THE APPLICATION OF RESEARCH RESULTS TO ANIMAL HEALTH AND DISEASE CONTROL

By

SIR THOMAS DALLING

(Consultant of the Food and Agriculture Organization of the United Nations Rome, Italy)

THE term "research" has a wide meaning and application, and it must not be thought that research work is confined to the laboratory. For many research projects, laboratory work, sometimes on an extensive scale, is essential but, on the other hand, it must not be forgotten that the observations made in the field, the testing out of ideas and the practical application of the results of laboratory work are all included in the term "research". Sometimes research work on problems of animal health and disease actually begins in the field and is extended and brought to fruition by the close collaboration of field and laboratory workers. Field observations are of the greatest importance to veterinarians whose activities are concerned mostly with laboratory work. Because of their clinical training, they themselves may actually make the initial observations leading to the development of ideas, which, in turn, give rise to the initation of research work on extensive lines.

Fundamental research work is highly valuable and the results may have far-reaching influences on many subjects, including problems which seem far removed from those for which the original work was undertaken, even the control of animal disease.

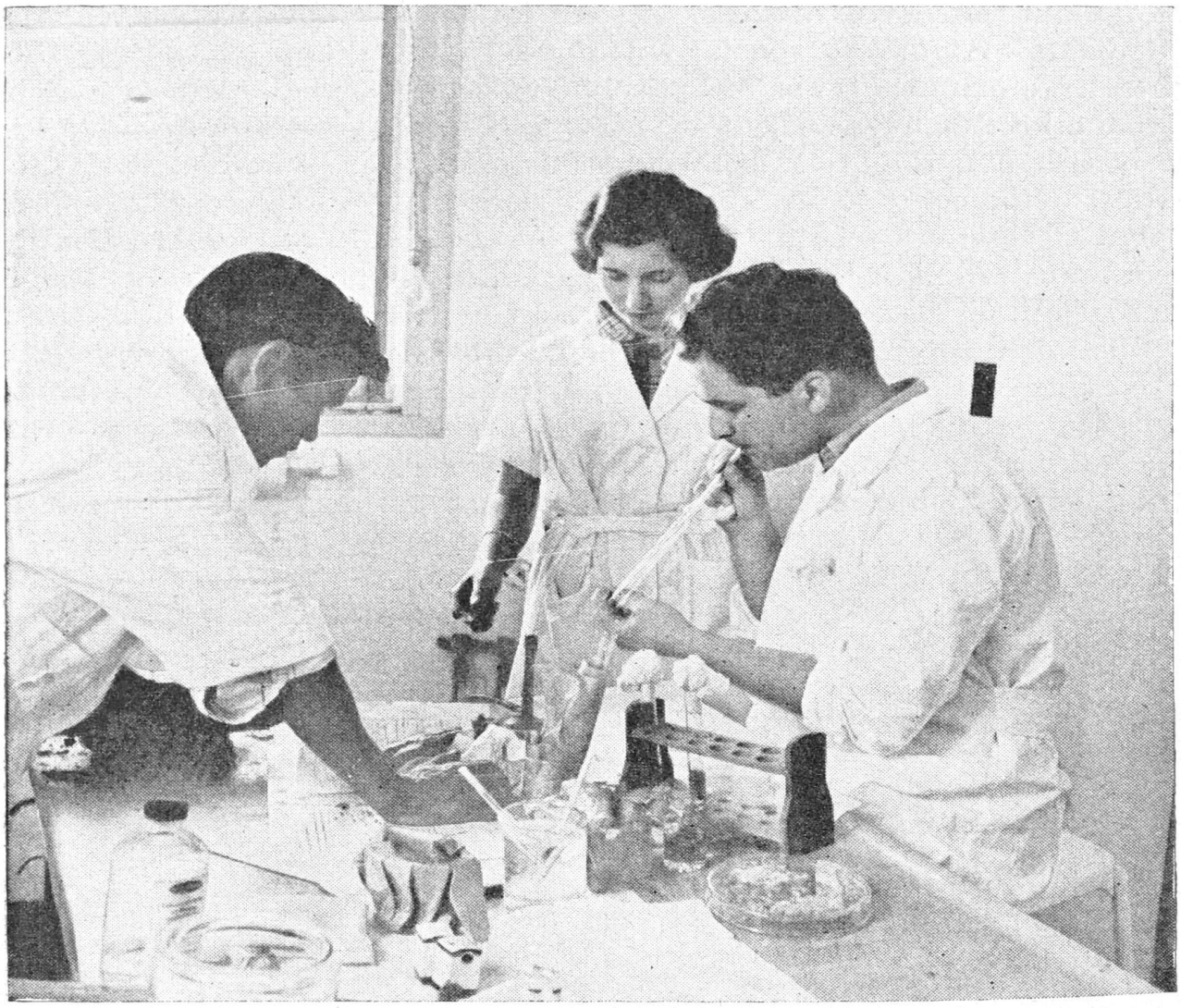
The results of some of the original research work carried out by veterinarians have been applied to the solutions of problems in other branches of science and veterinary medicine has gained much from reseach work in general. Many of the present problems on animal disease control will be solved only by research carried out by teams of workers trained and experienced on special subjects : veterinarians have an important place in such teams.

