GENETIC RESISTANCE TO DISEASE IN DOMESTIC ANIMALS

F. B. HUTT

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BY FREDERICK BRUCE HUTT

Professor of Animal Genetics

New York State College of Agriculture

Cornell University

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Preface

THIS little book is the outgrowth of a series of lectures given at North Carolina State College in 1956. They, in turn, grew out of my interest for three decades in the desirability and feasibility of breeding domestic animals that can withstand ordinary levels of exposure to disease. As a result of our studies here at Cornell University, that interest, at first little more than commendable curiosity, has become a firm conviction that the biological fitness of domestic animals to cope with their environment, including disease, can be greatly increased by selective breeding.

It is true that my own work on resistance to disease has been limited to my favorite species. However, in order to inoculate my veterinary students, whose preferences among domestic animals rarely include the fowl, it has been an absorbing necessity to keep informed on genetic resistance to disease in all domestic animals. Accordingly, while I have faithfully exercised the scientific virtue of citing my own research without any subtle beating about the bush, it has been possible to supplement those citations in this book, as in my lectures, with a review of what little is known about resistance to disease in other animals.

If it should seem to the reader that too much of this book is devoted to a marshaling of the evidence that animals do differ genetically in resistance to disease and that too little of it deals with the actual practical use of that resistance, let him remember that the chief purpose of the volume is to provoke some thinking, perhaps some controversial discussion, and eventually more research. If it succeeds in attaining these objectives, those who write later and better books on the same subject will have more to say about applications.

I am indebted to my colleague Dr. R. K. Cole, who read parts of the manuscript and made many helpful suggestions. I shall also be indebted to any readers who may be so kind as to report any conspicuous sins of omission or commission.

It seems a pity to toss this little book to those ubiquitous and inevitable arbiters—the reviewers. It has about as much chance as a turtle trying to cross Chicago's Michigan Boulevard. The veterinarians are likely to condemn it because of its rank heresy and because the author, who is not a veterinarian, should not have ventured to write about disease. Similarly, the authorities in animal husbandry will probably tear it apart, page by page, because the author, a mere chicken expert, should have stuck to his field, which is clearly poultry and not animals. Animals, as defined by the administrators of agricultural colleges and of country fairs, are horses, cattle, sheep, swine, and goats, while poultry are chickens, turkeys, rabbits, and canaries. In defense against the impending onslaught, the author can plead only that he wrote the book because none of those others who should have written it seemed much interested in doing so. It is to be hoped that its critics will at least find it interesting.

F. B. Hutt

New York State College of Agriculture
Cornell University, Ithaca, New York
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Chapter I

Why and Wherefore

IT seems desirable to begin by stating some of the reasons that led to the writing of this book. All geneticists are interested in variation. Some of us are concerned with variation in domestic animals, particularly with their differing abilities to produce milk, butterfat, eggs, meat, wool, or work. To measure adequately genetic differences in productivity, one must provide an environment conducive to the best possible performance by the animals under study. That optimum environment must include some degree of physical comfort. This is often assured by some simple shelter from the elements, is sometimes improved in specially ventilated and air-conditioned quarters, and, if we can believe what we read in the newspapers, may occasionally be enhanced by the administration of soothing selections from the nearest broadcasting station. The food supply must be adequate, both in quantity and quality, for the purpose intended. Thanks to the good work of the experts in nutrition, there is now little difficulty in providing a satisfactory diet for most species, for most purposes, in most parts of North America.

Finally, if the animals are to demonstrate what their genes permit them to do in the way of converting feedstuffs to milk, meat, or eggs, it is necessary that they be plagued by no more bacteria, viruses, parasites, and other organisms than they can tolerate without adverse effects upon their normal physiological processes. Here the problem is not so simple.

It would be nice for the farmer if all pathogenic organisms could be eradicated, but attempts to eradicate them have not been uniformly successful. The prospects of our attaining this utopian state of affairs are no better than are those of paying off the national debt. Programs for eliminating bovine tuberculosis have apparently been successful in this country, and happily so because some human beings are susceptible to bovine tuberculosis. One wonders, however, to what extent the causative bacillus is still carried by deer, whether or not it will ever be feasible to stop testing, and, also, what may happen a thousand years hence if cattle, unexposed for that time, again encounter the organism.

Attempts to eradicate *Brucella abortus* have not fared so well as the campaigns against *Mycobacterium tuberculosis*. Blood-tested herds from which all reactors are removed remain "clean" for a time, but when reinfected as frequently happens, they seem unusually susceptible. The resort to vaccination, which is now the more common method of control, suggests that the earlier attempt to eradicate *B. abortus* was not too successful. Vaccinated animals can live with the organism. Some cattle are undoubtedly able to do so without protective vaccination, but unless and until whole herds are made genetically resistant vaccination will continue to provide effective control at comparatively low cost.

