PROBABLY the most brilliant achievement of modern medical science has been the gradual disclosure of nature's methods of producing immunity against disease, and the use of these methods to protect human beings and animals by artificial immunization. Not only livestock producers but everyone should understand the fundamentals of this process.

**BACTERIAL AND VIRUS DISEASES**

In the prevention and treatment of diseases of animals a knowledge of the principles of immunity is highly desirable, especially when biological products, such as vaccines, bacterins, toxoids, and immune serum, are to be used.

In its true sense immunity denotes complete resistance to a disease, but since all individuals of a species can seldom be made resistant enough to withstand severe exposure, the term is now used chiefly in a relative sense; that is, it does not necessarily mean absolute resistance, but signifies that the natural resistance, if any, of an individual has been increased to a certain degree, which may be slight or marked, usually the latter. Susceptibility is the opposite of resistance, denoting that an animal of a certain species or the large majority of animals in a given species may contract a disease readily if exposed to it.

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NATURAL AND ACQUIRED IMMUNITY

Immunity may be natural or acquired. Natural immunity to a specific disease is inherited, and the degree of immunity varies considerably in different individuals. Just as no two animals are exactly alike in physical appearance and mental attributes, no two are exactly alike in susceptibility or resistance to disease. When a herd of swine has been exposed to hog cholera, for example, a few animals commonly die within 48 to 72 hours after the first symptoms develop; others—probably the majority—are sick for 4 to 10 days before dying; some recover after being slightly sick, and some after being very sick; and a few may show no indication of illness. The last group would be considered naturally immune.

Again, horses and cattle may be exposed directly to hog cholera, but they never contract this disease. Such natural resistance is known as species immunity, meaning that all or most individuals of a species of animals are resistant or immune to a specific disease.

Other factors operate in resistance to a disease, chief of which are the severity of exposure and the virulence of the germs or virus causing the disease. It can be readily understood, therefore, that resistance is a complex problem and that natural immunity may be broken down in many instances by severe exposure.

For an understanding of acquired immunity it is necessary first to be familiar with certain physiological processes.

The inroads of bacteria, parasites, and other foreign substances into the body of a susceptible animal stimulate three remarkable, complex, and somewhat related protective reactions: Inflammation, immunization, and repair. By means of these processes the body attempts to localize, neutralize, and ultimately destroy the foreign organisms or substances; to produce chemical substances—antibodies—antagonistic to or protective against the foreign materials; and to repair and compensate for injuries sustained.

Two types of physiological elements, namely, cells and antibodies, are chiefly concerned in these processes. Of primary importance, since they produce the antibodies, are the living, microscopic cells of which all tissues are composed, and especially those of the blood and connective tissues, including the specialized larger phagocytic, or devouring, cells called macrophages. Macrophages are present in all the connective or supporting tissues of the body and are concentrated in great numbers in the liver, spleen, and lymph nodes. The cells of this protective system are of great importance against infection, since they not only take up and devour foreign organisms and substances but also appear to be the main elements concerned in the production of antibodies.

Thus an animal’s body may be considered a battleground in which the invading forces seek to overcome the defenses. The aim of the livestock owner and his ally, the veterinarian, is to aid animals in acquiring sufficient immunity to resist the invading organisms.
ACTIVE AND PASSIVE IMMUNITY

Acquired resistance can be increased by one or a combination of several means. If the animal produces its own antibodies, the resultant immunity is called active immunity. If the resistance of an animal is increased by the injection of antibodies produced by another animal, the immunity is known as passive.

Animals acquire an active immunity to certain diseases when they have survived a natural or modified course of the disease produced either by infection with the particular germs or by inoculation with their specific vaccines, bacterins, or toxins. In these cases, the animal produces its own immunity, either because it had the disease naturally or because it sustained a less severe form of infection produced intentionally by artificial means. Intentional active immunization is commonly called vaccination, although the latter term, to be exact, signifies that a vaccine has been used to produce the protection.

Passive immunity is produced in an animal by the introduction of immunizing substances obtained from an actively immune animal. Such immunity is usually conferred by the injection of blood serum from immunized animals; such serum carries with it the substances by which the protection is conferred. The immunizing substances (antibodies) of an actively immunized animal are known also as immune bodies. In relation to infectious diseases, they comprise two classes. Those acting on bacteria are antibacterial, as, for instance, anti-white-scours serum and antianthrax serum, whereas those acting on toxins are called antitoxin, as, for instance, tetanus antitoxin.

Active immunity develops only after 1 or 2 weeks, whereas passive immunity is established immediately after the injection. Passive immunity does not protect animals for a long period; it usually disappears within 3 to 6 weeks. This is due to the fact that as soon as the injected immune bodies are eliminated from the animal organism, the immunity is ended. In active immunity, however, the stimulation of the infection on the body cells causes the prolonged development of immune bodies, and thus a more lasting immunity is produced.