There is a close linkage between human and veterinary medicine and many of the results of research work applicable to the human subject can, with necessary modifications, be applied to animals. Some of the newer methods and techniques used today in improving human health are the results of research work carried out in animals : new developments in human surgery and anaesthesia would not have been possible within so short a time without research work on some types of animals.

In this article there will be given some examples of the application by veterinarians of the results of research work.

Improvement in animal production throughout the world is closely related to breeding the types of animals most suitable for their required purpose, feeding them in such a way that the maximum conversion of the food into the desired animal product will be obtained and improving their health and preventing disease so that animals so bred and fed will be capable of providing the expected results in production.

The use of artificial insemination in the breeding of animals especially cattle, is one outstanding example of the application and rapid practical development of the results of research work. Techniques in which the artificial vagina is used for obtaining semen from bulls, handling, storage and dilution of semen so obtained and a knowledge of the oestrus cycle from which the optimum time to inseminate was found, have led to the adoption of artificial insemination as a successful method of breeding in many countries. The advantages of artificial insemination are so obvious that they only need a passing mention : the use of bulls of desired qualities for producing large numbers of improved offspring ; dispensing with the purchase and maintenance of bulls in breeding herds ; improvement of low-producing animals in less-developed areas ; and the practice of more detailed control of infertility which is now considered to be a part of the artificial insemination service in many countries. The rate of progress in the adoption of artificial insemination must, of necessity, vary in different parts of the world. In countries in which free-range, especially on an extensive scale, is the common method of keeping cattle, it may be possible only to use artificial insemination on a limited scale for, say, the breeding of special males for use in the future. On the other hand, in milk-producing herds and even in beef-producing animals kept under more controlled conditions, there has been a very rapid expansion of this method of breeding : for example, in Denmark it is stated that nearly 100 percent of cattle are so bred, in Holland some 65-70 percent, in England 50-60 percent and in the United States the figure for milking cows is given as 31 percent which is included in the total of nearly 8 million cows inseminated annually. The more recent



