum. The duty of these pharmacologists is to examine the action of the new chemical products of the factory, to reject those which are useless or poisonous, and to suggest possible improvements in those which promise to be of value. In this way many hundreds of new bodies have been tested, many rejected, and some submitted to trial by the medical profession.

The cruder drugs have been in many instances replaced by purer principles extracted from them, but these principles have all to be tested before they can be known to possess the virtues of the crude drug. This may be exemplified by the present position of ergot, a drug which has been in use for many centuries for its effect in causing contraction of the womb and



arresting hæmorrhage in labour. Ergot has always suffered from the fact that it is uncertain in action, some extracts appearing devoid of any influence on the uterus, while others have undoubted value. Attempts have been made for many years to obtain a more satisfactory body by isolating the active principle of ergot. Within the last year a German chemist has put on the market an apparently pure substance, clavin, which he supposes to be the essential factor in ergot. This view may be tested in two ways. Clavin may be injected into women in labour who show signs of hæmorrhage, and in course of years doubtless the question as to whether clavin is a valuable addition to therapeutics, an inert body, or a poison, may be determined. On the other hand, the effect of ergot on the uterus of animals is quite well known, and half a dozen experiments on anæsthetised animals would suffice to settle the question. As a matter of fact, clavin proved quite inert in experiments in which it was tested in animals, and on these grounds was withdrawn by its discoverer.

Another direction in which animal experiments have proved of the greatest importance is in discovering and testing remedies to be employed in cases of poisoning. Poisoning occurs so rarely that in practice it is impossible to test the value of antidotes, and even when a patient recovers after an antidote, the question always arises whether the quantity of poison taken was really a fatal dose, whether vomiting or slow absorption or some other factor was not really responsible for the recovery. In animals, on the other hand, the exact dose required to kill may be ascertained, and the effect of antidotes may then be examined with accuracy. In this way many supposed antidotal measures have been shown to be valueless, or worse, through the waste of time which



their administration involves. On the other hand, the value of the anæsthetics and hypnotics in convulsive poisoning has been demonstrated; the usefulness of the atropine treatment in opium poisoning, and its limitations, have been satisfactorily established; atropine has been shown to be the treatment in cases of pilocarpine poisoning and in some forms of mushroom poisoning, and so on.

#### STANDARDISATION OF DRUGS.

The strength of most drugs used in medicine can be ascertained by chemical methods, *e.g.*, the amount of morphine in opium and its preparations. These methods are not available in certain cases, notably in the group of cardiac tonics, including digitalis and strophanthus, in which the active principles are imperfectly known and cannot be assayed quantitatively. The strength of tincture of digitalis dispensed was quite indefinite up to a few years ago, and tinctures prepared by different druggists varied as much as 1:4 in strength. In 1896 a method of standardising these preparations by means of animal experiments was brought to the notice of manufacturing pharmacists by Houghton, and was adopted by most of the larger American manufacturers. It has recently been taken up by a number of pharmaceutical manufacturers in this country, and enquiry of one of these houses elicited the statement that apart from their natural desire to issue preparations of definite strength, it was found necessary to standardise their products in order to be able to compete with other firms, notably the Americans. The advantage of using standardised preparations thus appears to be realised both by the pharmaceutical and medical professions.

This method consists in finding the smallest dose of the preparation which induces a certain result in



animals. For example, digitalis is assayed by finding the smallest quantity required to arrest the heart of a frog in a given time. If the doses of two preparations vary 1 : 2 for the frog, they will also vary as 1 : 2 in man. No attempt is made to derive the actual dose used in therapeutics from the dose found active in the frog by a consideration of the relative weights of man and frog.

The activity of *strophanthus* and squills is determined in the same way as that of digitalis; that of ergot is found by experiments on cats, rabbits, or dogs; *cannabis indica* is assayed in the dog, which reacts much more exactly than the cat or rabbit; and adrenalin and products of the suprarenal gland are also assayed on the dog. The importance of standardisation of these drugs can be easily understood, and the ordinary pharmacist is quite helpless in the matter. For example, I have found that of two tinctures of digitalis supplied me by a perfectly reliable firm, the one was four times as strong as the other. If a patient were treated with the weaker for some time in the increasing doses which would be necessary to elicit the therapeutic effect, and then the treatment were inadvertently continued with the stronger in the same dose, the results might very easily be disastrous.

In the case of ergot the conditions are even worse, for much of this drug on the market is practically inert, and the preparations of course valueless. A physician may thus depend in an emergency on the action of a drug which is without action. Ergot is very largely used in cases of hæmorrhage in childbirth, in which it is absolutely essential to lose no time and to be certain of one's remedies if the woman's life is to be saved.



In regard to another drug, *cannabis indica*, I have personal knowledge that 20,000 pounds of it were offered for sale to a firm, which before closing the deal had a sample tested on animals, and finding it inactive refused the consignment. This firm informs me that since the introduction of physiological assay "we have had practically no complaints whatever as to the inefficiency of products of *cannabis indica*, quite a contrast to our experience previous to this time."



# THE HISTORY OF THE

REIGN OF

CHARLES THE FIRST

BY

JOHN BURNET

OF

THE UNIVERSITY OF OXFORD

IN TWO VOLUMES

LONDON

Printed by J. Streater, at the

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1679

By Authority

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## THE VALUE OF ANTITOXIN IN THE TREATMENT OF DIPHTHERIA

It is sometimes said, by the opponents of all experiments on animals, that these experiments have had no great result in the saving of life; and, by way of example, they point to the antitoxin treatment of diphtheria, denying that this has done anything to diminish the dangers of the disease, or even going so far as to say that diphtheria is often aggravated by the administration of antitoxin.

In support of this statement, they bring forward a number of statistics, obtained from the annual reports of the Registrar-General, showing that the death-rate from diphtheria in proportion to the whole population has risen rather than fallen since the introduction of antitoxin in 1894. The following extract from a recent magazine article will serve to illustrate their line of reasoning:—

“Average diphtheria death-rate per million persons living as recorded in the returns of the Registrar-General for the last thirty years in quinquennial periods:—

1st	Quinquennial Period	1876-1880	...	121
2nd	„	1881-1885	...	156
3rd	„	1886-1890	...	170
4th	„	1891-1895	...	252
5th	„	1896-1900	...	272
6th	„	1901-1905	...	204



From this it will be seen that the highest death-rate ever recorded took place in the five years of 1896 to 1900, which synchronises with the spread all over England of the antitoxin treatment. During the last five years, 1901-1905, the death-rate seems somewhat to have decreased, but it is still above the death-rate for the whole time from 1876 to 1890, during which time diphtheria patients escaped the attention of the vivisectors. . . . All these figures, which can be verified by anyone capable of simple arithmetical exercises, show the insidious and malignant inroads the Black Art of Vivisection has made upon human lives, wherever its familiars have succeeded in practising their sorceries and serums. . . . The Registrar-General records his dispassionate facts, and proclaims to the world that wherever the hand of the vivisector is stretched out over a disease, there that disease increases its hold upon life, and hurries men faster to the tomb."

These returns of the Registrar-General may seem at first sight to give convincing proof of the uselessness of antitoxin in the treatment of diphtheria. But, if we look below the surface, it will at once become evident that the figures will not for a moment bear this interpretation; and the purpose of this pamphlet is to show that the argument against antitoxin treatment is based on three entirely false premises.

i. *It is impossible to judge of the value of the antitoxin treatment from a study of the death-rate in proportion to the general population.*

The distribution of an epidemic disease such as diphtheria varies widely from time to time. The disease may be very common one year, and very scarce the next; or a cycle of bad diphtheria years may be



followed by a cycle of good years. Supposing, now, that during a period of 5 years the prevalence of diphtheria were to be twice as great as during the preceding 5 years. If the severity of the disease remained unchanged, the death-rate in proportion to the general population would be approximately doubled, and it is absurd to expect that treatment, either by antitoxin or by any other means, could counteract such a largely increased death-rate. Unless, therefore, we know the number of cases of diphtheria during the period under consideration, it is quite impossible, from a study of the death-rate in proportion to the general population, to estimate the efficacy of antitoxin treatment; this can only be deduced from the *case-mortality*, that is to say, the percentage of deaths from diphtheria occurring amongst those who have contracted the disease.

ii. *It is impossible to estimate from any death-rate figures the value of antitoxin, unless we know in how many cases it was given.*

The truth of this statement is obvious. If antitoxin were given only in 5 per cent. of all diphtheria cases, the results, however brilliant, would not be reflected to any appreciable extent in the death-rate; whereas if it were given in every case we ought to be able to discover its effect, whether good or evil, from an examination of the case-mortality. The returns of the Registrar-General contain no information as to the number of cases treated by antitoxin, and the writer just quoted apparently assumes that since its introduction in 1895 it was given in every case of diphtheria. But this is very far from the truth. For, at first, antitoxin was regarded with a good deal of uncertainty and suspicion by the medical profession, so that only a small proportion of patients were



treated in this way; and it is only of recent years, after passing through a long period of probation, that it has come into general use, and is now almost universally given in all municipal fever hospitals. Moreover, in the early days, even those who believed in antitoxin were afraid to use it often enough, or in sufficient amount; the doses then given seem ridiculously small by the light of our present knowledge, and it is certain that they could not have produced the best results.

iii. *The Registrar-General's returns as to the death-rate from diphtheria are admitted to be untrustworthy, on account of the confusion that existed until recent years between diphtheria and croup.*

Sixty years ago, diphtheria was not regarded as a distinct disease, and not till 1855 did it appear in the Registrar-General's returns under its own name. For many years after 1855, there was a great deal of uncertainty as to what was and what was not diphtheria; and, in particular, a large number of cases of true diphtheria were classed as croup. The Registrar-General himself refers to this confusion, and in 1885 writes:—"The registered deaths from diphtheria fell from an annual average of 185 per million to 121; but so much uncertainty attaches to the use of the term diphtheria by medical men, and there is so much confusion in their certificates between diphtheria and simple spasmodic croup, that the returns under this heading are extremely untrustworthy." In addition, each annual return contains some such statement as this:—"In order to obtain an approximate measure of the loss of life caused by diphtheria, it has been found necessary to class the deaths definitely referred to that disease with those referred to croup."



