Fowl Paralysis and Other Forms of the Avian Leukosis Complex

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FOWL PARALYSIS is one form of a very damaging disease complex that probably costs poultrymen in the United States as much as all other diseases put together. No one knows what causes it, how it spreads, or how to control it. This article tells about a concerted drive to discover more facts, with a view to reducing a tremendous annual loss.

The disease called fowl paralysis, together with several other allied conditions classed together as the avian leukosis complex,\(^2\) causes a tremendous loss to the poultry industry. The paralysis form of this disease complex was first recognized in the United States along the eastern coast about 1920.

During the last 20 years the avian leukosis complex has spread rapidly until few flocks of chickens in the United States have escaped its ravages. Its yearly toll in this country is believed to exceed that of any other poultry disease and it also causes great damage in other countries of the world where the production of poultry is conducted

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2 In the avian leukosis complex may be included in addition to so-called fowl paralysis, or range paralysis, also termed neurolymphomatosis, other forms of lymphomatosis; ocular lymphomatosis, or iritis; visceral lymphomatosis, or big-liver disease; lymphocytoma, myelocytoma, and leukotic tumors; osteopetrosis, or marble bone; and the leukoses—erythroleukosis, erythrosis, myeloleukosis, erythromyeloblastic or erythroblastic, and granuloblastic leukosis, etc. These diseases or expressions of disease show differences in various features; yet marked similarities exist among certain of their characteristics. These resemblances are taken as a basis for a common group or name, although the knowledge of the relationship which one type or form of disease may have to another within the complex is quite limited.
on a considerable scale. Although chickens from a few weeks old to a year of age or older may become affected, the disease usually does not appear to a great extent in flocks until after the expense of rearing has been incurred. It is partly for this reason that the disease exacts such a great financial toll. The control of the avian leukosis complex consequently is of major interest to all concerned with the poultry industry.

With the aim of finding some means to reduce losses from this disease, investigations are being actively carried out by various State and Federal workers.

**TYPES AND SYMPTOMS**

One of the most obvious symptoms of the avian leukosis complex is a paralyzed condition in one or more parts of a bird’s body. This led early workers to call the disease fowl paralysis. Later examinations and study revealed a great variety of apparently closely related disease manifestations. Practically all the tissues, organs, and other parts of the body have been found to be involved. The numerous expressions of disease make it desirable to use the more inclusive term “avian-leukosis complex,” of which paralysis, or nerve involvement, is only one type or manifestation.

The various types of the leukosis complex may be classified as (1) nerve (neural), (2) eye (ocular), (3) internal-organ (visceral), (4) bone, and (5) blood (leukosis). It should be emphasized that a bird may be affected by one or all these types at the same time. In addition, other unrelated diseases may also be present. These facts greatly complicate the already difficult task of determining the true nature of the disease or diseases present.

The various types described in the following paragraphs may be found in both males and females, and some may exist in a bird for long periods without producing any noticeable effect.

**NERVE TYPE (NEURAL LYMPHOMATOSIS)**

The nerve type of the disease is most familiar to the poultryman, Figure 1 shows a typical position of the legs (spraddling), which is considered characteristic. One or both legs or wings may be affected, with a resulting partial or complete paralysis of these parts. Examination of the nerves of the diseased part with the unaided eye may show great enlargement and a slight yellowish discoloration, but often the use of a microscope is necessary to detect the disease changes. The nerves of other parts of the body may also be affected, resulting in so-called sour crop, wry neck, and a general incoordination of the entire body. Partial or complete paralysis of the viscera occurs in many cases. Breathing through the mouth or difficult respiration may be observed when the vagus nerve, which serves the lungs and stomach, is involved. The length of time an affected bird may survive depends on the extent, location, and function of the nerve or nerves affected. Partially paralyzed birds have been
known to live many months in individual pens with access to feed and water.