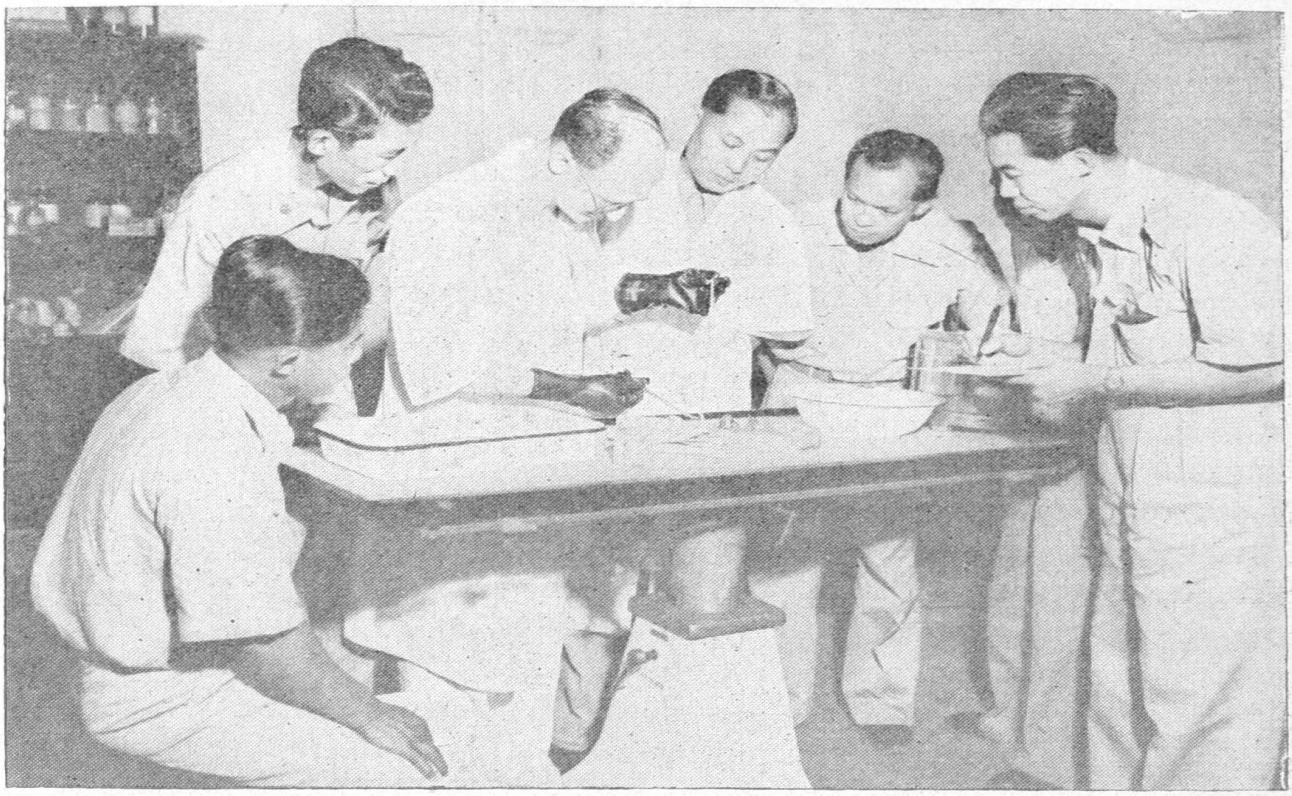
Block 17—Vaccine production in Honduras.
Photo by courtesy F.A.O. Rome.

discovery that semen can be successfully stored at low temperature for several years is an advance of such magnitude that the future possibilities of breeding satisfactory cattle in almost any part of the world is assured. Careful consideration has, of course, to be given to the selection of the most appropriate bulls, as far as possible including progeny-testing, as well as to the application of the most severe tests to ensure the freedom of the bulls and the semen from any agent likely to cause transmissible diseases in the inseminated females. Veterinary supervision of the health of the bulls is absolutely essential and although not carried out in all countries today, veterinary supervision of all the aspects of artificial insemination is a legal condition of its practice in some other countries. It is common now to include sexual hygiene and the control of infertility in artificial insemination services in some countries, the necessary examinations and treatments being carried out by veterinarians.

Research work on animal nutrition is receiving much attention throughout the world. Much of this work has to be done by individuals and teams of workers specially trained in the many aspects of the subject. Veterinarians are intimately concerned with the effects which introductions of new feeding systems and feeding stuffs may have on the health of animals. It sometimes happens, for example, that the earliest evidence that a pasture is deficient in some essential element or that a system of feeding is at fault, is reflected in the clinical health of animals. Much of the research work on deficiencies and excesses of trace or minor elements arose from field observations and the results of much of the research work in remedying these conditions was left to the observations of veterinarians in the respective areas. Veterinarians are greatly assisted by research workers in the many problems appertaining to nutrition. A veterinary research laboratory today would be very incomplete without a team of biochemists, some of

Block 18— Vaccination against Rinderpest in Ethiopia.
Photo by courtesy F.A.O. Rome.