The advance of bacteriology has done much to dispel this uncertainty ; and at the present time, when almost every large town owns a municipal laboratory, any doubtful case of sore-throat is submitted to the crucial test of a bacteriological examination ; a culture is made from the throat and examined for the diphtheria bacillus. In consequence of these improved methods of diagnosis, a great number of cases which would previously have been classed as croup are now returned as diphtheria. This has naturally led to a decreased record of mortality from croup, and a corresponding increased record of mortality from diphtheria, as is shown by the following table :—

			Average annual mortality from		
			(a) Diphtheria.	(b) Croup.	
1861-1870	...	...	3,945	...	5,254
1883-1894	...	...	5,617	...	3,331
1895-1906	...	...	7,586	...	860

It is evident, therefore, that in order to determine from any statistical data the influence of antitoxin in the treatment of diphtheria, three conditions must be satisfied as far as possible :—

- i. It is necessary to know the case mortality.
- ii. It is necessary to know the number of cases in which antitoxin was given.
- iii. The diagnosis of diphtheria in all cases under consideration must rest on the surest foundations.

These conditions are not likely to be fulfilled except in public institutions and hospitals, where

- i. Accurate records are kept as to the progress and termination of every case.
- ii. Antitoxin is given almost invariably as a matter of routine.
- iii. The diagnosis of every doubtful case is verified by a bacteriological examination.



We may turn, then, to the statistics of recognised hospitals, with the assurance that here at last may be found an answer to the question, What is the value of diphtheria antitoxin? A few examples of these statistics are given here; they could be multiplied almost indefinitely.

Statistics of cases of diphtheria treated in the Metropolitan Asylums Board Hospitals<sup>1</sup>:—

Year.	Cases treated by Antitoxin ;		Mortality ;	
	per cent. of all cases.		per cent. of all cases.	
1888-93	...	—	...	28·5
1894	...	—	...	29·6
1895 <sup>2</sup>	...	61·8	...	22·5
1896	...	71·3	...	20·8
1897	...	80·2	...	17·5
1898	...	81·4	...	15·5
1899	...	—	...	13·95
1900	...	—	...	12·01
1901	...	—	...	12·5
1902	...	—	...	11·0
1903	...	—	...	9·7
1904	...	—	...	10·1
1905	...	—	...	8·3

<sup>1</sup> 65 per cent. of all cases of diphtheria in the County of London are treated in these hospitals.

<sup>2</sup> Commencement of the antitoxin period.

Statistics of cases of diphtheria in New York City from 1891-1899:—

Year.	Cases.		Deaths.		Mortality per cent.
1891	...	5,346	...	1,970	36·7
1892	...	5,184	...	2,196	40·6
1893	...	7,021	...	2,558	36·4
1894	...	9,641	...	2,870	29·7
1895 <sup>1</sup>	...	10,353	...	1,976	19·1
1896 <sup>2</sup>	...	11,399	...	1,763	15·4
1897	...	10,896	...	1,590	14·6
1898	...	7,593	...	923	12·2
1899	...	8,240	...	1,087	13·

<sup>1</sup> Antitoxin introduced.

<sup>2</sup> Use of antitoxin became general.



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Statistics of cases of diphtheria treated in the Paris Hospitals, 1893-1898 :—

Year.				Case mortality per cent.
1893	...	...	...	45
1894 <sup>1</sup>	...	...	...	31
1895	...	...	...	12
1896	...	...	...	15·2
1897	...	...	...	13·2
1898	...	...	...	14·5

<sup>1</sup> Commencement of antitoxin treatment.

The opponents of all experiments on animals object to hospital statistics on the grounds that the cases are selected, that a great many mild and favourable cases are admitted, and that the hospital patient has an advantage over the patient treated at home as regards careful nursing and skilled attention. Those who hold these objections seem to be unaware that until 1894 the diphtheria death-rate in hospital patients was always higher than in cases treated at home, because the former belonged to the poorer classes, who were less able to resist the attacks of any disease. Antitoxin treatment was at first almost confined to the hospitals, with the result that the mortality among hospital patients fell rapidly, and for the period 1895-1900 was slightly lower than among home-cases. Subsequently the death-rate among the two classes of patients became equalised, coincidently with the general use of antitoxin. This is shown by the following table :—

Case mortality from diphtheria in London.

	Hospital Patients.		Home Patients.	
1889-1894	...	30·1 per cent.	...	24·2 per cent.
1895-1900	...	16·0 "	...	17·0 "
1901-1906	...	10·0 "	...	10·0 "

### *The value of antitoxin in laryngeal diphtheria.*

In some cases diphtheria spreads from the throat to the larynx, whereby the disease at once becomes more



serious, because the diphtheritic membrane may easily block the narrow orifice of the larynx and cause fatal suffocation. Under these circumstances the correct treatment is to perform tracheotomy. The death-rate in these laryngeal cases has always been much higher than in others; consequently, in testing the effect of antitoxin on laryngeal diphtheria, there is no possibility of the inclusion of a number of mild cases, which would have recovered if left to nature. The following figures show the influence of antitoxin under these conditions:—

Previous to 1894, the mortality among 8,927 hospital cases of laryngeal diphtheria was 71·6 per cent.

After 1894, the mortality among 2,374 cases, in which antitoxin was given, was 36·6 per cent., showing a reduction of nearly 50 per cent.

In Germany, an even greater reduction was obtained. There, before the introduction of antitoxin, the death-rate among cases of laryngeal diphtheria was 86 per cent.; whereas of 2,041 children, treated with antitoxin, on whom tracheotomy had to be performed, 778 died, giving a death-rate of 33·6 per cent. Similar results have been obtained in other European countries and in America.

One other point, having an important bearing on the subject, is the varying effect of antitoxin according to the stage at which it is given. The ideal treatment is to give antitoxin on the first day. If this be done, any risk of death is almost obliterated; unfortunately, this is often impossible, as a diagnosis can rarely be made so soon. The later the administration of antitoxin is deferred, the less will be its effect in checking the



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disease, as can be seen from this table, compiled from the records of the Brook Hospital, London :—

No. of cases treated.	Day of disease on which antitoxin was given.		Fatal cases.		Case mortality.
2,135	...	1st day	...	0	0
1,441	...	2nd „	...	62	4.3
1,600	...	3rd „	...	178	11.12
1,276	...	4th „	...	220	17.24
1,645	...	5th „ or later	...	308	18.72

If the antitoxin were of no value as a remedy, whether it were administered on the first or on the fifth day of the disease would be immaterial.

We have touched on only a few of the arguments in favour of antitoxin, but it is hoped that enough has been said to show that the claims put forward on its behalf are based on a solid foundation of use and experience. Those who still remain sceptical may be advised to seek the opinion of some officer in charge of a fever hospital.

NOTE.—The statistics for 1906 and 1907 (Metropolitan Asylums Board Hospitals) are as follows :—

Year.	Cases treated by Antitoxin; Per cent. of all cases.			Mortality; Per cent. of all cases.
1906	...	...	84.0	8.9
1907	...	...	91.2	9.8



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## THE VALUE OF ANTIMENINGITIS SERUM IN THE TREATMENT OF EPIDEMIC CEREBRO-SPINAL MENINGITIS

By A. GARDNER ROBB, M.B., D.P.H.

*Visiting Physician in Charge of the Belfast Fever Hospitals*

OF all the epidemic diseases met with in English-speaking countries, the most terrible in its manifestations and the most disastrous in its death-rate is cerebro-spinal meningitis. Outbreaks of this malady have been comparatively rare and comparatively short-lived. We have as yet no certain knowledge of the conditions under which it arises; but, if we are to judge by the history of its incidence in America during the past ten or twelve years, its occurrence in epidemic form is becoming more frequent, and the tendency to linger where it has once gained a footing is becoming more marked.

Within the past two years extensive outbreaks have occurred in some parts of Scotland and Ireland. The larger cities have suffered most, Glasgow and Edinburgh and Leith in Scotland, and Belfast in Ireland. Commencing with great suddenness in these cities, cases rapidly appeared in widely separated districts having no apparent connection with each other. It is true, and fortunately so, that the total number of the inhabitants attacked in these places has been but a small proportion



of the population, but the disease is so terrible in its consequences that it causes more widespread alarm than any other form of epidemic outbreak. Although the microbic cause of the disease is now definitely ascertained, but little is known of its method of spreading, and no theory of its propagation as yet suggested can be accepted as satisfactory; hence the public health authorities can do very little to cope with it, and this adds much to the dread caused by its appearance in a community. This alarm is only natural, when it is remembered with what terrible rapidity many of the cases proved fatal, and the fearful havoc wrought amongst those who did survive. Many of those attacked died within a few hours of the onset, and that after terrible suffering, while many of those who survived the acute attack lingered on for weeks and months, going steadily downhill in spite of every effort to save them. Again, many of those who did survive were left permanently maimed.

Until recently it must be confessed that no known treatment could be said to produce any marked effect on the course of the disease; for, while it could with justice be claimed that treatment and careful nursing did turn the tide in the patients' favour in some instances, the proportion of cases so influenced was so small as to be almost inappreciable.

#### THE ADVENT OF ANTIMENINGITIS SERUM FOR INTRASPINAL INJECTION

After prolonged and patient experiments on the lower animals in the laboratory, Dr. Simon Flexner and Dr. J. W. Jobling, of the Rockefeller Institute for Medical Research, New York, produced an antimeningitis



serum, obtained from the horse, for use by intraspinal injection in this disease. This serum was first tried in the spring of 1907 ; and the complete revolution, brought about by the adoption of this method of treatment, will be readily appreciated by contrasting the results obtained in cases before its use with those obtained since its introduction. Fortunately, accurate statistics are available from all the more recent epidemic outbreaks.

#### RESULTS BEFORE THE USE OF THE SERUM

Of 4,000 cases in New York in 1904, 75 per cent. died.

Baker reports from Greater New York, 2,113 cases with 1,636 deaths, giving 77·4 per cent. mortality.

Chalmers reports from Glasgow (1907) 998 cases with 683 deaths, giving 68·4 per cent. mortality.

Bailie reports in Belfast (1907) 623 cases with 493 deaths, giving 79·2 per cent. mortality.

Ker reports that in the Edinburgh epidemic there was 78 per cent. mortality.

Robertson reports from Leith (1907) 62 cases with 74·4 per cent. mortality.

Turnour reports from the Transvaal 200 cases with 74 per cent. mortality.

Amongst patients treated *in hospitals* the death-rate was not better, for of

202 cases in Ruchill Hospital, Glasgow	79·2% died
108     ,,     Edinburgh Fever Hospital	80·5%     ,,
275     ,,     Belfast Fever Hospital	72·3%     ,,

and Dunn reports that in the Boston Children's Hospital, during the eight years 1899-1907, the mortality varied from 69 per cent. to 80 per cent.



