RESEARCH IN ANIMAL GENETICS.*

BY

SIR EDWARD SHARPEY-SCHAFER, F.R.S., P.R.S.E.,
PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF EDINBURGH.

THE Animal Breeding Research Department at Edinburgh was established some ten years back to investigate the principles which should govern the breeding of animals employed in agriculture. The first step was to select someone to carry out and direct research on the subject—no easy task, and our choice was fortunately fixed on the present director, Professor F. A. R. Crew, who had already made a name for himself as an authority on genetics. As a result the department has already become an unqualified success, not only in the objective sense, as manifested by the buildings we are assembled to inaugurate, but much more in the personnel which the director has been able to gather round him, and in the work they have already effected.

Research Problems in Animal Breeding.

It might be thought that as the department was established for the encouragement of agriculture, and that the avowed object was to improve the breeds of animals used for agricultural purposes, the choice of a director would have fallen upon an agriculturist accustomed to the breeding of stock, who would surely have been best able to judge what results were required and how these could be arrived at. Those who hold this opinion would consider that in appointing a purely scientific man, with little or no experience in the breeding of farm animals, the committee made an initial mistake. But the breeding of animals, like all applied sciences, must be founded upon a basis of pure science. Moreover, it is essential that it should, like every other branch of science, be based upon experiment. Now it would be possible for experiments in breeding to be carried out on ordinary farm animals with a certain amount of success. But the length of time one has to wait for the result of experiment in animals which have a gestation period of many months greatly limits the number of experiments which can be made, and renders the progress of research very slow; moreover, from the interbreeding which has been going on for long periods in most domestic animals, the results may be uncertain. As a concrete example we may cite the Pencyuik experiments on telegony by Professor Cossar Ewart. By telegony is meant the influence exercised upon the mother by the foetus *in utero*. Not long ago every breeder in the country believed that if a female of pure breed was crossed by a male of the same species, but of another breed or of no breed at all, the resulting progeny would so influence the maternal organism that this particular female would never again—even if crossed by a male of exactly the same breed—produce pure progeny; that, for example, a mare of the purest blood would be permanently ruined for stud purposes if she were in foal to a stallion which had no pedigree behind him. The circumstance was thought to be proved by the observation of Lord Morton, communicated to the Royal Society in 1820, that a mare which had produced a hybrid foal to a quagga—a species of zebra—and was afterwards crossed by an Arabian horse, happened to produce a foal which exhibited distinct stripes: these stripes were supposed to have been caused by an influence exercised upon the mother by the hybrid foal *in utero*. The question of telegony was, however, definitely settled in the negative, so far as the equidae are concerned, by Professor Ewart, who crossed mares, first with zebra stallions, producing hybrids which showed distinct stripes, and subsequently with ordinary horse stallions. The progeny of the second crossing never showed signs of the zebra influence, although faint stripings were sometimes visible in the foals, but not more than in ordinary foals, in which stripings are sometimes noticeable—an indication that the horse had at one time a striped ancestor. These experiments took years to bring to a conclusion

and cost hundreds of pounds; but similar experimental results can be obtained in a comparatively short time by selecting small animals with short periods of gestation. Nor is it necessary to employ mammals alone for such experiments. For many purposes birds are even better adapted. And as the experiments of T. H. Morgan and others have shown, the laws which govern heredity and the morphological conditions which accompany and determine the transmission of bodily characters may be even more advantageously studied in certain invertebrate types, such as *Drosophila*. Nor are these laws essentially different in the animal and vegetable kingdoms. The law of heredity discovered by Mendel was the result of experiments upon crossing varieties of sweet peas. And of late years a vast amount of work of the same kind has been carried out on different kinds of plants, which in some particulars lend themselves even better than animals to the elucidation of the principles governing heredity. It may be added that these experiments illustrate the fallacy of the saying "*Natura non facit saltus*." Rather would it seem that nature frequently does work by leaps, and that intermittence is often the rule, continuousness the exception.

Application of Genetics to Man.

Just as the principles of genetics are applicable to plants as well as to animals, can they equally well be applied to man. I suppose that nowadays all educated persons admit that mankind is only the highest type of animal; and therefore that all laws which regulate the lives of animals, including those which determine heredity, apply equally to him. If we were able to use the knowledge acquired in breeding animals for the improvement of our own race, we might eventually succeed in eliminating much that tends to keep the race physically and mentally far lower than is desirable. At present all that we can do is to educate the individual. Much, no doubt, can be effected in this way, but education is useless unless there is an inherent power to be educated.