Other diseases of the fowl that produce similar or identical symptoms of paralysis may be confused with the nerve type of the avian leukosis complex. Among these are certain of the nutritional diseases, including several vitamin deficiencies, and infectious diseases, such as epidemic tremor, or avian encephalomyelitis. The fact that several other diseases may show all the gross symptoms and changes

![Figure 1. Typical spraddling position of the legs in neurolymphomatosis, the nerve form of fowl paralysis.](image)

of the nerve type of the avian leukosis complex indicates the need for careful diagnosis and makes it evident that the term "fowl paralysis" refers to a symptom of disease and not a disease. A final differentiation between so-called fowl paralysis, or neurolymphomatosis, and paralysis resulting from other causes often requires microscopic and various additional laboratory examinations and procedures.

**Eye Type (Ocular Lymphomatosis)**

The eye type is quite common and is frequently manifested in the bird by loss of color in the iris and development of gray eyes and "fishy," or bulging, eyeballs (fig. 2). Changes in the size and shape of the pupil are also commonly seen in ocular lymphomatosis. In some cases the nerves leading to the eyes are affected, with partial or complete blindness as the usual result. There is a considerable amount of variability in the time when eye disorders are manifested. They may first be observed as early as the fourth month of age, but the majority of cases occur between the fourth and twelfth months. New cases may appear, however, even after the birds are a year or more old. It should be remembered that though the iris of the eye of the adult fowl is normally pigmented, during the first
few months after hatching the eye is gray or unpigmented. Thus the lack of pigment during the early period should not be confused with loss of pigment resulting from the eye type of the leukosis complex. Since the eye changes usually develop slowly, an affected hen may remain in production until almost complete blindness interferes with its obtaining feed and water.

**INTERNAL-ORGAN, OR VISCERAL, TYPE (VISCERAL LYMPHOMATOSIS)**

Laboratory examinations indicate that all the internal organs of the bird are affected by the avian leukosis complex. The liver, lungs, heart, spleen, ovary, testicles, kidneys, intestines, skin, and in fact every tissue or organ may show disease manifestations that are part of this complex (fig. 3). All of these organs may not, however, be affected at the same time. The disease may be seen in birds from a few weeks to several years of age.

On examination the various internal organs of diseased birds frequently show gross tumorlike masses, though in some cases these "tumors" may be seen only with the aid of a microscope. An infiltration of young or immature blood cells into the liver may cause a general enlargement of this organ without a nodular, or spotted, effect. The liver may increase to several times its normal size. Livers weighing more than a pound have been found in affected birds weighing less than 4 pounds. This condition is frequently called big-liver disease. The external symptoms shown by a bird vary according to the location and extent of the disease condition. For
example, when the liver is seriously affected the blood circulation and digestive system do not function normally, and the bird generally loses flesh, becoming weak and nonproductive. As in other forms of the leukosis complex and in other diseases, a diarrhea often develops either as a direct consequence or as a result of complications. Death may occur either before serious external symptoms are observed or after a long period of sickness.

Various unrelated diseases may cause symptoms identical with those shown by birds affected by the visceral type of the leukosis complex. The lesions, or tissue injuries, of tuberculosis may be so similar that frequently differentiation can be made only by laboratory examinations. The fact that other forms of the leukosis complex, the nerve type, for example, may be seen in a flock suggests but does not prove that the organ, or visceral, type is present also.

**BONE TYPE (OSTEOPETROSIS)**

A bone condition (25, 27)\(^3\) in which the long bones (leg and wing) are thickened and enlarged without any increase in length taking place has been found to be associated with the avian leukosis complex (fig. 4). The walls of the bone become thickened and very hard, and the amount of space normally occupied by the bone marrow is greatly diminished. In advanced cases the bone deformity of the shanks is readily noticed, and affected birds have a stilted

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\(^3\) Italic numbers in parentheses refer to Literature Cited, p. 960.
or jerky gait. The scientific name of this bone condition is osteo-
petrosis (literally, hardening of the bone).

![Figure 4: Marble bone—such enlargement of the shanks and other bones in fowls is caused by osteopetrotic lymphomatosis.]