whom are veterinarians, whose special work concerns research into the causes of ill-health in animals related to nutrition. Hypomagnesaemia or " grass tetany " is an example of a condition which, in some seasons, causes much concern especially to dairy farmers. The disease is associated with a fall in the blood magnesium levels, the actual cause of which has not yet been determined. It occurs on pastures which have a relatively high magnesium content and thus, although the recognised amounts of magnesium may be present, there apparently exists some mechanism whereby they are not available or are not in a satisfactory state to meet the requirements of the animal tissues. Research work has shown that the daily consumption of two ounces of calcined magnesium will probably prevent the occurrence of the condition, if fed for a period beore animals are given access to a pasture in which hypomagnesaemia is likely to occur. The daily feeding of this medicament is stressed, for it has been found that a single large dose given soon before turning the animals on to the pasture does not prevent the disease. It has also been shown that top-dressing of pastures with magnesium compounds is beneficial : the condition under which the compounds should be applied and the amounts to be used vary with circumstances, and advice on the subject should be obtained. Copper deficiency in lambs causes the disease known as " enzootic ataxia " in Australia and as " swayback " in Great Britain : the condition is characterised by lesions in the brain of affected lambs consisting of cavities, often present at birth, which should contain white matter. The feeding of copper sulphate to the pregnant ewes prevents the disease. A deficiency of the amount of cobalt in the pasture, necessary for the formation of vitamin B12 in the rumen of sheep occurs in some parts of the world. The intensity of infestation with worms in the alimentary tract is sometimes related to this deficiency. The addition of as small an amount as 0.1 parts per million of cobalt in the diet provides all the requirements. Excess of molybdenum in feeds or in pastures, especially on soil composed of peat where there is a deficiency of copper, may cause poisoning in cattle, sheep and goats. The feeding of small amounts of copper sulphate as well as the application of fertilizers containing small amounts of copper to the grazing land prevents the condition. Vitamin deficiencies may give rise to diseases in animals. In nutrition of poultry they may be marked and cause serious trouble. Vitamin A deficiency, for example, interferes with normal growth and egg production with the occurrence of recognisable symptoms and lesions, while deficiency of vitamin D interferes with the normal metabolism of calcium and phosphorus leading to abnormal bone development or rickets in young growing birds even although the diet contains adequate amounts of



Block 19—Diagnosis of Poultry Diseases
Photo by courtesy F.A.O. Rome.

these elements. These are but a few examples of the results of research work on the nutrition of animals, the application of which is improving animal health and animal production.

Research work is resulting in many improvements in our knowledge of the causes, distribution, prevention and treatment of diseases of animals. The list is long : only a few examples can be given but they will serve as illustrations of veterinary activities in this direction. Serological tests are in daily use for diagnosing some of the important animal diseases : the nature of the test varies with the type of infection. They show the presence of substances in the blood, produced by tissues of the infected animal in efforts to deal with the invading agent. One of the simplest of the serological tests demonstrates agglutinating anti-bodies in the serum of infected animals. The test is widely applied, for example, in the detection of " carriers " of pullorum disease among breeding fowls and in the diagnosis of *Br. abortus* infection in cattle.

Research work has resulted in the application of the test by rapid methods actually on poultry farms when only a drop of whole blood, instead of blood serum, from individual fowls, is used by the " rapid " or " slide " method and " carrier " birds, diagnosed on the spot, can be disposed of at once. While sero-agglutination tests have been and

are widely used in diagnosing brucellosis, research work has led to the now well-known ring or ABR test on samples of milk in which a blue-stained emulsion of *Br. abortus* is added to the milk. A positive reaction is shown by the appearance of a blue ring, consisting of the cream to which the agglutinated coloured organisms are adhering, which rises to the top of the sample. This test is valuable for screening infected herds, the finding of a positive reaction in mixed samples of milk from a number of animals being followed later by the application of the sero-agglutination test to samples of serum from individual animals to detect those actually infected. There is now in existence an international standard anti-*Br. abortus* serum against which national standards can be tested for use as control sera in agglutination tests. Recommendations on the techniques of carrying out the tests and the interpretation of the results have been made in order that there may be uniformity in the results reported in different countries : this seems necessary in connection with the export and import of live cattle.

Sero-agglutination tests are also used in determining the actual type of salmonella and leptospira infecting animals. In the test for such purposes, cultures of the organisms recovered from the infected animals are used and stocks of the sera, known to cause agglutination of the different types, are prepared and kept in readiness for use in the tests.

Sometimes for the diagnosis of some diseases it is necessary to carry out more elaborate serological tests than the simple agglutination test : for example, the complement-fixation test used in the diagnosis of dourine in horses and the conglutination test in the diagnosis of Johne's disease. An interesting and important extension of the use of the agglutination test for the diagnosis of trichomonias and genital vibriosis in cattle followed an understanding of the stage of the oestrus cycle when agglutinating substances are present in the vaginal mucus, which is used in the test instead of blood serum.