RESULTS IN CASES TREATED WITH FLEXNER AND  
JOBBLING'S SERUM.

	Cases.	Died.	Mortality. Per cent.
City Hospital, Cincinnati ... ..	45	14	31·1
Dr. Dunn, Boston ... ..	40	9	22·5
Johns Hopkins Hospital, Boston	22	4	18·1
Rhode Island Hospital ... ..	17	6	35·2
Lakeside Hospital, Cleveland ...	29	11	37·7
Edinburgh Fever Hospital ... ..	33	13	42·3
Mount Sinai Hospital (Children)	15	2	13·3
Municipal Hospital, Philadelphia	21	9	42·7
Belfast Fever Hospitals ... ..	98	29	29·6

Flexner and Jobling have collected statistics of 411 cases treated with the serum, of which 151 died: a mortality of 36·7 per cent. This series embraced all the available figures up to that time, and included many cases in which the serum was given too late to allow of hopeful results, and also many cases at the early stage of its employment which are now known to have received inadequate doses. It is confidently hoped that with increased experience of the amount and frequency of the injection necessary, even better results will be obtained.

From these figures it will be seen that the death-rate in the cases not treated with the serum averaged some 75 per cent. This has been reduced in cases treated with the serum *to less than half*, and in many instances much below that figure.

My own experience has been that of 275 cases under my care in hospital before the use of the serum was commenced 72·3 per cent. died; while of the 98 cases treated with the serum 29·6 per cent. died. No selection of cases was made: *every* case sent into hospital since September, 1907, has been treated in



this way. No change in the severity of the attacks was observed: in the three months *immediately before* the serum arrived with us, 45 cases came under treatment, of whom 37, or 82 per cent., died; and in the first four months after we began its use in hospital 30 cases were treated, of whom 8 died, a mortality of 26·6 per cent.; while of the 34 cases occurring in the City *in the same period* but not sent into hospital, and not treated with the serum, over 80 per cent. died.

Great as this change in the death-rate has been, it is not more striking than the improvement in the course run by the cases; for whereas it was common to have cases running on into weeks and even months, such cases are no longer met with; the duration of illness in those who do recover has been greatly reduced, and with this reduction there has also been a marked diminution in the number of serious complications and sequelæ occurring.

More recently similar antisera have been produced in other places, notably in Germany, and encouraging reports are being collected from districts in which they have been employed.

It is true that sufficient serum for the treatment of hundreds of cases can *now* be produced from a single horse with what amounts to little more than inconvenience to the animal, but it is also true that this serum could only, in the first instance, have been obtained, and sufficiently tested to warrant its use in human subjects, by repeated experiments on animals in the laboratory.

BELFAST, *January*, 1909.







## ADVANCE IN KNOWLEDGE OF CANCER

*(The Editor of NATURE has kindly allowed the Committee of the Research Defence Society to reprint for the Society's use the following article by Dr. Bashford, Director of Imperial Cancer Research. Dr. Bashford, also, has kindly agreed to let the article be thus used.)*

IN conformity with a scheme of inquiry embarked upon in October, 1902, the third scientific report of the Imperial Cancer Research Fund, recently issued, treats, like its predecessors, of cancer as a problem of general and experimental biology. It contains no definite answer to the questions, What is the nature and what the cause of cancer? and beyond demonstrating that systematic experiment justifies the early surgical removal of a tumour as the only possible treatment at the present time, the report is silent as to remedial and preventive measures. These shortcomings will almost certainly arouse misgivings on the part of those who cannot appreciate how progress is made in any field of knowledge. They will also, no doubt, be seized upon by persons who, in their ignorance, assert that all scientific efforts should be concentrated on utilitarian ends, and they will be exploited by the charlatan, to whom for a space a free field is still left for his nostrums. The sustained efforts of the past six years to penetrate the mysteries of cancer have been accompanied by a corresponding activity on the part of faddists and quacks who advertise themselves by proclaiming the failure of scientific investigation to yield "practical fruits." The danger of their literary activity is but



enhanced by the powers of diction and of exposition possessed by some of the writers. They could profitably devote their literary ability to expounding to the public the true facts and difficulties of the cancer problem, instead of the ridiculous causes they maintain before a jury of the credulous and the suffering. In the absence of this enlightened attitude on their part, it is my duty, since the second scientific report was followed by volumes of nonsense on the part of such persons, bluntly to inform the general reader of the folly of ignoring the necessity for the early surgical removal of cancer, and of running from one faddist or quack to another yet more ignorantly sanguine. If, in the future, the progress of scientific investigation provides a substitute for or an adjunct to surgical treatment, there will be no needless delay in placing it within the reach of the cancer patient.

✓ Meantime, the importance of the investigation of cancer is only too grimly emphasised by its frequency as a cause of death. The number of deaths *recorded* from cancer increases from year to year throughout the world, civilised and uncivilised, human and animal. Taking England and Wales as an example, in 1889, on an average, the chance of a man above thirty-five years ultimately dying of cancer was one in twenty-one, and for a woman above the same age one in twelve. The increase in the number of deaths *recorded* from cancer makes the corresponding chances to-day one in eleven for men and one in seven for women. Scarcely a family of large size escapes attack. There is no circle of acquaintances, no chance assemblage of persons at a *table d'hôte* or in a tube lift, but contains prospective victims. But is cancer really increasing? The accurate use of statistics, and the careful scrutiny of scientific value of the data upon which they are based, still withhold an



affirmative answer. If it be further asked, Is not cancer much more frequent in races living under European civilisation than in the rest of mankind? recent investigation has disposed of the fiction that many races of mankind are exempt. Where the disease was said to be rare—*e.g.*, in Japan—there are excellent statistics, of which Europeans were previously ignorant, proving the great frequency of cancer among the Japanese; and, taking another example, investigations in Indian hospitals show that certain forms of cancer very common in London hospitals are probably not less common in hospitals throughout Hindustan. In the case of most other races there are insurmountable difficulties in the way of even thus roughly estimating its frequency among them. Therefore it is idle to affirm or to deny that cancer may be more common in some races than in others. The disease occurs throughout the human race, and its association with forms of chronic irritation having nothing in common beyond this association is a fact of more moment than any futile discussion of the relative liability of different races. The additions, during six years, to our knowledge of its occurrence in man, as well as in tame and wild animals, tell hard against those who, at the close of the nineteenth century, argued that the increase in the number of deaths attributed to cancer was real, and merely a penalty for living under the influences of European civilisation.

Much additional evidence has been obtained of the extent to which cancer pervades the vertebrate scale. The similarity of the disease throughout vertebrates is illustrated most diagrammatically by a series of preparations of skin-cancers from mammals to marine fish living in a state of nature. Wherever data are available, for animals as for man, the liability to cancer is shown to be greatest in the last third of



the span of life, whether it be short or long; the "age-incidence" of cancer in man has acquired enhanced significance by the establishment of this generalisation.

The widening of our knowledge of the occurrence of cancer is only one example of how revived interest in mere observation has put an end to the era of unverified, and often unverifiable, speculation which characterised the last twenty years of the nineteenth century, when exact methods of studying the clinical course, the anatomy, and the microscopical structure of tumours had reached their natural limitations. The study of cancer solely from the standpoint of its being an infective disease had yielded equivocal and self-contradictory results. Statistical methods had become barren from want of data to work on. No point vulnerable to an attack in the rear by the experimental method could be discerned.<sup>1</sup> In short, there was a standstill in the advance of knowledge. As is usual in all similar epochs in the progress of science, observation, hypothesis, and experiment had ceased to advance hand in hand. The armchair speculator had the field to himself. With only the knowledge derived from the bedside, the study of the structure of tumours in man, imperfect data of its incidence in Europeans, and hearsay statements of its absence elsewhere to guide him, he little comprehended the futility of the explanations he so lightly advanced, and others of his kind equally lightly refuted. A general feeling of the hopelessness of penetrating to

<sup>1</sup> As a matter of fact, such a point of attack had existed since the time when Hanau and Morau had successfully inoculated cancer from one animal to another, but those engaged in cancer research had either failed to realise the significance of this imperfect work or had been baffled by the difficulties which had to be overcome in attempting to imitate it.



the truth was abroad, both among the public and the medical profession, who, the limits of surgical aid having been reached, were despondent in the extreme. The universality of this conviction led to the spontaneous and independent formation of "cancer research committees" in different countries at the end of the nineteenth century.

The whole outlook of the cancer question has been changed by the successful application of the comparative biological and experimental methods to its study, and by the restoration of the legitimate relations of observation, speculation, and experimental verification. In this revival the committees formed in different centres have played very unequal shares, according as their proceedings have conformed to the methods which advance natural knowledge. To demonstrate fully the adequate evidence upon which the claim—cautiously advanced in the first and second scientific reports and earlier papers—is based, that a new and rational era of investigation has been inaugurated, and to urge continued confidence in the investigation of cancer, are the primary objects and the main justifications of the third scientific report of the Imperial Cancer Research. The time has not come when practical applications of the additions to knowledge are to be expected, nor has accident yet yielded any.

Although the rapid accumulation of new facts forbids the premature formulation of a generalisation attempting a unification of the mass of new and old knowledge, many results of far-reaching importance have been attained. The work of recent years has made it more certain than it ever was before that cancer contains no virus or other parasite foreign to the living organism. One is often asked if a relative suffering



from cancer is dangerous to others—*e.g.*, a grandmother to her grandchild, the chief solace of her old age—or if an historic family mansion should be burnt down because many progenitors inheriting it had died of cancer. During six years many tens of thousands of mice suffering from cancer have been under the most stringent observation. If cancer were communicable in the sense in which infective diseases are communicable, animals housed along with those naturally suffering from, or inoculated with, cancer would be the first to suffer. In an experience extending over six years, *i.e.*, almost three times the average length of a mouse's life, exhaustive investigation has shown that this risk does not exist. This fact of itself satisfies those handling the animals. They incur still less risk in passing many hours daily dealing with cancerous animals in a room in which 10,000 of such mice and rats are usually housed at one time. If such a "cancer house" as never before existed has no dangers to human beings who spend their days in it, *a fortiori* other persons have no ground for apprehension. These results are of great practical value. They reinforce opinions often expressed in the past for other reasons. The presence, every day in the year, of some 50,000 persons suffering from cancer in England and Wales constitutes no menace to the health of those near and dear to them, nor to the health of the population generally, as would a smaller number of people suffering from smallpox. Notwithstanding the unwise assertions irresponsible enthusiasts will continue to make from time to time, what was a justifiable cause of public alarm has been removed by experiments on the transference of cancer from one animal to another, and on the housing of large numbers of cancerous with sound animals over a prolonged period. It has



been demonstrated completely that artificial transference from animal to animal is due to the implantation of living cells. This is a factor which does not come in at all in reference to the frequency of spontaneous cancer in man or animals. In corresponding observations on mice suffering from spontaneous cancer no case of transference has occurred.