**Blood Types (Leukosis)**

In one type of the avian leukosis complex the blood and blood-
forming organs and tissues, especially the bone marrow (where blood
cells are made), are affected. The blood is the direct means for
carrying oxygen and nourishment to the different body tissues as
well as for removing waste. Consequently, when the blood shows
evidence of disease, there is a general disturbance of the body
functions.

Affected birds become anemic—thin, weak, and pale. The wattles,
comb, and skin may become intensely yellow. The blood is often
pale and watery. In the late stages of the disease the bird is fre-
quently too weak to stand, and this extreme weakness and inactivity
are sometimes mistaken for paralysis.

Unlike the other types of this complex, which seldom show pro-
gressive changes in the blood cells, the blood types are largely limited
to alterations developing within the blood-vessel system. Alterations
of the blood or blood circulation may occur which quickly endanger
the life of the bird. Frequently great numbers of immature blood
cells collect in the smaller blood vessels of the various organs and
cause an enlargement which may resemble that in other forms of the
leukosis complex. Parts of the bone marrow may be swollen and may vary in color from dark to white or chalky.

**OTHER TUMORS**

Various tumors, or neoplasms, of poultry are found in flocks affected with the avian leukosis complex. The tumors are often localized in muscle tissue or are attached to some part of the viscera. Little is known of their origin, and though they are frequently classed under the avian leukosis complex, there is some doubt that they are actually connected with it.

**CAUSE OF THE AVIAN LEUKOSIS COMPLEX**

The cause of the avian leukosis complex with all its various manifestations is not definitely known, even though a great deal of work has been done both by workers concerned with the disease because of its great economic importance to the poultry industry and by those interested in it for the information it might yield on the problem of leukemic diseases in man and other mammals. Most authorities have expressed the opinion that it is caused by a virus or a viruslike agent. The fact that the various types of the avian leukosis complex have been transmitted from bird to bird by various means under suitable conditions strongly suggest that it is of an infectious nature and may spread readily.

Present knowledge would eliminate improper nutrition as a direct cause of the avian leukosis complex. Parasites, such as coccidia and tapeworms, do not cause the disease, although they produce injury that may favor entrance of the leukosis complex agent into the body. Claims that bacteria or their products will induce the disease have not been confirmed. Neither can an unfavorable environment, with faulty ventilation or poor housing, be held responsible.

**HOW IS THE DISEASE TRANSMITTED?**

To the poultryman probably the most pressing question pertaining to the avian leukosis complex is that of the method of transmission, or spread, of this disease or group of diseases from bird to bird and flock to flock. Effective control measures must await further knowledge of the ways and means by which the disease is spread. Experimental work has shown that it is not difficult to transmit various forms, or types, of the disease by inoculating young birds artificially with blood or material from the organs of diseased birds. It is exceedingly difficult, however, to be sure how the disease is spread under farm and commercial conditions. Under field conditions transmission of the avian leukosis complex would appear to occur in various ways. The observation that the disease seems to have been introduced into clean flocks by hatching eggs or baby chicks from affected sources points to spread through the eggs, possibly in a manner similar to that in which pullorum disease spreads. The fact that the offspring of hens showing various forms of the disease com-
plex sometimes develop the condition at an early age would also favor this possibility.

The fact that the avian leukemia complex has first appeared in a flock after the introduction of birds from flocks where the disease was present suggests spread by contact. Some investigators report transmission of the disease by means of feed contaminated with droppings of affected birds, whereas other workers obtained negative results in similar experiments. In general, however, the common eye, nerve, and visceral forms appear to spread more readily under ordinary conditions than the blood, or leukotic, forms. On the other hand, the leukotic forms seem to be more easily transmitted by artificial means, as, for example, by injection of the blood or organs of diseased birds (50).

Resistance to the avian leukemia complex increases rapidly with age, so that special precautions against exposure during the first several months after hatching are justified. Worms, coccidia, and other parasites may lower the vitality of the birds and produce injury through which the disease agent may enter the body tissues. Transmission by mites and ticks has been suggested, and different experiments have yielded both positive and negative results.