The diagnosis of bovine tuberculosis in cattle has been much improved by the results of research work by biochemists, in the production of tuberculins in a higher state of purity than those formerly used. Investigations into the nature and extent of reactions following the intradermal injection of appropriate amounts of purified tuberculins, prepared from mammalian and avian cultures of the tubercle bacillus, are assisting in the differentiation between sensitivity to tuberculin due to bovine tuberculosis and that arising from other types of tubercle bacilli and other micro-organisms. In the research work, veterinarians have played an outstanding part.

Notable advances in the control of some diseases of animals have followed the application of research results to the production of

vaccines from viruses passed through animals of less susceptibility than that of animals commonly infected, and the conservation of such " attenuated " vaccines in a freeze-dried condition. There are several examples, two of which are now referred to.

One concerns the control of rinderpest (cattle plague). In earlier days, protection against the disease was accomplished by the use of serum from cattle which had recovered from the infection, the injection of which was followed by protection for a comparatively short period ; or by injecting infected blood and controlling the resulting infection by the simultaneous injection of protective serum, which resulted in immunity of long duration. Vaccines composed of inactivated tissue from artificially-infected cattle became available. While, on the whole, these methods gave good results, difficulties and inconveniences were experienced in their use. Research into the effects of passing the virus through animals other than cattle resulted in the production of virus in an attenunated state so that its injection did not set up the disease in cattle but was followed by high and lasting immunity. The goat was and still is used for this purpose and goat-attenuated virus is the most common vaccine now available. It was found, however, that passage through the goat did not render the virus sufficiently attenuated to prevent undesirable reactions in highly susceptible cattle and buffaloes in some countries. Rabbits and, later, developing chick embryos in fertile hen eggs, or a combination, were used for purposes of attenuation. The result of all this research work is that there are now available vaccines in states of attenuation likely to be satisfactory for immunising animals in almost any part of the world. The application of freeze-drying has resulted in the conservation of the virus in this form over long periods, its availability on demand and its easy transport in serviceable condition.

The production of vaccine for the control of Newcastle (Ranikhet) disease in poultry is the other example. The cultivation of the causal virus in the developing chick embryo is usually sufficient for its attenuation to a degree suitable for use for immunising fowls. This virus vaccine is also preserved and issued largely in a freeze-dried state. For very young chicks, the susceptibility of which may often be greater than that of adult fowls, a virus of natural low virulence is used in the preparation of vaccine.

The cultivation of cells of body tissues apart from the living body has been steadily developed over a considerable number of years and such cultures are now being used to grow disease-producing viruses. This method has been recently used for the cultivation of the virus of foot-and-mouth disease in prepartion of vaccine for the prevention of the disease in cattle. In preparing foot-and-mouth disease vaccine

plentiful supplies of suitable virus are required. For many years this virus was produced by infecting the tongues of susceptible cattle and harvesting the tongue membranes in fact, this method is still very extensively used. It was found, however, that if the cells in the deep layer of the covering membrane of the tongue were removed from the newly-slaughtered animal and placed in suitable nutrient material, there was still sufficient " life " in them to enable the virus of foot-and-mouth disease to grow in them : and so, a new successful method of cultivating the virus was introduced. The latest method is to use growing cultures of cells, kidney cell cultures being found suitable. Thus, by the application of results of research work, large amounts of the virus, found suitable for vaccine preparation, are now produced by methods which exclude the use of the living animal.

Some disease-producing micro-organisms form toxins which are the actual causes of the diseases. In animals, this is the position with many of the anaerobic bacteria, e.g., those causing tetanus (lockjaw) and especially some diseases of sheep. At one time it was thought that each of the different anaerobes produced one toxin only. Careful research work, however, showed that, given the necessary conditions, different toxins can be produced by the same organism. This was a big step forward in understanding the nature of some of the anaerobic infections of sheep and cleared up some of the reasons for failure in attempts to immunise animals against them. An outstanding example is the anaerobic organism which causes gas gangrene in man following the infection of wounds and which was responsible for so many casualties and deaths in the First World War. An apparently similar organism was shown to be associated with different diseases of lambs and adult sheep, viz., entero-toxaemias, in which its multiplication and toxin production takes place in the intestine. Research work showed that the organism which responded to many of the tests for that causing human gas gangrene had the power of producing a variety of toxins and that these different toxins were largely responsible for the different diseases of lambs and adult sheep. By further research work, much of which was carried out in veterinary laboratories, there were evolved vaccines which protected against either one or a mixture of the toxins : such vaccines are now in general use in controlling some of the diseases of sheep in some countries and are giving satisfactory results.