In this respect cancer presents a marked contrast to other diseases—*e.g.*, tuberculosis—equally widely disseminated and common to man and the whole vertebrate phylum, for although no race of mankind is exempt, and cancer extends down the vertebrate scale to marine fish living in a state of nature, there are the most striking limitations to its communication from one individual to another. There is no connecting link, as it were, between the disease as it presents itself in nearly allied species, nor yet even in individuals of the same species. There is nothing which, while foreign to the animal body, is nevertheless common to cancer wherever it occurs. There is nothing equivalent, *e.g.*, to the characteristics of tuberculous tissues which, no matter what the species of animal, are stamped with unmistakable common features by the presence of the tubercle bacillus. The properties of the tubercle bacillus obscure all the natural properties of the tissue containing it, and they confer upon such tissue new properties essentially the same in all species of animals. Tubercular tissue has common properties in all animals; the distinctions of species, and of individual tissues of one and the same species, are submerged in their acquirement of a new property, conferring on them the power of conveying the disease to previously healthy tissues, not only from one animal to another of the same species, but also to others of different species. The tuberculous *tissues* themselves, however, die when transferred to a new



animal; they do not grow, they merely hand on the cause of the disease, viz., the bacteria, which continue to grow in new soil. How, then, is the pervasion of the animal kingdom by cancer explicable? It is intelligible because experiment has proved that cancerous tissues retain, not only the characters of the species of animal, but also those features distinguishing the several normal tissues of an individual, and because the general conclusion from comparative and experimental investigation is that cancer arises *de novo* in each individual attacked, by a transformation of healthy tissue, one case of cancer having no relation to any other. This general conclusion is based upon observations and experiments of very varied but confirmatory nature.

When a piece of cancer-tissue of a mouse is implanted into another mouse, certain of the cells continue to grow in the new animal and others die. The cells which continue to grow are the cancer cells proper. The other cells which die formed the scaffolding of supporting connective tissues and blood-vessels. The process of transference can be repeated *ad infinitum*, the powers of growth of the cancer cell being inexhaustible; they set at defiance the laws determining the specific sizes of the bodies and the organs of vertebrates, and determining the specific duration of the lives of different vertebrates. The cancer cells retain their characters unaltered in the course of artificial propagation, and the connective tissue scaffolding, supplied afresh by each successive host, remains identical with that which the cancer cells had in the animal where they originated. This scaffolding is called forth by the cancer cells themselves, and is of the nature of a specific reaction on the part of the ordinary connective tissues and blood-vessels of the host. The scaffolding is characteristically different for different tumours, and, as will be stated



below, the cancer cell is unable to continue to live and grow without it. The propagation of cancer is only possible in animals of the same species—*e.g.*, from mouse to mouse, or rat to rat, but not from mouse to rat or *vice versa*.

Since the limits to transplantation are the same as those which limit the transplantation of normal tissues—*e.g.*, the grafting of skin—the facts are of themselves evidence that cancer tissue contains nothing extraneous to the animal in which it appears. The distinctive differences in the new scaffolding which different tumours even of the same organ—*e.g.*, the mamma—re-acquire after every transplantation are inexplicable on the assumption that the tumour cells contain a common virus endowing them with their peculiar properties. Thorough investigation of questions of metabolism has shown the relations of a tumour to its host to be merely those of nutrition, similar to those of the foetus *in utero* to its mother. More than seventy transplantable tumours of very varied nature have been studied in the laboratory, and the above facts hold for them all.

The features of growth and of histology exhibited by different spontaneous tumors remain distinctive in the course of continued propagation, and they give weighty indications of the nature of the changes responsible for the acquisition of cancerous properties, since there is neither progress to a uniform histological structure nor a gradual advance to the exhibition of uniform biological behaviour, nor acquisition of a uniform rate of growth. The transformation of normal into cancer cells really covers a scale of changes which do not pass into one another. Permanent features are stamped upon cancer cells at the outset. There is no transition from one degree of the cancerous change to another.

In the transplantation of a tumour into a new host,



success or failure is determined primarily by two factors. These are the qualities of the tumour cells, and the nature of the "soil" the new animal offers. During continued propagation, the cells of the tumours of a single organ—*e.g.*, the mamma—exhibit other differences corresponding to those mentioned above with reference to the "supporting" scaffolding, and together with them pointing still more strongly to primary qualitative differences in the cells of different tumours. Although cancer occurs spontaneously mostly in old animals, young animals are more suitable for growth. The introduction of a minute particle of cancerous tissue into a normal animal leads to all the consequences which accompany the growth of a spontaneous tumour. Thus the adequacy of the assumption with regard to man, that the origin of cancer is primarily circumscribed, is demonstrated. A consideration of all the results proves that the genesis of a tumour and the growth of a tumour are two different things.

The "soil" which different races of mice offer, as it were, for the growth of cancer varies naturally in suitability; but tumours can gradually or rapidly adapt themselves to a soil which was unsuitable; *e.g.*, when a Danish tumour was first transplanted in England it grew in only 5 per cent. of the mice inoculated, but later the success rose to 90 per cent. There are natural constitutional conditions which are favourable, and others which are unfavourable, to the growth of a tumour. The unfavourable conditions act as sieves, permitting certain kinds of cells to pass, and once they have passed they can multiply beyond our powers of measurement.

The "soil" can, however, also be modified experimentally. It can be made absolutely unsuitable for growth, or rendered more suitable than normal



Mice and rats can be rendered unsuitable for growth only by vaccinating them with malignant new growths of their own species, and by vaccinating with *normal* tissues of their own species. In the latter case the degree of "resistance" normal tissues produce directly corresponds to the closeness of the relationship between the normal tissue vaccinated and the tumour subsequently inoculated; *e.g.*, skin protects best against skin cancer. These facts refer us back again to the limitations to the transplantation of tumours, and together with them demonstrate the retention, by malignant new growths, not only of the tissue characters of a species, but also of the biochemical as well as of the histological characters distinctive of the several species. A sarcoma of a rat or cat, vaccinated into a mouse, lacks the power of protecting it against subsequent inoculation of a mouse sarcoma; this fact shows, as clearly as the method permits, the absence of any extraneous agent common to the growths of these different species. The growths of different species of animals resemble one another just as much, and differ just as much, as their respective organs and tissues do. As differences exist in certain properties of tumours already alluded to above, so corresponding other differences are revealed by the extent to which tumours, when vaccinated, induce protection against one another. A tumour does not vaccinate so well against other tumours as it does against itself or against those of its own kind. A lesser degree of protection which one kind of mouse-tumour induces against other kinds is due, probably, not to cancer-tissue as such, but to its properties *qua* mouse-tissue.

Animals which are absolutely protected against inoculation do not yield a serum which, when introduced into new animals, has a power of protecting them against



inoculation; still less is there any evidence of immune sera having a power to cure animals of tumours already growing. Highly immune mothers do not transfer immunity to their offspring as do animals immune to diphtheria or other poison of infective disease. Indeed, the mechanism of the protection which can be induced against cancer is of a kind quite unknown before. Most painstaking observations have been necessary to penetrate somewhat into its nature. Artificially protected animals do not supply the cancer cell with the peculiar scaffolding of supporting tissues it requires in order to grow into a tumour. It dies because it cannot grow into an organised tissue, and hence cannot nourish itself; being damaged, it falls a prey to the natural guardians—the phagocytes—of the body. The process is the same whether vaccination has been made with cancer or with normal tissue. The way in which this protection becomes general in the body fluids or tissues has not yet been fully ascertained; nevertheless, so far as it is known, it helps to elucidate the spontaneous healing of primary and secondary growths in man, and its further study gives promise of our being able ultimately to enhance the powers of resistance of the body to a degree which will prevent the dissemination of a primary growth.

Before so much can be attained there are many difficulties to be overcome, not the least of which is the discovery of the fact mentioned above, that the soil may be rendered more than normally suitable for the growth of cancer. Hypersensitiveness can be induced by many different agencies; indeed, as contrasted with the induction of protection, it is not specifically induced.<sup>1</sup> The

<sup>1</sup> The variety of the agents which render an animal hypersensitive for the growth of cancer acquires added interest when regarded in association with the variety of causes of chronic irritation related to the development of cancer in mankind, as referred to above.



growth of one tumour does at times make the "soil" of an animal more favourable for the growth of a second tumour, and therefore, presumably, for dissemination. It is much more difficult to protect an animal already bearing a tumour against the transplantation of a second tumour than it is to protect an animal which has not already got one.

Animals spontaneously attacked with cancer make efforts, which are sometimes successful, to cure themselves both of primary and of disseminated growths; *e.g.*, in the vessels of the lungs. There is no longer room for scepticism regarding the statements which have been made from time to time of similar occurrences in man. The process of spontaneous healing is much more common in animals bearing transplanted tumours. In their case it can be studied in great detail, and it has been found to follow the same course as in man. A weighty factor contributing to its occurrence resides in the properties of the cancer cells themselves, for it has been discovered that they multiply with unequal rapidity at different times. They alternate regularly between positive and negative phases of growth. They are much more vulnerable to attack in the negative phase; *e.g.*, through the heightened unsuitability or resistance which can be induced in the soil as described above. The further study of the relations obtaining here will ultimately assist us to prevent a primary tumour from disseminating and establishing offshoots in remote parts of the body.

A startling phenomenon has been stumbled upon during the artificial propagation of epithelial malignant new growths (carcinomata). In the course of time some of these tumours have been replaced by connective tissue new growths (sarcomata). There is no question of the conversion of epithelial into connective tissue cells.



All the facts point to the acquisition of cancerous properties by what were previously normal connective tissues, viz., cells of the supporting scaffolding or "stroma." It appears probable that in this way malignant new growths have been produced for the first time experimentally. The development of sarcoma in this way occurs in circumstances throwing much light upon why cancer in man is so frequently associated with chronic irritation, as referred to above, and resulting continuous or intermittent attempts at regeneration and repair in man. Together with other facts, notably the differences in incidence of cancer in different races of mankind as determined by the application of irritants to different parts of the body, it gives the *coup de grâce* to the generalisation of the idea that cancer is of congenital origin.