Recent observations on the avian leukemia disease complex, as well as on leukotic diseases in other animals, also emphasize the important influence which natural or inherited differences in susceptibility may have on the spread of various infectious and parasitic diseases. Some individuals of a family, or entire families, or even strains of birds develop disease after apparently very mild exposure, whereas others do not become affected even when severely exposed. That such resistance may be greatly lowered by unfavorable conditions of housing, handling, or feeding must, however, be fully recognized:

WHAT IS KNOWN ABOUT CONTROL MEASURES

Despite the economic importance of the avian leukemia complex and the fact that it has been recognized and studied to some extent for over 20 years, adequate means of control are not known. This situation may be attributed in part to the insidious nature of the disease and in part to the lack of funds, facilities, and personnel to study the many aspects of the problem.

The poultry raiser, therefore, cannot at present rely on any definite practical control measures as a protection against serious and recurring losses from the avian leukemia complex. There are, however, two methods, namely, sanitation and breeding, either or both of which hold some promise of being effective.

IMPORTANCE OF SANITATION

Sanitation and hygiene are the keystones of successful management of poultry flocks. Better management is sorely needed on the vast majority of farms where poultry are kept. Poultry will be more thrifty, and consequently more profitable, if they are fed a complete diet and housed and yarded in clean, sanitary quarters.
Furthermore, where clean quarters are provided, there will be less chance of exposure to disease agents. Poultry raisers who foster disease through continued neglect and mismanagement not only jeopardize their own interests but maintain a menace to the flocks of those who have adopted sanitary practices.

Sanitation assumes a major role in the transfer of stock from farm to farm and from State to State. The enormous exchange in breeding stock, hatching eggs, baby chicks, and live market poultry provides an excellent opportunity for dissemination of disease. Specific management recommendations, though admittedly inadequate in controlling the avian leukosis complex, suggest the adoption of quarantine measures and a minimum exchange of poultry stock.

Distributors of poultry, in any form, must realize that they are handling an animal that is susceptible to a large number of diseases, many of which are infectious and highly contagious. They must see the problem of disease dissemination as it now exists and by united effort attempt to solve it.

Breeding Methods Offer Promise

Careful breeding procedures hold some promise of eventually reducing the incidence of the avian leukosis complex. This may come about in two ways, by mating birds that have the proper hereditary resistant factors and by selecting parents that will not indirectly or by way of the egg transmit the disease to their progeny. Both of these possibilities are supported by sufficient evidence to warrant exhaustive study. Roberts and Card (47), reporting on data obtained over a 10-year period on more than 29,000 birds, present evidence that heredity is an important factor in resistance and susceptibility to pullorum disease. Lambert and Knox (31) have demonstrated that five generations of selective breeding decreased the mortality from fowl typhoid from 85 to 10 percent. Gildow et al. (18, 19) reported a reduction of fowl paralysis at the Idaho Experiment Station flock by selective breeding. Marble (37) gives data indicating a 50-percent decrease in mortality over a 5-year period when selective breeding was practiced.

Asmundson and Biely (2) indicated that there are inherited differences in susceptibility and resistance to fowl paralysis. Patterson and associates (45) stated that decided strain differences were found in birds susceptible or resistant to paralysis. These experiments and many others (3, 10, 11, 32, 36, 57) with both fowls and mammals indicate that resistance or susceptibility to disease has a genetic basis. It should be emphasized, however, that the absence of disease manifestations does not necessarily indicate genetic resistance, since individual birds or all progeny of certain parents may not have been exposed at all. Such conclusions are warranted only when an adequate number of inoculated controls are available for comparison. It is entirely possible, also, that acquired immunity may account for the failure of many individuals to show manifestations of the disease.

That the egg is a means of pullorum disease transmission has been
fully established, and the possibility that the avian leukosis complex may be transmitted in a like manner should not be overlooked.