Chickens, vaccines, and genes. In other cases vaccination can be an expensive nuisance. To protect the author's White

Leghorns from the various respiratory diseases prevalent in his part of the world, a maker of vaccines advises the following treatments:

Against Newcastle disease: Three inoculations intranasally, or in the drinking water, by 16 weeks of age;

Against infectious bronchitis: Two treatments, which can be given along with two of those for Newcastle disease;

Against fowl pox: (*a*) vaccination once, in the web of the wing, or (*b*) pigeon-pox vaccine (in a feather follicle) followed 10 days later by fowl-pox vaccine;

Against laryngotracheitis: vaccination once, in the cloaca.

By these five to eight treatments, administered fore, aft, and amidships, the birds would presumably be protected against these four respiratory diseases. For a fifth one, infectious coryza, there seems to be no effective vaccine, and the usual recommendation when that strikes is to "depopulate" (i.e., market the whole flock), clean and disinfect the premises, leave them vacant for several weeks or months, and then start over with a new batch of chicks.

In addition to these five respiratory diseases, there is "chronic respiratory disease," which we are currently advised to eliminate by dosing our breeding flocks with antibiotics, so that they will not put the causative organism in their eggs. Should any chicks thus hatched free of that pleuropneumonia-like organism subsequently react to tests for it, they and the rest of the chickens in their pen can be slaughtered.

For the commercial poultryman some or all of these procedures may be indispensable if he is to remain in business with the kind of stock now available to him. Vaccines differ, however, as do directions for using them, and there is no assurance of complete freedom from respiratory diseases.

The author, having seen all six of these respiratory diseases go through his flocks at one time or another (fortunately not all at once), doubts that such elaborate protection is necessary. Certainly some birds need it, but others do not. While some hens die of these diseases, or stop laying, others in the same flock, in the same pen, are completely unaffected and continue to lay well. Can it be that they are not exposed? Not likely. It is much more probable that they are able to tolerate the infectious organisms, to resist them in some way, and thus to withstand a bit of the environment that may be disastrous to other birds.

Can the resistant birds be multiplied to produce a resistant strain? They can if their resistance is determined by their genes, and there is evidence that this is so. Within one breed two strains intermingled in the same flock can differ significantly in susceptibility to respiratory disease. Within a strain there can be remarkable differences among sire families in susceptibility. These facts show that heredity plays an important role in determining whether a bird will withstand disease or succumb to it.

To the best of the author's knowledge, no one has yet tried to breed a strain of fowls resistant to any one of these respiratory diseases. Strains of fowls resistant to lymphomatosis have, however, been developed by selection, and there are good indications that the same process would be effective against other diseases.

Real animals. Some of the best demonstrations of the feasibility of breeding disease-resistant animals have been made with the common house mouse. Unfortunately, some of my students find it difficult to consider the mouse as anything more important than a geneticist's plaything. To be sure, it is better than a fruit fly, but the question still remains: Is it feasible to breed disease-resistant strains among the *real* animals? As all veterinary students know, the real animals are dogs and cats and anything bigger. Hens qualify, but just barely.

It is the purpose of this book to review some of the evidence showing that domestic animals vary in genetic susceptibility to disease. Much of that evidence points the way to effective control of some diseases by the development of genetically resistant stock. It is *not* the purpose of this book to suggest that genetic control of disease is the only method of control or even the best way, or that it should supplant other methods now effective and satisfactory. In some cases it may be the best way; in others it may be entirely impractical. For at least one disease (lymphomatosis in the fowl) both genetic control and other methods can be effectively combined, and there are probably other cases to which the same applies.

Disease-resistant plants. Before proceeding further with domestic animals, perhaps we should see a little of what plant pathologists and plant breeders have done in the way of developing disease-resistant varieties of important cultivated plants. Varieties of wheat resistant to stem rust provide good examples. As that disease spread over the spring-wheat areas of the United States and Canada, varieties of wheat once reliable became economically undesirable because of their susceptibility. Through the co-operative research of plant pathologists and plant breeders, new varieties were developed that combined resistance to most forms of stem rust with other essential qualities like high yield, stiff straw, and good milling and baking qualities. Dr. R. F. Peterson (5) of the Canadian Cereal Breeding Laboratory at Winnipeg has kindly provided the following brief history of that work:

Basic rust-resistant breeding stocks of bread wheat were developed in the U.S.A. by transferring genes for rust resistance from other species to bread wheats. Thus Marquillo and related varieties were developed from crosses of bread wheat with durum wheat, while Hope and sister strains resulted from crosses with emmer wheat. Further crosses with this basic material resulted in such outstanding varieties as Thatcher, Rival and Mida in the U.S.A., and Renown, Regent and Redman in Canada.