Many new facts recorded above are of fundamental importance in enabling us better to comprehend the nature of cancer. Two factors have been proved to be of prime importance in its development; one is the alteration within a circumscribed area of what were normal into cancerous cells, either under the influence of unknown causes in the body itself or through the mediate intervention of diverse external chronic irritants, which may be actinic, chemical, bacterial, mechanical, in short, are legion; the other factor is the constitutional condition of the living body which may favour or hinder growth of the limited number of altered cells into a tumour. Extensive observations on inbreeding stocks of cancerous mice show that inborn predisposition plays only a very subsidiary, if any, part in determining both the one and the other; both are acquired. Cancer is a foe to all men, and the liability to it being in all probability acquired may ultimately be found to be avoidable.



A sudden revolution of all former views on the nature and treatment of cancer has not been effected. Much of the knowledge inherited can be utilised, much of it must be discarded. I have not dwelt on the initiative, the sacrifices, and the patient toil of my colleagues Bowen, Cramer, Gierke, Haaland, Murray, and Russell, nor on the enlightened and generous encouragement of the executive committee of the Imperial Cancer Research. It will be evident to all who read my colleagues' papers in the report how much they have contributed to raise the British national investigations of cancer to the premier position among similar institutions abroad. I have not made reference to work by other distinguished investigators, but full credit is given to them in the report itself. Slowly feeling the way from one certain step to another has often simply meant being met by new and unsuspected difficulties. Each hitherto unsuspected difficulty when overcome has, however, brought us more nearly face to face with the realities of cancer genesis, cancer growth, and the natural means by which the body protects itself against them ; they all are better comprehended and nearer solution to-day than ever before.

E. F. B.



The first part of the history of the United States is the history of the colonies. The colonies were founded by Englishmen who had come to America in search of a better life. They were at first dependent on England for everything they needed, but as they grew in number and power, they began to assert their independence. They fought the Revolutionary War and won, and in 1776 they declared their independence from England. The second part of the history of the United States is the history of the Union. The Union was formed by the joining of the thirteen original states. It was a great achievement, and it has since been the foundation of the United States. The third part of the history of the United States is the history of the present. The United States has grown in power and influence, and it is now one of the most powerful nations in the world. It has fought many wars, and it has won many victories. It has also made many mistakes, but it has always been able to learn from its mistakes and to move forward. The history of the United States is a story of progress and achievement, and it is a story that we should all be proud of.

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## YELLOW FEVER AND MALARIA

EVIDENCE GIVEN BEFORE THE ROYAL COMMISSION BY  
WILLIAM OSLER, M.D., F.R.S., REGIUS PROFESSOR  
OF MEDICINE, OXFORD

*Reprinted, by permission of the Controller of His Majesty's Stationery Office,  
from the Appendix to the Fourth Report of the Royal Commission, p. 157-159.*

*(The questions put by the Commissioners are printed in italics.)*

I THINK that the story of yellow fever illustrates, perhaps, more satisfactorily than any other, the remarkable way in which experiments, carefully devised and carried out, may influence not only our knowledge of the etiology of a disease, but may influence extensively the commercial relations of nations, and save not only thousands of lives but millions of pounds annually. Yellow fever has been the great scourge of the regions round the Caribbean Sea, more particularly Mexico, the West Indian Islands, Brazil, and every few years it has spread into the Southern States of America, and occasionally has reached Philadelphia, and even as far north as Boston. In the early part of the last century on several occasions it reached Europe, and there were extensive outbreaks in Spain, costing some thousands of lives. Many attempts had been made to find out the cause of the disease, but all had failed up to the year 1900, when a Commission was sent to Havannah by the United States Government, especially to investigate the cause of yellow fever.



That Commission, composed of Drs. Watten Read, Carroll, Lazear, and Agramonte, recognised particularly the relations of the mosquito to the disease, and they went out with the specific object of determining, if possible, to discover the germs of the disease. The experiments which they devised were carried out in a United States Army Camp in Havannah, and they are among the most remarkable that have ever been made. The camp was entirely isolated, so that there could be no possibility of communication with the outside. It was composed of a certain number of immunes, that is to say, persons who were no longer susceptible to yellow fever—

*In consequence of having had it, do you mean?—*  
In consequence of having had it—and of non-immunes. That is a common division of the population in Brazil and Havannah—namely, into immunes and non-immunes. A man is asked whether he is immune or not.

*Does one attack confer immunity as a rule?—*One attack confers immunity. In this camp a house was constructed with two compartments, divided from each other by a wire mosquito-proof screen. There were two sets of experiments made in connection with this little house. In the first place, into one side of this hut, 15 infected mosquitoes were placed. Those were mosquitoes that had bitten a yellow fever patient within the first three days of illness. Men were selected, partly from the Army and partly from civil life, who had expressed and signed their willingness to submit themselves to experiments. I may state that one or two of the medical men also volunteered. Into the compartment with the 15 mosquitoes a non-immune went in the morning, in the afternoon, and on the



following morning, and submitted himself to the bite.

*For an hour, or something of that kind?*—I do not know how long, but long enough to get a number of bites. Within five days he had the disease. At the same time, in the adjacent compartment, which was simply screened from these mosquitoes by a wire netting, for 21 consecutive nights two non-immunes slept. They did not get the disease.

*Were any precautions taken to keep the ordinary mosquitoes from them?*—Yes, of course; the compartment was double-doored and very carefully screened, so that there was no possibility of that. I may say that experiments of that nature were repeated on several occasions, demonstrating quite conclusively that, so long as these infected mosquitoes were kept from biting, though there was only a screen between them, the individuals did not get yellow fever. Then experiments were made on a very extensive scale to determine whether the disease was conveyed by fomites, that is to say, whether, as was usually supposed, the disease was carried by infected clothing and by the excreta of the patients and by the vomit. For that purpose the clothing and material soiled by the vomit and by the blood, and by the stools of the patients, were placed in one of these rooms, and a group of non-immunes slept in contact with this clothing, in some cases between the actual sheets of the beds in which these patients had died, for 21 consecutive nights. That experiment was repeated with a second set of non-immunes sleeping, as I say, with the bed linen and with the soiled materials of patients who had died of the disease. Not one of them took yellow fever.



*What were the numbers of the non-immunes that slept in connection with the fomites?*—I think two or three, two soldiers and one surgeon, for 21 consecutive nights; and a second party for the same period. Then these men were subsequently experimented upon by placing them in the section of the house with the infected mosquitoes, and in each instance they took the disease. Altogether twenty-two soldiers subjected themselves to the experiment and twenty-two took the disease; fortunately none of those cases proved fatal. One fatal case was a former assistant, Dr. Lazear, who had been for several years in charge of my clinical laboratory. He submitted himself to the bite of an infected mosquito, and three days subsequently developed the disease and died.

*May I ask what interval there was between the exposure to the fomites, and individuals being put into the place with the infected mosquitoes?*—Some days, possibly weeks, intervals: I cannot say exactly.

*What is the incubation period of yellow fever?*—From three to five days. The mosquito to become infective must bite a patient within the first three days of the disease—*Of its having been in contact with the disease, do you mean?* I mean that the mosquito must bite the yellow fever patient within the first three days of the patient having the disease. The mosquito itself is not infective under a period of twelve days; the mosquito may bite an individual anywhere, up to the twelfth day after receiving the infection, without being infective; then it remains infective all through the rest of its life.

Of course, the interesting practical point comes out, that this series of experiments has already revolutionised



life in those regions. Havannah within the next two years was cleared of yellow fever, the first time in the 300 years of its existence. The French Academy sent a Commission to Brazil to study the disease, and they have reported in harmony with the American Commission—namely, that the disease is transmitted by the mosquito, and by the mosquito alone, and only by a mosquito that had bitten yellow fever patients within the first three days, and that the mosquito did not become infective until after ten or twelve days subsequently.

*I think in yellow fever the transmission of any organism from the mosquito to man has not yet been followed out?*—No, we do not know the organism; but it must be a protozoon, possibly a spirochæte, which undergoes a slow evolution in the body of the mosquito.

*But nothing has hitherto been discovered comparable with the plasmodium of malaria?*—No, but it is possible that it is a very minute spirochæte, which passes through an ordinary filter.

This is the kind of discovery that will revolutionise conditions of life in the tropics. The discovery of the malarial parasite, and the discovery of relations of yellow fever with the mosquito, will enable the Panama Canal to be built. Without those two investigations, the probability is that it could not be built. *Or, if built, would cost a tremendous sacrifice of human life?* It would cost an enormous sacrifice of human life, just as happened with the French. Now, there are 20,000 whites on the Isthmus at work; of course, nearly all of those are non-immune. There has been practically no yellow fever, and what is much more important, because



it was not the yellow fever that killed the French to the same extent, there is no malaria.

*In these experiments that you have been detailing to us, animals do not come in; the animal experimented upon was man?—*That is so, only as man is an animal. I am referring to those experiments only as an illustration that it is through the experimental side of medicine, the experimental spirit in medicine, that these great revolutions have been effected, revolutions with which there is nothing else in human endeavour to compare from the standpoint of humanity. There is not anything else in the whole development of the British nation that is going to have so much importance as the discovery of the mode of transmission of malaria. It is going to make the tropics habitable. And all this has come about through the experimental method and the experimental spirit. Without these, such investigations could not have been made, and these perfectly phenomenal results could not have been achieved. It was the same spirit that gave us anæsthesia, and the same spirit that has given us antiseptic surgery, and the same spirit which has given us preventive medicine—three things which stand out in the record of human achievement, with which nothing else may be compared—I mean from the standpoint of everyday, common humanity.

*Then your contention would be that this experimental investigation, into the interaction between the mosquito and man producing yellow fever, would never have been thought of, if it had not been for previous experiments on animals?—*Never. The men who made these investigations spent their lives in laboratories, and their whole work has been based on experimentation on animals. They could not otherwise, of course, have



ventured to devise a series of experiments of this sort.

*Could you experiment with yellow fever on animals?*

—Yes, recently Wolferston Thomas, from the Liverpool School, working in Demerara, I think, has shown that it is capable of transmission to one of the higher anthropoid apes.

*Do the natives take yellow fever?*—Yes, everywhere ; but they often have it in such a mild form, and have it as children. *Still, even in that mild form, the mosquito would transmit it?*—Yes.