It is recommended that breeding flocks be closed to unrelated birds. The closing of flocks to outside breeding should be practiced more widely than it is. Whenever unproved birds are introduced into a flock, there is great danger of bringing in not only the avian leukosis complex but many other diseases. From a strictly genetic standpoint, uniformity for almost any character will be difficult to attain if birds from new sources are consistently introduced into the breeding pens. The average breeder is reluctant to return to the same source for breeding stock year after year because of the prevalent belief that new blood must be introduced frequently to obtain the best results. This is certainly a misconception on the part of any breeder when large numbers of birds are involved. Marble (37) demonstrated the possibility of reducing losses from disease by using proved blood lines and closing the flocks to outside breeding. Many of the most successful breeders in the United States have maintained closed flocks for years with no loss in either reproductive ability or general health.

The use of older birds for breeding purposes would appear to have some advantage in that they have at least proved their ability to live for a long time. This procedure would be of little value, however, if the hen were a carrier able to transmit the disease to her progeny. Possibly the better recommendation would be to use hens from families showing high viability, or livability, or from hens that have produced progeny showing high viability.

**No Treatment Known**

Specific agents or measures for the prevention or treatment of the avian leukosis complex are not known. No feed, vaccine, drug, combination of drugs, or other agent has been found to be of value for the control of this group of diseases. The claim that wheat-germ oil would prevent and cure the nerve type of the leukosis complex has not been confirmed by investigations carried out at a number of experiment stations. Consequently, any claims for direct or specific benefits from medicinal, biological, or other agents or products against the avian leukosis complex must be regarded with extreme caution.

**HISTORY AND OCCURRENCE**

A form of transmissible avian leukosis was described by Ellermann and Bang (7) as early as 1908. In 1907 Marek (38), in Austria, first described a disease in chickens which he called polyneuritis and which is now known as neural lymphomatosis or neurolymphomatosis—the so-called fowl paralysis. The same disease was apparently first described in America by Kaupp in 1921 (28). It was subsequently reported from Holland by Van der Walle and Winkler-Junius in 1924 (65); from England by Galloway in 1929 (16); from Germany by Seifried in 1930 (49); and from Japan by Emoto and Miyamoto in 1930 (8). Today there is evidence that the avian leukosis complex is widespread throughout the world and that the disease is a serious
problem in all areas where the practices of the modern poultry industry (large-scale hatching and distribution) are followed.

Chickens are most commonly and seriously affected by the avian leukosis complex. The disease has been reported also in turkeys, guinea fowl, pheasants, and various ornamental birds. Transmission from one species to another seems to occur rarely, if ever. The first 2 to 3 months of life appear to be the period of greatest susceptibility, although exposure to artificial inoculation indicates marked variation in susceptibility among older stock. Great variations, from several days to many months, are observed in the period of incubation (the time from exposure until symptoms or disease changes appear) as well as in the course or duration of the disease, even in the relatively rapidly developing leukoses. In some flocks only a few birds may show signs of the disease, whereas in other flocks a high proportion become affected. Few of the visibly affected individuals recover.

Differences in susceptibility, as determined by the number of affected birds and the time of development of the avian leukosis complex, have been observed among breeds as well as within strains and among families of a breed.

That there are significant sex differences in susceptibility to the avian leukosis complex has not been fully demonstrated.

**SCIENTIFIC INVESTIGATIONS**

Scientific study and research dealing with the avian leukosis complex began with the finding of so-called Marek's disease or fowl paralysis in 1907 (38) and of a transmissible leukosis by Ellermann and Bang in 1908 (7). As already pointed out, the leukosis complex in its various forms was recognized as a major enemy of poultry in various countries before 1930. The malady has attracted the interest and enlisted the energies of many research workers, both abroad and in this country. Progress in the attack on the perplexing problem has, however, been slow and somewhat discouraging.