But civilization has not progressed enough to permit even an endeavour to promote amelioration of the race by breeding from the highest types. All that seems possible is the prevention of breeding from the lowest types. Unfortunately there is a grave risk of an inferior type becoming established, for it happens that the reproductive faculties are better developed in mentally inferior than in superior types. It is the object of eugenics to combat this downward tendency of the race, though how this predominance of the unfit can be prevented is a difficult and controversial problem. It is, however, a problem which urgently demands solution, since the future welfare of the human race hinges upon it.

Study of Sex Hormones.

The study of animal genetics depends in the main upon physiology: probably that is the chief reason why I have been asked here to-day. Particularly it concerns the physiology of the sex cells and the organs in which these are produced. The sex cells are not the only elements produced by the gonads. Both in the male and in the female there are other cells which exert a profound influence upon the organism. This influence is the chief cause of what may be termed "maleness" or "femaleness," these qualities showing themselves not only in the physical features characteristic of the respective sexes, but also in the psychical attitudes which are equally sex-distinctive. One of the most interesting advances in the science of genetics has been to prove that these so-called secondary sex characters—whether corporeal or psychical—are dependent, not on the sex cells themselves, but on the other cells just mentioned. These other cells, however, do not exert their influence directly, or even through the nervous system, but they manufacture specific chemical substances which are passed into the blood and, circulating throughout the organism, are brought into contact with every cell in the body. These chemical substances belong to the class known as autacoids; they either stimulate activity (hormones) or restrain activity (chalones). They are of relatively simple composition; some have been obtained in a crystalline form. The

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administration of extracts of the gonads to immature animals (or to animals deprived of their gonads) is followed by the development of the special secondary sex features, both physical and psychical, characteristic of the sex from which the extract has been obtained. The substances in question are zoologically non-specific; in other words, it matters not how different the species of animal from which they have been obtained, the same results are yielded as if they had been derived from an animal of the same species as that to which they are administered. From this it is clear that genetics involves the study not merely of the structure and functions of the sex organs, but also that of their chemical products; this branch of the subject is increasing in importance every day.

Genetics has, however, not merely to do with the activities of the sex organs themselves; it is concerned also with the effect upon them of the nervous system and of internal secretions other than those produced by the gonads themselves. It has been recognized from the earliest times that the nervous system exerts a profound influence upon the sex organs and is in its turn profoundly influenced by them. But it is a matter of comparatively recent observation that there are influences acting from outside upon the sex organs which are not nervous. We term such influences "humoral," indicating thereby that they are conveyed to the sex organs by the blood: in other words, they belong to the class of autacoids to which we have been alluding. Those of which I am about to speak, however, are not to be confused with the autacoids producing secondary sex characters, though some are also manufactured in the gonads. For example, the ovary manufactures hormones which cause ripening and discharge of ova and changes in the uterus which are not responsible for the development of the sex characters. That autacoids related to the reproductive function should be formed in the sex organs themselves is not an altogether unexpected result; but the remarkable observation has lately been made that the pituitary body produces autacoids which are carried by the blood to the ovaries, and excite the internal secretion of those organs so as to cause a ripening and discharge of ova and the accompanying changes in the uterus even in immature animals.

The story of the pituitary body is a real romance—with the distinction that there is nothing of fiction about it. Long known to be present in all vertebrates, its functions, like those of most of the internally secreting organs, were until recently unrecognized. But the clinical observation of cases in which the gland had undergone enlargement and in which there was overgrowth of the skeleton and of the body generally suggested that it might yield an internal secretion which is concerned with growth. This could be tested by experiments on young animals—experiments involving on the one hand administration of pituitary substance, and on the other suppression of the secretion by removal of the gland, or of the larger anterior part which is recognized as the part concerned with growth. If it is yielded to the blood in undue proportion growth may be so much stimulated that a giant is produced. On the other hand, if from any cause this internal secretion of the pituitary body is not passed into the blood or not in sufficient amount, growth will be arrested. Administration of this part of the pituitary has been found to increase the animals' size above normal, whereas destruction of the same part arrests growth and produces dwarfs. Whether there is also a material in the internal secretion of this or some other gland which actively prevents growth is not determined, but is not altogether improbable.

The internal secretion of the pituitary not only influences the general growth of the body, but especially the growth and maturation of the generative organs. A young animal deprived of its pituitary not only ceases to grow but remains infantile; its sex organs do not mature. On the other hand, the administration of anterior pituitary stimulates general growth, and especially the development and maturation of the gonads, causing an immature animal rapidly to mature sexually. In a young female pituitary will cause the production of ripe ova; this it does by acting as a stimulus to the internal secretion of the ovary itself,

causing that organ to produce those substances which in adult animals effect maturation of ova and their fixation in the uterus.