*I understand that when the mosquito has once bitten a patient suffering from yellow fever, after the first ten or twelve days it remains capable of transmitting the disease during its short life?*—Sometimes it is a comparatively long life—many months. *Has that been determined?*—Yes, it will live through many months ; it will live through the winter.

*As the fever has disappeared in Havannah, may I ask whether the special stegomyia mosquito has also disappeared?*—No, they have made an active warfare against it, but I think the mosquito itself has not disappeared. *But if the mosquito is capable of transmitting the disease during its existence, after it has bitten a patient suffering from the disease, how can you get rid of the disease, so long as the mosquito lives?*—That is only a matter, I think, of eight or nine months. I do not know definitely what the life of a mosquito is. I do not think it is more than over the succeeding winter.

*Is there anything further you wish to add about yellow fever?*—No, I think not. The work in Brazil



lately has shown that even in large centres, like Rio, by the mosquito brigades thoroughly carrying out measures such as were introduced in Havannah by Gorgas, the reduction in mortality and in the number of cases has been very striking. *By taking steps to prevent the breeding and multiplication of mosquitoes?*—Yes, and by carefully reporting and carefully isolating the very earliest cases I look forward to the total abolition of yellow fever within five years, and that, from the commercial standpoint alone, will revolutionise the trade of those districts. Every few years that a terrible epidemic arrives and spreads, New Orleans and the Southern States, and the commerce of the whole country, has been paralysed for long periods.

*How do you account for the epidemic's rise and fall, because the mosquitoes were always there and the yellow fever on which they feed is always there?*—That is the difficult point; it is not easily explained. It depends very much upon how large the immune population is. The greater the proportion of non-immunes, the heavier will the epidemic be, because in a city like Havannah every non-immune within a year of his arrival there took the disease—he could not escape.

*Now that you have discovered that the mosquito is the cause, how do you ensure protection against it?*—By screening the houses properly and scouring out all the pools and protecting the water tanks. *By destroying the habitat of the insect?*—Yes, and particularly in Havannah, by covering up and protecting the water tanks, and by the active energetic fight against the mosquito which has been made so successfully. *Then the object is the extirpation of the mosquito?*—Yes.

*The mosquito does not fly very far, I suppose?*—Some of them go long distances, particularly when



carried by the wind. Then of course, they are carried by ships, and get into the holds, and get from one country to another in this way. *Is it not the case that in the mosquito which is connected with yellow fever the changes from the egg to the complete insect occur very rapidly?*—Very rapidly. *And also that its breeding places especially are not running waters or large pieces of water, but small pools, and even the water left in hollow utensils, which are not thrown away around private houses?*—Yes.

*Might I ask, has there been at present any distinct diminution in the multiplicity or numbers of mosquitoes?*—Yes, in all these regions, particularly where an active crusade has been waged, as in Havannah, in cleaning out these places where they have been breeding. *They have become diminished in number?*—Yes.

*I suppose they never swarm as the midge does in this country?*—Oh, yes, they do, and even in the cities, in countless myriads. *Is it held to be possible to exterminate them?*—Yes, I do not think there is any question about it. It has already been done in many places. Ross worked at that in Ismailia; and even in the West of India, under the most unfavourable conditions, the reduction in the numbers of mosquitoes has been very remarkable.

*Do you suppose that if it were a fact that disease of a serious nature could be communicated by the midge in England or Scotland, their numbers could be seriously attacked and diminished upon the moors and bogs, and places where they swarm?*—In the immediate neighbourhood of houses it could be done. A thing which has been demonstrated, parallel with that,



is the reduction in the number of cases of malaria. Take, for instance, a place called Sparrow's Point, in Chesapeake Bay ; within the last five or six years, since we have known how malaria was transmitted by the mosquito, the number of cases has been diminished almost to vanishing point there, entirely by clearing up the pools and waging war against the mosquito. There has been a remarkable reduction in the cases of malaria there. *The mosquitoes, of course, have been diminished too?*—Yes. *Are those pools the breeding places?*—Yes. This discovery is making Africa, of course, habitable for the white man. Many of the young men who have been out on the recent scientific expeditions have by carefully protecting themselves lived for years there without having an attack of malaria.



## THE EXTINCTION OF MALTA FEVER

BY SIR DAVID BRUCE, K.C.B., F.R.S.

### INTRODUCTION.

THIS short pamphlet has been written at the request of the Research Defence Society, to assist in bringing to the mind of the public the necessity of animal experiment in the investigation of human diseases. In it will be described the various steps in the study of Malta fever which led up to the discovery of its mode of spread, and so to its prevention and extinction. It will be shown that the success of this work depended altogether on experiments on animals. Without them the Malta garrison would still be groaning under the incubus of this fever. This island, situated as it is in the middle of the sunny Mediterranean, should be the healthiest of places. On the contrary, it was one of the most unhealthy of foreign stations, and was feared alike by officers and men. Now all this has been changed. The naval and military hospitals in Malta are almost empty, and the island has become, as it was meant to be, the healthiest of garrisons. This has been done by the experimental method, and by the experimental method alone, without which there cannot be any true or safe advance in our knowledge of human diseases.



## HISTORICAL.

This fever has been studied in various ways for the last quarter of a century, but it was not until 1904 that the Government, alarmed by the great wastage in men, took the question up, and asked the Royal Society to undertake a thorough investigation of the matter. This the Royal Society agreed to do, and early in the summer of the same year sent out to Malta a Commission for this purpose. The work was carried on for three years before the discovery was made which led to the extinction of the fever.

It seems a pity that this research was not undertaken twenty years earlier, as during this time some 14,000 or 15,000 soldiers and sailors have suffered from the disease.

## DESCRIPTION OF MALTA FEVER.

At the outset it will be necessary to give a short description of this fever.

Malta fever is no trivial complaint, but is a severe and dangerous disease, which lasts a long time, and is accompanied by a good deal of pain. Our soldiers remain under treatment in hospital with it on an average for 120 days, and it is by no means uncommon for a patient to suffer almost continually from it for two or even more years. During the whole course of his illness the patient is apt to suffer from severe rheumatic pains in the joints, and neuralgia in various nerves, and this, combined with the long-continued fever, brings about a condition of extreme emaciation and weakness, from which recovery is slow.



## THE EXTINCTION OF MALTA FEVER 199

In order to show to what a degree of emaciation a few weeks of this fever may bring a man, the photograph of a soldier who has been suffering from it is here reproduced (Fig. 1).

### INCIDENCE OF MALTA FEVER IN THE GARRISON.

Among the soldiers, who number about 7,000, there have been on an average 312 admissions to hospital every year from Malta fever alone, and among the sailors about the same number. This means that 624 soldiers and sailors have been treated in hospital 120

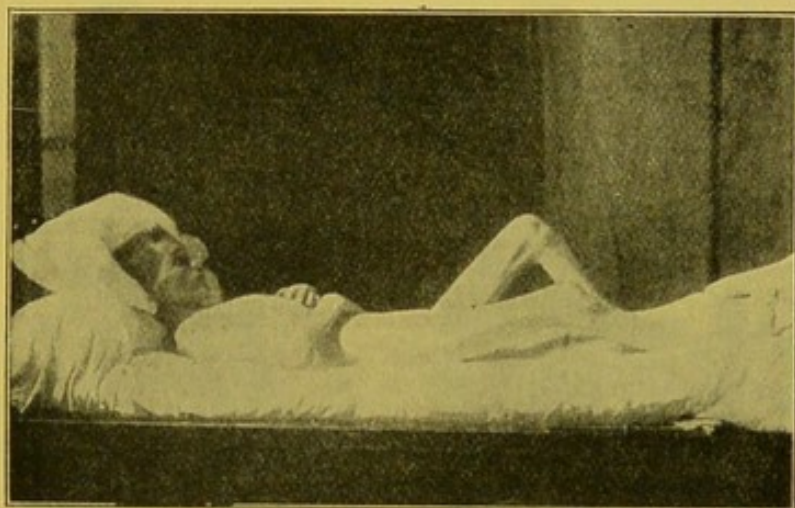


FIG. 1.

days each, which makes about 75,000 days of illness per annum.

The accompanying diagrams (Fig. 2) show the number of admissions to hospital for Malta fever among the soldiers. The first diagram gives the average for seven years (1899 to 1905), and it will be seen, for example, that on an average 18 men were admitted to hospital each January and 45 each August. The average number of admissions for these years is 315. But this represents a low average, as some of these years were occupied by the South African war, when



most of the regiments were away on active service, their places being taken by the so-called Garrison Regiments, composed of old seasoned soldiers. The second diagram shows the number of admissions to hospital among the soldiers for one year (1905). This reaches the startling number of 643, the best part of a regiment, incapacitated by this fever alone. During

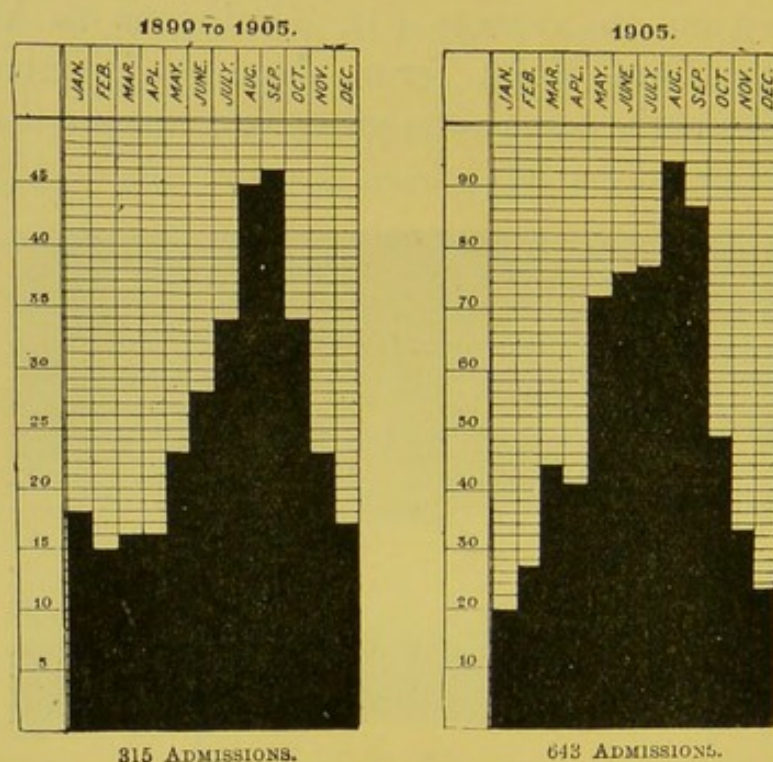


FIG. 2.--Charts of Incidence in 1899-1905 and 1905.

the same year as many as 403 officers and men were invalided to England as the result of Malta fever.