Observations on various aspects of the problem made by workers in Europe, the United States, and Canada, and other countries have been largely in agreement. The earlier investigations of the avian leukosis complex in this country were directed chiefly toward study of the nature of the disease and its transmission or spread. Schmeisser (48) in 1915 reported artificial transmission of a case of myeloid leukosis to about half the chickens inoculated. May, Tittsler, and Goodner (39) gave a preliminary report of field and laboratory findings in so-called fowl paralysis. Doyle (4, 5), in spite of negative transmission experiments, suggested the infectious nature of the disease, as well as a relationship between the nerve and eye types. He indicated that the disease was spread by the introduction of stock and through the egg. Pappenheimer and coworkers (42, 43, 44) in extensive studies clarified various features of so-called fowl paralysis. They proposed the term "neurolymphomatosis gallinarum" and recognized an apparent relationship between lymphomatosis lesions in the nerves and in other tissues. The disease was transmitted by injection with diseased nerves. No relation was found between paralysis and infestation with coccidia and intestinal worms. Pat-
Persen and associates (45) presented evidence of the spread of the avian leukemia complex by means of manure and contaminated litter. Work at other stations (Ohio (29), Idaho (18, 19), South Carolina (1), Illinois (54), and Connecticut (26)) tended to confirm this observation. Ratcliffe and Stubbs (46) failed to transmit leukemia by mosquitoes and mites. Johnson (24) concluded that mites could carry the disease from affected to healthy birds and that it might be mechanically transmitted during the process of vaccination against fowl pox.

The work of Furth (12, 13, 14), Furth and Breedis (15), Stubbs (51), and Stubbs and Furth (52, 53), dealing with various manifestations of the disease grouped as the avian leukemia complex, indicated differences among strains of the agent or agents causing leukemia, as well as between the agents responsible for leukemia and lymphomatosis. This view was supported by the findings of Feldman and Olson (9, 10), Olson (40, 41), Fenstermacher (11), and Jungherr (25, 26, 27). The Iowa workers (Patterson and associates (45), Lee and associates (33, 34)), as well as Johnson (22, 23), hold the view that all manifestations of the avian leukemia complex are associated with a common causative agent. Wilcke and coworkers (58) found that cod-liver oil, yeast, green feed, iodine, and various ratios and amounts of calcium and phosphorus had no effect on the incidence or course of the disease.

Observations on the influence of heredity on susceptibility and resistance to the avian leukemia complex have already been alluded to. This phase of the problem is now receiving much attention. The recent work of Durant and McDougle (6) suggests the importance of egg transmission and the almost continuous infectivity of the blood of chicks from clinically affected dams. Lee reported in 1940* that affected hens apparently are much more likely to transmit the disease through the egg than are diseased males. Gibbs (17), Kirschbaum and Stern (30), Hall and associates (20), and Brandly and Cottral 5 were able to induce manifestations of the avian leukemia complex by inoculating incubating chick embryos or their membranes with the blood, tissues, and extracts of diseased birds.

Though the findings of these and other investigations have added materially to the information on the disease or diseases designated as the avian leukemia complex, it is clear that much additional information is desirable and necessary. Some of the lack of agreement in work and opinions may be ascribed to difficulties peculiar to the study of diseases with long incubation or developmental periods, irregular manifestations, and undetermined causes. Likewise, studies with hosts or birds of unknown genetic background magnify the difficulties. These problems obviously demand a more comprehensive and coordinated program supported by proper facilities and suitable personnel if they are to be successfully attacked.

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* In a paper presented at seventy-sixth annual meeting of the American Veterinary Medical Association

5 Unpublished data, 1940
A Coordinated Program of Research Begun

In view of the seriousness of the poultry-disease situation as represented by the avian leukosis complex and various other conditions, recommendations were drawn up during 1937 in a conference of 25 directors of experiment stations in the North Central and Northeastern States. The Secretary of the United States Department of Agriculture was subsequently petitioned to establish a regional laboratory for the improvement of viability in poultry. The Regional Poultry Research Laboratory was approved and was established at East Lansing, Mich., March 25, 1938. Its work is done in close and active cooperation with that in each of the 25 North Central and Northeastern States and that of the Animal Disease Station, Beltsville, Md., where investigation of this disease has been carried on for several years. In this research program, experiment station workers and the Regional Poultry Research Laboratory staff are collaborating in the investigation of various ways and means for the control of the avian leukosis complex. Such collaboration will eliminate needless duplication of effort and at the same time provide the laboratory with active and advisory assistance.