Direct evidence that the pituitary substances which thus act on the ovary are poured into the blood can be obtained. They happen to be present in larger amount during pregnancy than at other times. Their effect can then be got simply by injecting a few drops of blood from a pregnant female into a young female mouse. A short time after such injection the mouse's ovaries, which were very small and immature, become enlarged and exhibit unmistakable signs of maturation; the Graafian follicles become large and haemorrhagic like those which, in mature animals, are ready to discharge their ova. Even more remarkable is the fact that these substances do not remain in the blood of the pregnant female, but are got rid of by the kidneys, being passed into the urine, in which they occur in considerable amount. So that, instead of blood, a drop or two of urine injected under the skin of an immature female mouse will easily furnish unmistakable evidence of the existence of pregnancy, even at so early a stage that none of the ordinary signs of that condition is exhibited. This is known as the Zondek-Aschheim test for pregnancy.

Animal Experiment in Medicine.

Everyone can appreciate how important it may be to make an early diagnosis of pregnancy. Yet, by the laws of this country, no medical man is permitted to carry out the Zondek-Aschheim test unless he has a licence to practise vivisection, and even then he may only do so in a place registered under the Act. He must also obtain from the Home Secretary a special certificate permitting him to keep a mouse alive for the few days necessary to enable the result of the experiment to be observed. It happens that the laboratory, which we are now assembled to declare open, is at present the only one in the country which undertakes this duty, though, strictly speaking, the resources of an establishment intended to be devoted to research pure and simple should not be diverted to a routine method of diagnosis which might as well be done anywhere else and by any medical man who has been instructed in the method.

It seems still more extraordinary that hospitals should debar themselves from making such necessary observations. This applies not only to the diagnosis of pregnancy, but even more to that of diseases the rapid and efficient diagnosis of which depends upon experiments involving the inoculation of animals. But even when the hospital possesses a well-equipped laboratory experiments upon living animals, whether for diagnostic purposes or not, are usually barred by the authorities responsible for the administration of the hospital. Samples of blood, of morbid growths, of urine, must be sent away to be tested on animals; no such experiments are allowed under the same roof as the patient whose condition has to be diagnosed. The reason for such a state of affairs is only too apparent; it is due to apprehension that the subscriptions of antivivisectionists will cease to be forthcoming, and that the revenue of the hospital will suffer. On this account hospital authorities will not permit any part of the premises to be registered under the Act, or any operations, or even inoculations for diagnostic purposes, to be made on living animals. A mouse may not even receive a hypodermic injection, although the operation on the mouse may lead to the cure of the man. This is not only wrong in principle; it is not honest, and honesty is always the best policy. A hospital is provided for the treatment of disease, for which rapid and accurate diagnosis is of major importance. Considerations of finance or misapplied sentiment should never be allowed to override this fundamental principle. The time is long past when a surgeon was bold enough to declare that no experiments on animals had ever contributed to his knowledge or influenced his surgical procedures; the declaration merely showed his ignorance of the history of medicine, and of physiology, on which all medicine is based. The science of medicine, the operations of surgery, the action of drugs, the application of preventive and sanitary measures to the health of the community, are all bound up with animal experimentation. Even if the Secretary of State is opposed to experiments on animals, he cannot choose but issue permits for them, for he soon finds on

assuming office how essential such experiments are for the progress of medical knowledge and for the public health. The antivivisection societies have, and can have, no real influence; their propaganda will never prevent a sick person from calling on the services of a doctor whose knowledge is founded on vivisection.

It must be understood that all the work of this and kindred institutions is based upon vivisection. Literally the word means the dissection of living animals, and therefore every surgical operation is a vivisection. But technically and legally it means any experiment on a lower animal of any kind, whether by operation, or by injection, or merely by feeding. This definition of vivisection is not mine; it is that given by the Act of Parliament regulating the practice. No one can make any sort of experiment, whether it is painful or not, upon a vertebrate animal—even upon a fish or tadpole—without a licence from the Home Secretary. That is to say, provided the experiment is made to advance knowledge and not for sport. No farmer may test the effect upon his stock of a novel food without a licence; if he conducts such a test he makes an experiment for the purpose of advancing knowledge, and, if his animals suffer from the change of diet, he renders himself liable to prosecution. Thousands of experiments on animals are recorded every year and reported to Parliament by the inspectors under the Vivisection Act. At least 99 per cent. involve no operation; they consist merely of feeding, or at the most of hypodermic injection. By far the greater number are done in connexion with, and by the direction of, the Public Health Services of the country. All operations which involve incision are performed, like surgical operations, under profound anaesthesia; and if an animal is kept alive after operation it is treated in exactly the same way as a hospital patient, the only difference being that if the animal appears to be suffering pain it is killed painlessly by chloroform. We who experiment upon animals have every regard for the sufferings of animals, but we have a greater regard for the sufferings of humanity. Very appropriate, therefore, are the words which Professor Crew has caused to be carved at the entrance of this institute, which I now formally declare to be opened: "To the advancement of science and to the service of mankind this building is dedicated."