No wonder, then, that our soldiers looked on Malta as a place to be avoided.

#### STUDY OF MALTA FEVER FROM THE EPIDEMIOLOGICAL POINT OF VIEW.

Before this fever was studied by the modern experimental methods, many years had been spent in trying



to arrive at a knowledge of its causation by the old statistical methods. Doubtless a good deal of light may often be thrown on the natural history of a disease by these means, but in this case they completely failed to solve the problem. The epidemiologist asks himself in what parts of the world the disease is found; under what conditions of climate; whether any connection can be made out between it and the temperature or rainfall; whether age or sex renders a person more liable; whether occupation or social position has any bearing on it; whether a difference in sanitary conditions has any effect, as, for example, Do people living in small villages without any proper system of water-supply suffer more than those living in towns supplied with pure water and a modern drainage system? Of course, all these questions can be answered without having recourse to animal experiment.

In a short paper such as this, it is clearly impossible to enter in detail into this side of the subject, but a few facts, some of which greatly puzzled the old workers, may be stated.

*Geographical Distribution.*—For example, it is interesting to know that Malta fever is not confined to Malta, but occurs in most parts of the world.

*Climatic Conditions.*—Then, again, in regard to the effect of climate. Malta is extremely hot and dusty in the summer, and correspondingly cold and wet in winter. But, although the number of cases of Malta fever do show an increase in summer, yet it is a disease which is prevalent all the year round, one-third as many cases occurring in the coldest and rainiest months as in the hottest and dustiest.



Another fact of importance is, that if we study the occurrence of Malta fever in individual years, we are struck by its irregularity, a number of cases appearing in December or February or other of the cold and rainy months.

*Social Position.*—Another curious fact in regard to this disease is, that the better the social position of a person the more risk is there of catching this fever.

**MALTA FEVER IN THE GARRISON**  
**RATIO per 1000.**  
**1897 TO 1905**

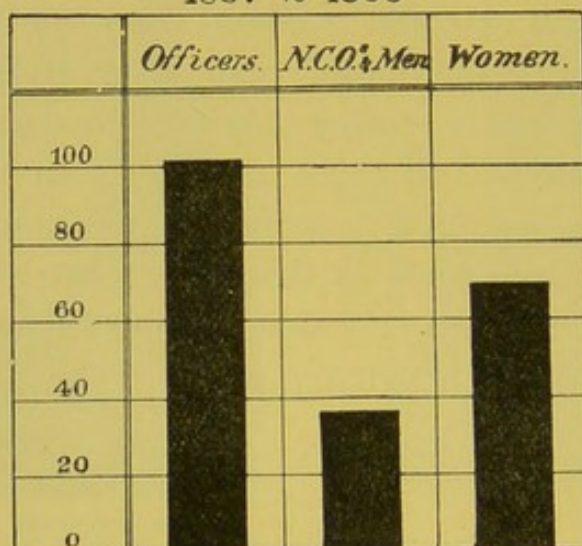


FIG. 3.—Incidence in Officers, Men and Women, for 1897–1905.

Officers and their wives and children, living in large, airy and clean houses, suffer more frequently than the rank and file in their more crowded barrack rooms. In fact, the chance of a naval or military officer taking this fever was more than three times as great as in the case of the non-commissioned officers and men.

The above diagram (Fig. 3) shows the incidence of the disease, from 1897 to 1905, among officers, N.C.O.'s and men, and women.







disease in Malta is very striking. It is not the cities round the Harbour which are struck most heavily, some of the inland towns and villages showing a much higher fever-rate.

This is illustrated by Fig. 4, where the number of cases is represented by different-sized squares. The larger the square the larger the number of cases of Malta fever, reckoned, of course, in proportion to the population of the town or village.

It will be seen that the squares representing Valletta, Cospicua, Senglea and Vittoriosa, the cities surrounding the Grand Harbour, are much smaller than the squares representing some of the inland towns; and so the supposition that the poison which causes this disease was generated in the Harbour was exploded.

#### SUMMARY OF EPIDEMIOLOGICAL EVIDENCE.

What, then, was learned from the study of this fever by the old statistical method?

It was found that Malta fever depends on no local conditions, as it occurs in many parts of the world. It could not have any great dependence on climatic conditions, as it occurs in the cool and rainy months almost as frequently as in the hot, dusty and rainless. Poverty and insanitary surroundings do not predispose; in fact, the well-to-do classes were shown to be more liable to take the fever than the poor. It has no connection with water supply or systems of drainage, as it breaks out as frequently in the smallest country village as in the large cities.

What, then, is the cause of this fever? The epidemiologists could give no answer to this question. They were sure the fever could not be traced to water,



or any food-stuff and so on, or any kind of dwelling, so they remained satisfied in thinking the disease was caused by some air-borne poison.

#### STUDY OF MALTA FEVER BY THE EXPERIMENTAL METHOD

*Discovery of the Parasite.*—Let us therefore approach this problem from the modern experimental side. The first step to be taken is to discover if any parasite or micro-organism is associated with this fever. To do this we examine the blood and the tissues of the various organs, both microscopically and by means of culture on various media, to find out if anything can be seen or grown. The blood and various organs are also inoculated into different animals to ascertain if any of them will take the disease. This is to try and discover if there is anything in the blood or organs which when injected into a healthy animal will give rise to symptoms resembling the fever under investigation.

In this way, as long ago as 1887, it was discovered by an Army medical officer that a minute living organism, to which the name of *Micrococcus melitensis* was given, is the cause of this disease.

*Description of Micrococcus melitensis.*—There is not much to be said about this micro-organism, except that it is very minute, only becoming visible under a magnification of 1,000 diameters.

But it is very important at the outset of an investigation such as this to be quite sure that the parasite found in the tissues is really the cause of the disease, and is not there by accident. If the history of malaria, yellow fever, sleeping sickness, and many other diseases



is studied, it is surprising to find how often scientific men were misled by finding organisms which they thought to be the cause of the disease, but which, on further knowledge, were found to have nothing whatever to do with it. This is especially true in the investigation of diseases to which human beings alone are susceptible. Happily, in the case of Malta fever, one of the lower animals, the monkey, is also susceptible, and so it could be made quite certain by animal experiment that this micrococcus is the true cause of the disease. Monkeys injected under the skin with this organism develop symptoms similar to those of Malta fever in man, and if they die or are killed their blood and organs are found to be swarming with the *Micrococcus melitensis*.

Without this animal experimentation it is often quite impossible to know whether a particular micro-organism is or is not the real cause of a disease.

#### CHARACTERISTICS OF THE MICROCOCCUS MELITENSIS

*Behaviour Outside the Body.*—Now, having found the micro-organism, it is necessary to study its characteristics.

It is found to survive outside the body for some time. For example, it can retain its vitality and virulence in a dry condition in dust or on clothing for at least two or three months. It can also live in a moist condition, in water—tap-water or sea-water—for a somewhat shorter period. This power of retaining vitality and virulence is proved by the injection of the various substances under the skin of susceptible animals, and the setting up of the disease. One important thing noted was, that the *Micrococcus melitensis* does not increase outside the



body, it merely survives for some time, and then dies off; and that, if exposed to direct sunlight, it disappears in a few hours.

Many attempts were made to discover it outside the body, under natural conditions. As the generally accepted theory was that it was conveyed in air, naturally the air of fever wards or of places where cases had occurred was examined with great care. Here, again, animal experimentation comes in. When a parasite is too small and featureless to be recognised by the microscope, or so mixed up with other organisms as to render its recognition by cultivation improbable, then the injection of the mixed material into an animal will often show its presence by setting up the disease. It is in this way that the germ of consumption is found in milk. The suspected milk is injected into guinea-pigs, and if this disease is set up, then the milk is condemned. Up to the present time, no other way has been discovered of testing milk for this germ of consumption.

So in the search for the germ of Malta fever in the air of fever wards, or of drains or sewers, a large quantity of the air was drawn by a suitable apparatus through water, and this water was afterwards tested on animals. If the animal showed symptoms of Malta fever, then the air contained the *Micrococcus melitensis*; if not, then the air was free from this micro-organism. In the same way it was looked-for in the dust of suspected places, and in the water of the Harbour, but with no success. It was evidently a parasite which depended on some warm-blooded animal for its continued existence.

Thus, then, the first important step in the discovery of the way to rid our garrison in Malta of this fever had been taken. The cause of the disease was known and could be recognised without difficulty when met



with, so that now an attempt could be made to find out where human beings got it from.

The next steps in the investigation were to find out how this micrococcus leaves and how it gains entrance to the body.

#### HOW DOES THE MICROCOCCUS MELITENSIS LEAVE THE BODY?

In regard to this, it is conceivable that it might leave the body by way of the expired air, in the saliva, in mucus from the lungs, as in consumption, in the secretion of the skin, as in scarlet fever, in the renal secretion, or by way of the intestinal tract. Or it might leave the body by way of the blood, by the agency of mosquitoes or other biting flies. Many inoculation experiments on animals were made along all these lines, and it was decided that this micro-organism leaves the body principally in the renal secretion, and in the blood taken out of the body by blood-sucking insects.

The result, therefore, of this experimental work was to give rise to the belief that the disease was conveyed from the sick to the healthy either by personal contact, or by inhalation of infected dust, or, lastly, by the agency of mosquitoes.

#### HOW DOES THE MICROCOCCUS MELITENSIS GAIN ENTRANCE TO THE BODY?

The investigation of these various modes of infection was therefore undertaken.

Let us first consider infection by contact. Experiments were made by placing monkeys, one affected by Malta fever, the other healthy, in more or less intimate contact, and it was found that if the monkeys lived



together in the same cage infection did take place. If, on the other hand, the monkeys were kept in the same cage, but separated by a wire screen, so that, although they could touch each other, contamination of the healthy monkey's food by the sick monkey could not happen, then infection did not take place.

In regard to this question of conveyance by contact, there is one argument against it which has always seemed to me unanswerable, and that is, that thousands of cases of Malta fever have been invalided home to England, and treated in our naval and military hospitals without, so far as I am aware, a single case of the fever arising among the patients, orderlies, or nursing sisters.

It was therefore concluded that mere contact with Malta fever patients is not the mode of infection.

Then the question of infection by contaminated dust was taken up.