Of the 31 State experiment stations in the United States which have undertaken studies of the avian leukosis complex, 21 are in the group of States designated as the major region of the Regional Poultry Research Laboratory program. Besides these experiment stations, numerous other institutions in various States are investigating the avian leukosis complex particularly as it relates to leukemia and similar conditions found in other species, including man.

At the present time, 10 States within the major region have cooperative projects with the Laboratory. These States are conducting work either in combination or separately on various phases of pathology, breeding, and nutrition.

Investigations Under Way

The work project of the regional program has four aspects: Genetic and physiologic, management, nutritional, and pathologic. Because there are neither funds nor facilities available to undertake at the start all the phases of the research that need attention, the genetics and physiology and the pathology (the study of the nature of the disease itself) will receive first attention.

The Genetic Approach

A genetic approach to this problem calls for the formation of families inherently resistant or susceptible to fowl leukosis and possessing to a marked degree characters of general economic value (56). Though susceptible families would be of little economic importance, their genetic value would be great, for without such lines the mode of inheritance of resistance and the influence of the environment would be difficult to determine. In addition, susceptible noncarrier stocks are necessary for pathologic studies, including epizootiology (the
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study of the disease as an epidemic among animals), immunization, and various nongenetic control methods.

Careful consideration was given to the selection of birds to be used for experimental purposes at the Regional Laboratory. A survey of breeding stock in the United States indicated that it was possible to obtain from widely separated geographic regions many strains of Single Comb White Leghorns about the viability and production of which much was known. The White Leghorn was therefore selected as the most suitable material for the research on fowl paralysis.

In the spring of 1939, more than 1,000 hatching eggs were introduced from each of 10 different White Leghorn flocks. Upon hatching, the chicks were divided into two groups. One group, unexposed to the avian leukosis complex, used as a control, was confined in strictly quarantined houses on the west, or control, side of the plant. The other group was subdivided into an inoculated group and a noninoculated, pen-contact group, which was confined in the same pens with the inoculated chicks and quarantined in similar houses on the east, or infection, side or unit of the plant. All the chicks, except those from one flock which were subsequently discarded, were of known ancestry. This fact permitted a distribution of chicks from the same dam to both control and inoculated groups. The inoculated birds were to provide an estimate of the resistance or susceptibility of their unexposed sibs (sisters and brothers).

Only birds from the noninoculated control units were to be used for breeding purposes. It was decided to close the entire flock to all outside breeding and to attempt a breeding program which would as quickly as possible segregate the birds with the greatest number of desirable characters and those with the fewest. In a breeding experiment with a closed flock, no inherited trait can be incorporated into a group of birds, except for possible mutations unless the genes exist in the original foundation stock. This emphasizes the importance of starting with suitable material.

One of the main objectives of the breeding program is to segregate birds resistant or susceptible to fowl paralysis as quickly as possible while sacrificing valuable economic characters as little as possible. On the basis of incomplete family performance, therefore, birds of the original 1939 population within families showing the most resistance and those within families showing the most susceptibility were mated to obtain a 1940 population. The chicks hatched in 1940 were divided into inoculated and control groups as in the case of the 1939 population.

Pathology Phase

The pathology program includes studies planned or under way on methods of diagnosis, both before and after the appearance of symptoms; possible means of detecting carriers; means of transmission, including the role that parasites, bacteria, and other agents may play; the nature, properties, and tissue distribution of the causative agent or agents; embryo and chick susceptibility; the mechanism of acquired immunity; and the development and improvement of experimental methods and procedures for the study of the avian leukosis complex.
The initial study at the Laboratory was projected jointly toward a study of the susceptibility and resistance of the 10 strains of chickens on the one hand, and on the other, of the properties of several strains or causative agents of the avian leukosis complex.

Extensive examination of all the birds that developed disease during the course of the experimental work was recognized as necessary in order to make accurate diagnoses. The data collected from the examinations indicate the nature and distribution of the lesions. The value of such information from the practical as well as the experimental standpoint is apparent.