WATER POLLUTION.

ADVISORY COMMITTEE'S REPORT.

THE second report¹ of the Joint Advisory Committee on River Pollution, under the chairmanship of Mr. Herbert Brooks, with Dr. H. Maclean Wilson as medical member, deals with the reception of liquids from industrial and manufacturing processes into the sewers of local sanitary authorities. The growing tendency of factories to settle on river banks conflicts with the necessity of conserving all sources of water supply and with efforts to safeguard the amenities of life. No drastic measures are advocated by the committee. Easily adopted changes are considered advisable at present, and suggestions are outlined for new legislation.

General Legislation Regarding Trade Effluents.

The position of local authority and trader in regard to the disposal of trade effluents is regulated to some degree by the Public Health Act of 1875 and by the Rivers Pollution Prevention Act of 1876. The first required sanitary authorities to provide sewers to drain their districts effectively, and permitted any occupier of premises within the area to allow his drains to empty into those sewers. The second enacted that the sanitary authorities should afford facilities to manufacturers within the district to conduct to sewers the liquids resulting from their trade processes. No authority, however, was compelled to admit fluids potent enough to injure the sewers or to cause any sanitary trouble. Nor was it bound to allow these facilities if its

sewers were no more than adequate to the needs of the district. The two Acts were vague enough to create ambiguity as to what the trader might demand and the authority refuse. Legal opinion has made it apparent that the obligations of the sanitary authorities are defined by Section 7 of the Rivers Pollution Prevention Act, with the limitations already stated. But these limitations are so comprehensive that they almost cancel the general obligation, and they are so imprecisely framed that their intentions have sometimes been questioned. Moreover, the powers of the local authority in regard to expenditure and the fixing of conditions are uncertain; and agreements with traders willing to pay for facilities and observe regulations are inhibited by the fact that other traders may claim admission for their effluents without promising to observe the same conditions and without payment. Meanwhile other Acts of Parliament—for example, the Public Health Amendment Act of 1890—help to protect the sewers from liquids that are actually or potentially dangerous to health.

Trade Effluents and Local Legislation.

Local legislation and practice supplement with varying success the indications of general law. In some districts the position has been clarified by special legislation. Many of these local Acts cope with some special difficulty rather than deal with the general principle of right of access to sewers. But corporation Acts of a comprehensive kind prevail in seven districts, including Halifax, Huddersfield, Dewsbury, and Salford. The codes embodied in these statutes are evidently based on the third Report of the Royal Commission on Sewage Disposal, issued in 1903. Where they are in operation, their practical effect is to supersede Section 7 of the Rivers Pollution Prevention Act, and to substitute for it a more detailed machinery to regulate the relations of local authority and trader. They give the trader a definite right to discharge his effluent into the sewers, and impart to the local authority such powers and obligations of disposal as it already possesses in regard to ordinary sewage. They also authorize local authorities to co-operate with each other in the exercise of certain rights and duties. None of these provisions, however, affect the existing water rights of a riparian owner. This system assumes that the local sanitary authority should deal with trade effluents, and it appears to operate smoothly and effectively by working through discussion between the two parties.

Recommendations for New Legislation.

The committee is convinced that the general law concerning trade effluents is at present too indefinite. There is marked necessity for a new code, stating precisely the rights and obligations of the trader and of the local authority, uniform in application, but flexible enough to vary in detail to suit local requirements. The codes of the Huddersfield and Dewsbury pattern suggest the kind of general law required for populous cities. The central recommendation of the committee is that the local authority should everywhere accept the responsibility for the disposal of trade effluents. Its standard of purification will undoubtedly be higher and less expensive than in any system arranged by an individual trader. A single centre, under skilled and constant supervision, will protect the river more thoroughly than the independent control exercised by those whose interests are concerned with their products, and who can hardly afford a skilled supervisor. Besides, some effluents are best disposed of when diluted with domestic sewage. There are effluents, of course, which may be properly debarred from entering the sewer. Rivers bordered by a line of industrial works will need exceptional consideration. But no objection seems cogent enough to affect the recommendation that the local sanitary authority should receive and dispose of trade effluents as simply and as completely as it deals with domestic sewage.

¹ H.M. Stationery Office. 6d.