As new biological races of the rust fungus arose from time to time, new genes for resistance had to be discovered to combat them. Race 15B, with its ability to infect all commercial varieties, was a threat during the 1940's and became a serious problem in 1950. However such new varieties as Selkirk, developed in Canada, and Conley, produced in the U.S.A., have given adequate resistance to this race. Even before these varieties were released, however, hitherto unknown rust races were discovered to which the new wheats were susceptible. Other varieties now under test are resistant to all races known in North America. While the examples here given are from the spring-wheat area of U.S.A. and Canada, many other countries and regions have protected their wheat crops from rust attacks by breeding resistant varieties.

It is probably safe to say that, had the plant breeders not developed varieties of wheat resistant to stem rust, there would be in North America today neither a wheat surplus nor cheap bread.

In other crops other fungi cause rusts, blights, mildews, wilts, and leaf spots. A list of varieties of grains, vegetables, and fruits genetically resistant to these ineradicable pathogens would cover many pages. One can hardly pick up a farm magazine without reading of some new oat resistant to crown rust, a strawberry resistant to yellows, a bean resistant to anthracnose, or some disease-resistant variety in other plants. Some varieties once resistant lose that valuable property when new forms of pathogens arise by mutation. In such cases new varieties must be developed to resist the new agent of disease.

On the other hand, some varieties have retained their original resistance for many years. A good example is the Martha Washington asparagus, developed about 1912 for its resistance to rust, which soon became the most important variety in the United States and still retains that distinction. Varieties of cabbage bred at the University of Wisconsin for resistance to yellows have made it possible to produce that crop in areas where other cabbages could scarcely be grown. Similarly, the Congo watermelon and other varieties resistant to anthracnose have quickly replaced the susceptible kinds grown earlier in the southeastern states. Tomato growing in southern states, where fusarium wilt is a serious menace, would scarcely have been feasible without the use of comparatively resistant varieties like Rutgers, Marglobe, and others.[1]

Many diseases of plants and animals are caused by viruses. A good example of the utilization of genetic resistance to permit an industry to live with a virus, and to flourish in spite of it, is provided by the cane-sugar industry in Louisiana. A mosaic disease of cane proved fatal to practically all the "noble" varieties of the species of cane (*Saccharum officinarum*) used for the commercial production of sugar. A single variety, Wit Ceram, was fairly resistant. Wild sugar cane (*Saccharum spontaneum*) is practically immune to mosaic but is not grown commercially because of its low yield of sugar.

By crossing Wit Ceram with the wild species and repeatedly backcrossing the F_1 hybrids and their descendants to *S. officinarum*, a process called "nobilization," a cane can be produced of the desired noble type that carries also the all-important resistance to mosaic. Interspecific hybrids thus

[1] I am indebted to Dr. H. M. Munger for information about these disease-resistant vegetables and fruits.

produced have now displaced the susceptible noble varieties, and the cane-sugar industry has, if not an assured future, at least a reprieve until stricken by some other disease.

Other examples could be given of cultivated plants resistant to virus diseases, but this book must give more space to animals than to plants. Reviews of genetic resistance to plant diseases are given by Hayes *et al.* (2) and by Walker (6).

Plants resistant to insects. Insects are animals. Some of them feed on plants and some feed on other animals. Many act as vectors carrying disease from plant to plant or from one animal to another. Plant breeders have made remarkable progress in developing varieties resistant to insects (and to other animal parasites, including even nematode worms), but as yet animal breeders can show few similar achievements, if any. The grape phylloxeran, a plant louse that ravaged the vineyards for years, was finally overcome by the discovery of resistant varieties, some of which are said to have maintained their resistance for over 70 years. Pawnee wheat combines resistance to the Hessian fly with other desirable traits of economic value. Some varieties of maize are resistant to the chinch bug; others are completely destroyed by it. Details of these and other examples of genetic resistance to insects are given by Hayes *et al.* (2) and by Painter (4).

Some contrasts. An important point to remember is that the development of all these disease-resistant cultivated plants (and of many others too numerous to list) has resulted from recognition of these simple facts:

1. The pathogen, be it a virus, a fungus, a bacterium, or an insect, is not likely to be eradicated.
2. Within a species (or genus) some plants are generally able to live with the pathogen while others are not.