The fact that a very high percentage of birds less than 3 weeks of age (approximately 1,700) inoculated in April and May 1939 with lymphomatosis material from two different sources developed the disease is not particularly significant. Under the conditions that prevailed, however, the occurrence of the disease among each of the 10 strains of the uninoculated, or control, population would tend to incriminate egg transmission of the avian leukosis complex as important. In this connection it is pointed out that only hatching eggs representing the 10 different strains were brought onto the Laboratory premises. Live poultry and other birds as well as animals and human beings, from the outside were excluded. Furthermore, all buildings were under quarantine, and strict sanitary precautions were followed. The caretakers were limited to the separate units and required to change clothing and footwear before going from one unit to another, and other rigid quarantine measures were observed. Complete confinement of all birds has been practiced since the beginning of the experiment. Despite all these precautions, cases of the avian leukosis complex began to appear among birds in the west or control unit of the Laboratory as early as 40 days after the first hatching of eggs from the original 10 strains of White Leghorns. The disease did not appear any earlier in the birds in the east or infection unit, even though approximately two-thirds of the latter stock were inoculated at an early age with the blood of birds showing disease changes characteristic of some form of the avian leukosis complex. Furthermore, the mortality from the avian leukosis complex among the 1939 population was not significantly less in the birds in the control unit than in the birds reared in contact with the inoculated stock.

The results obtained, under strict quarantine and sanitary measures, may be regarded as satisfactory despite the appearance of the avian leukosis complex among the control birds, because no other diseases or parasites, with the exception of sporadic cases of coccidiosis, have been found on the premises. The first outbreak of coccidiosis, in several houses and among both controls and inoculated birds, occurred in November 1939, 8 months after the work was started. The manner in which coccidiosis first appeared suggests contamination by way of feed or litter, or both.

In serial-passage experiments, the inoculation of different groups of chicks with lymphomatotic material from widely separated sources

\* Serial passage is passage of the disease from bird to bird by artificial inoculation of a healthy chick with tissues from an individual affected with the disease.
has consistently reproduced both nerve and visceral types of the disease. One of these strains of inoculum has associated with it the bone changes termed “osteopetrosis.” The bone changes have been seen in about half the chicks inoculated with that particular strain, or agent. Furthermore, when the material was inoculated into incubating eggs, the resulting chicks showed about the same percentage of bone changes as the birds inoculated after hatching. Osteopetrosis has not been seen in uninoculated birds kept continuously in the same pens with affected individuals for long periods. Another of the strains of material used for inoculation in the serial-passage work has induced a high percentage of blood, or leukosis, cases. In the serial-passage experiments with strains showing osteopetrosis and leukosis, respectively, the nerve and visceral forms of the disease were also manifested. This might be accepted as proof of the capacity of a particular strain to induce all manifestations and types of the disease complex if it were not for the development of similar numbers of cases of nerve and visceral types of the disease in uninjected control birds.

These observations do not clarify the question whether all types of disease classed within the avian leukosis complex are due to one causative agent or whether each type or a combination of types is caused by a separate and distinct agent. The observations on the source, or strain, of the material used for inoculation do, however, emphasize clearly that progress on this entire problem will depend to a large extent on securing disease-free stock for experimental purposes. In order to identify the agent or agents causing the avian leukosis complex and to measure the resistance or susceptibility of birds, there must be reasonable assurance that the disease has not been introduced either by way of the egg or by any other means. This phase of the problem, therefore, is being studied intensively.

Other Phases of the Investigation

Many other phases of the problem presented by the avian leukosis complex have been outlined as a part of the long-time laboratory program. Some work that has been outlined cannot be undertaken at present because of lack of facilities and personnel. Other parts of the program must await the results of investigations under way in other branches of science before they can be approached properly and to the best advantage.

Poultry management factors that demand study and clarification include (1) the value of sanitary procedures and (2) the time required for the infection present in contaminated areas and premises to die out.

Nutritional aspects of the problem to be studied embrace the effect of diet on the incidence of the avian-leukosis complex in stock of known genetic background.
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