*By Dust Contaminated by the Micrococcus melitensis.*—For some time it was considered highly probable that this would prove to be the common method of infection. The fact that the micrococcus withstands drying for a long time, the dusty nature of Malta, and the probability that gross contamination of the surface of the soil takes place by infected discharges, rendered this view likely.

Experiments were made to put the theory to the test. Dust was artificially contaminated with the micrococci of Malta fever and blown about a room in which monkeys were confined, or blown into their nostrils or throat. Several of these experiments were successful. It was therefore proved that dust *artificially* contaminated with *Micrococcus melitensis* could give rise to the disease.



This, however, was no proof that this mode of infection occurs in Nature. The artificially-contaminated dust contained myriads of micrococci. Under natural conditions, they could seldom be numerous, and the powerful Maltese sunlight would tend to kill them off rapidly. The dust blown about by the wind must also dilute the micrococci to an enormous extent, so that it is only possible to conceive of a micrococcus here and there in a vast quantity of dust. Experiments were therefore made with dust naturally contaminated, in order more closely to resemble natural conditions. Dust contaminated in this way, and also that collected from suspicious places and blown about the cages, sprinkled on food, or injected under the skin of the experimental animals, always gave negative results.

The conclusion was therefore again come to that conveyance of the infective germ to human beings by means of contaminated dust could only rarely, if ever, take place.

*By Mosquitoes or other Biting Flies.*—As already mentioned, the theory has been strongly advanced that Malta fever, like yellow fever and plague, might be conveyed by blood-sucking insects. The fact that the micrococci are almost always found in the blood drawn from the skin gave some colour to this belief. This point was therefore fully investigated and numerous animal experiments made with the different species of mosquitoes found in Malta, and also with other blood-sucking insects.

The results, again, were all negative, and it was therefore decided that Malta fever is not conveyed by contact, by contaminated dust, or by mosquitoes.

What, then, could be the mode of spread?



*By way of the Alimentary Canal.*—It had long been known that the smallest quantity of the micrococci introduced under the skin or applied to a scratch would give rise to the disease in man or monkeys, but some work by previous observers had led to the belief that infection did not take place by way of the mouth in food or drink. They had fed monkeys on milk, in which they had mixed the micrococci, and asserted that in no case did infection take place. This observation kept the Commission at first from making feeding experiments. As infection, however, did not appear to take place by contact, by the inhalation of infected dust, or by mosquitoes, it was clearly necessary to repeat these feeding experiments.

#### FEEDING EXPERIMENTS.

The table on the next page shows the result of some of these feeding experiments, and it will be seen that it is abundantly proved that Malta fever can be conveyed to healthy animals by way of the alimentary canal. Even a single drink of a fluid containing but a few of the particular micrococci almost certainly gives rise to the disease.

From the result of all these experiments, then, it seemed most probable that the poison of Malta fever gains an entrance to the body by way of the mouth, and therefore by some infected food or drink.

This led to an examination of food-stuffs, and among these the milk of the goat is one of the most important in the island.



TABLE. (FIG. 5.)

Species of Animals.	Mode of Infection. M. = M. melitensis.	Probable time which elapsed before infection took place. In days.	Result. Infection. + - No infection.
Monkey.	Feeding on potato containing M.	30	+
"	" " "	31	+
"	Accidental feeding	"	+
"	Milk and M.	"	+
"	Dust and Malta fever urine. Dried	"	-
"	" " "	"	-
"	Dust and Malta fever urine. Moist	"	+
"	Potato and M.	"	+
"	" " "	"	+
"	" " "	"	+
"	" " "	"	+
"	Milk and M.	"	+
"	" " "	"	+
"	" " "	"	+
"	" " "	"	+
"	Culture of Malta fever	"	+
"	" " "	"	+
"	" " "	"	+
"	" " "	"	+
"	" " "	18	+
"	" " "	32	+
"	" " "	"	-
Kid.	Milk	"	-
"	Goats' milk	"	-
Goat.	Culture from milk	"	+
"	Malta fever urine and dust	"	+
"	" " "	"	+
"	Milk and culture	"	+

## INFECTION BY MEANS OF GOATS' MILK.

The goat is very much in evidence in Malta, and supplies practically all the milk used. There is, it is said, one goat to every ten of the population, so that, as there are 200,000 inhabitants, there must be about 20,000 goats. Flocks of them wander about the streets from morning till night, and are milked as required at the customers' doors (Fig. 6).



It must be confessed there seemed little hope that an examination of these animals would yield any result. The goats appeared perfectly healthy, and they have the reputation of being little susceptible to human disease of any kind.

To put the matter to the test, however, several goats were inoculated with the micrococcus, and the result watched. There was no rise of temperature and no sign of ill-health in any way, but in a week or two the blood was found to show signs of being infected by Malta fever.

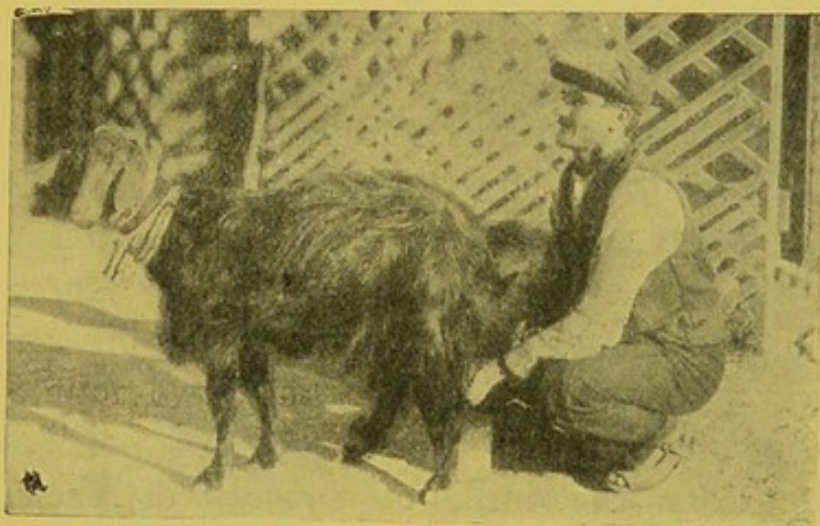


FIG. 6.—Milking Goat.

This raised suspicion, and a small herd of apparently healthy goats was then procured and their blood examined to see if they were all healthy. Several of them were found not to be beyond suspicion, and this led to the examination and the discovery of the *Micrococcus melitensis*, not only in their blood, but also in the milk of the milch goats.

#### THE POISON OF MALTA FEVER IN GOATS' MILK.

Some thousands of goats in Malta were then examined, and the astounding discovery was made that



quite half of them were affected by Malta fever, and that actually 10 per cent. of them were secreting and excreting the poison in their milk.

Monkeys fed on milk from an affected goat, even for one day, almost invariably took the disease.

S.S. "JOSHUA NICHOLSON."

At this time, curiously enough, an important experiment on the drinking of goats' milk by human beings took place accidentally. Shortly, the story is as follows: In 1905 the s.s. *Joshua Nicholson* shipped sixty-five goats at Malta for export to America. The milk was drunk in large quantities by the captain and the crew, with the result that practically everyone who drank the milk was struck down by Malta fever. Sixty of the goats (five having died) on arrival in America were examined, and thirty-two found to be affected, while the deadly *Micrococcus melitensis* was isolated from the milk of several of them. This epidemic of Malta fever on board the s.s. *Joshua Nicholson* therefore clinched the fact, that the goats of Malta act as a reservoir of the poison of Malta fever, and that human beings are infected by drinking the milk of these animals.

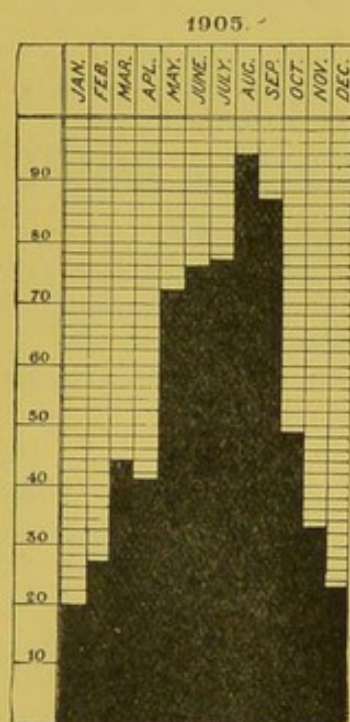
Here, then, at last was discovered a mode of infection which explained the curious features of Malta fever—the irregular seasonal prevalence, the number of cases which occur during the winter months, when there are no mosquitoes and little dust. It is true there are more cases in summer than in winter, but this may be explained by the fact that more milk is used at that time of the year for fruit, in ice-creams, etc. It also explains the fact that officers are more liable



than the men, as the former consume more milk than the latter. It also explains the liability of hospital patients, milk entering so largely into a hospital dietary.

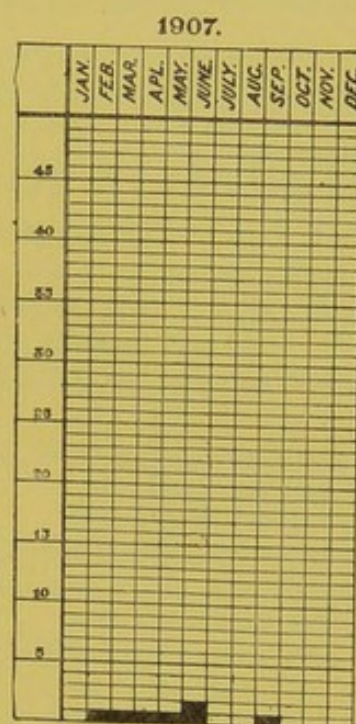
### RESULT OF MEASURES DIRECTED AGAINST THE USE OF GOATS' MILK.

As soon as goats' milk was discovered to be the source of infection, preventive measures were begun.



643 Cases.

FIG. 7.



7 Cases.

FIG. 8.

Incidence of Malta Fever in Malta during 1905 and 1907.

The result is very striking, as is shown in the diagrams (Figs. 7 and 8), which give the number of cases of Malta fever among the soldiers in the garrison before and after the preventive measures came into force.

Fig. 7 represents the incidence of Malta fever in 1905 among the soldiers before the preventive measures



were put into force, while Fig. 8 shows the number of cases of this fever which have occurred among the soldiers in Malta since goats' milk has been banished from their dietary.

In conclusion, I have no hesitation in asserting that this happy result, this blotting out every year of 75,000 days of illness, this extinction of Malta fever from our garrison in Malta, could never have been accomplished without the aid of animal experiment.



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