An interesting discovery was made in studying methods for protecting very young lambs against the disease lamb dysentery, in which the infection takes place and the disease becomes established during the first few days after birth. It was shown that lambs born

from mothers which had been vaccinated and had developed protective substances, were protected against lamb dysentery. One of the methods introduced to protect the young lambs against this disease was, therefore, to use vaccine on the pregnant sheep. The results were highly satisfactory. It had been quite generally believed that the protective substances developed in the mother passed to the lamb before birth. Research work showed, however, that transference of the protective substances did not take place before the lamb's birth but that they collected, in high concentration, in the ewe's udder and were thus readily available for the newly-born lamb in the colostrum. It was also shown that these protective substances were absorbed from the intestine into the lamb's general blood circulation during the first few days after birth and that, thereafter, little absorption took place ; and further, that as milk replaced the colostrum the amount of available protective substances gradually became less and less and they finally disappeared.

Much research work has been done on the preparation of vaccines for the production of immunity. Such vaccines must be safe to use and, at the same time, be capable of introducing a high degree of immunity. With some organisms, it was found that heating to a certain temperature for a definite period produced the required result. With some others, and with toxins, research work showed that treatment with a chemical agent was satisfactory and this led to the introduction of formolised toxins or " anatoxins " as immunising agents, followed later by formolised cultures or " anacultures ". Examples in vaccines used in animals are these for producing immunity against some of the diseases caused by toxins formed by anaerobic organisms. Although formalin is largely used for inactivation purposes, research work is continuing with other chemical substances which, it is hoped, may give even better results. Research also showed that by absorbing anatoxin or anaculture to a chemical substance, the injected material was slowly released from the site of injection and that this caused steady production of protective substances by the responsible mechanism in the body. Hence, a number of vaccines in use today, including those used for protection against some virus diseases, consist of the inactivated absorbed toxin, bacteria or virus. Some virus-vaccines, as already mentioned, consist of the virus in a living but attenuated state, the attenuation having taken place naturally or by artificial means, e.g., passage through another species of animal.

The many aspects of research work are, of course, being continued all the time. New medicaments, including antibiotics, are being fully tested and used to full advantage when found suitable and satisfactory

in the control of animal diseases, e.g., in mastitis in cattle associated with certain micro-organisms. Antibiotics and other new drugs together with new operative techniques have made possible surgical work, often major in character, in all species of animals—operations which, at one time, were thought impossible to carry out.

Following upon research studies, much progress has also been made in our knowledge of reproductive disorders in animals and their control.

This progress concerns not only infectious diseases, transmitted venereally, but has been made from the results of study of the genital systems and the influence of the many substances secreted by glands and other tissues, on the reproductive organs and their functions. It is now possible to restore many animals with impaired fertility, at one time believed to be permanently sterile, to normal breeding capacity. Much of the present-day information on the subject relates to cattle. Infertility in sheep is also receiving attention. An example is the research work in New Zealand which has shown that the widespread infertility in rams is caused by infection of the genital organs with an organism of the brucella group, peculiar to sheep. The infection is mostly transmitted from rams to ewes at mating and, in turn, infected ewes transmit the disease to healthy rams. In addition to impaired fertility in rams the infection is responsible for abortion in ewes and deaths in lambs at about the time of their birth. Recent work shows that this disease in rams can be prevented by the use of suitable vaccines before the breeding season.

Studies of the life cycles of parasites is leading to a better appreciation of the stages of development at which it is most convenient to apply measures to prevent further development, taking into account control of any intermediate hosts and the most appropriate time to use drugs to destroy the parasites within the host. The recent work on the immunisation of calves against lung-worm infection by the injection of the worm larvae partly inactivated by "X" irradiation opens up a new and important field in the control of some internal parasites.

These few examples illustrate the part played by research work in the development of measures for the control of animal diseases. They also show the part which veterinarians are taking not only in the application of the results of research work but also in the studies themselves.