It can be seen from this brief description that active immunity has a great advantage over passive immunity, and the tendency is to produce active immunity whenever possible. On the other hand, there are times when it becomes necessary to employ means by which the spread of a disease can be immediately checked, and in such instances passive immunity has the advantage, since it affords immediate protection against infection; in some instances it also exerts a curative action. Frequently, both methods are used in a combined inoculation by which the animal is given immediate and also lasting protection against an infectious disease. This form of immunization is known as the simultaneous method, a familiar example of which is virus-serum inoculation against hog cholera.

Scientists the world over have expended much effort in attempts to discover and perfect effective and at the same time practical
means of immunizing animals against the more destructive of the infectious diseases. Large sums have been appropriated for the advancement of these researches, both from governmental sources and by private gifts and endowments. The goal sought is the discovery of some means by which immunity may be conveyed to a large number of animals at the least expense. After successful vaccination, the animal is sufficiently protected to withstand exposure that would have proved deadly before vaccination was performed. The same principle is used in protecting man from many diseases; for example, smallpox and diphtheria.

It appears natural, then, that the best and surest results from immunization should be expected in those diseases in which the specific cause has been definitely established and for which means of effective protection are known. This is the case in actual practice.

**Vaccination**

In localities where a disease appears year after year it is advisable to vaccinate susceptible animals while they are healthy; that is, before exposure. It is not advisable to delay the immunization until the disease actually makes its appearance. Such a practice may prove costly because of the time required before actual protection is established and also because some of the animals may already have become infected though not yet showing symptoms.

The object of vaccination, as already noted, is to induce in the animal a reaction, sometimes a mild form of the disease, which stimulates the body to develop antibodies against the infective agent. It is very important that the vaccination be undertaken when the animal is in a healthy condition, as any devitalization will adversely affect the immunization. It is well known that the presence of the infection is not the sole cause of a diseased condition. In most cases the combined effects of various contributing factors are necessary. Immediately after the invasion of the infective agent, the protective mechanism of the body is set in motion, and the disease results only if the attack is stronger than the defense; that is, if the animal is not capable of producing sufficient antibodies.

Influences that tend to weaken the normal functioning of the body include overwork, exposure to cold, lack of proper feed, and shipment of animals over long distances, especially in stormy weather. Chronic infections also may lower resistance. In particular, a disease condition or a parasitic infestation may predispose an animal to infection, because while it is still fighting one disease it is called upon to combat a new invader. The failure under such circumstances explains the frequent occurrence of two diseases simultaneously, or of one following immediately after another. A disease devitalizes the body and prepares it for an attack by either latent or invading germs of a secondary infection. This situation is often observed in hog cholera, equine influenza, canine distemper, and other maladies. The formation of antibodies is influenced also by the age of the animal; neither very young nor old animals respond to vaccination so well as those between these extremes.
Susceptibility to disease is also influenced to some extent by breeding practices, such as inbreeding, as well as by selection for high productivity or performance. (See the article The Relation of Genetics to Disease, p. 167.) Feeding, discussed later, also plays an important part.

To increase the chances of success in vaccination, therefore, it is advisable to eliminate all debilitating influences before the immunization is carried out. In vaccinating against hog cholera or canine distemper, for instance, the animals should be freed of parasites if any are present and should be protected from exposure to cold and dampness. Any vitamin or mineral deficiency in the diet should also be corrected. It is a mistake to depend solely on vaccination; every effort should be made to eliminate all adverse conditions that might interfere with its success.

**Preparations Used in Producing Immunity**

For the production of immunity to various kinds of infection, veterinary research has developed numerous biological products. The preparation and distribution of these biologies in pure and potent form contribute greatly to the safety of modern livestock production. Probably the most familiar class of biologies is the vaccines.

A vaccine is an attenuated, weakened, or even apparently dead virus of the disease, specially prepared so that it will perform its function with the least possible danger to the animal. The reduction of virulence is accomplished by subjecting the virus to heat, desiccation (drying), or other unfavorable influences strong enough to weaken but not to destroy it. Examples are anthrax vaccine and blackleg vaccine. In some instances an organism modified in virulence is used for immunizing purposes, as, for instance, in bovine brucellosis (Bang's disease); or, again, an unattenuated virus may be used when it has passed through certain species of animals, a procedure that increases its virulence for that particular species but reduces it for other species. For instance, suspensions of a brain emulsion of fixed rabies virus passed through rabbits are used for immunizing other species of animals against rabies. In the use of viruses for immunizing purposes, the general opinion formerly was that immunization with "killed" virus had not been successful. Recently, however, very dependable immunity has been produced with such virus, as illustrated by successful immunization against equine encephalomyelitis with chick-embryo vaccine, in the preparation of which the virus is killed (fig. 1). The vaccine has proved highly effective not only in experimental tests but also in extensive field use.

Bacterins, another class of biologies, are standardized suspensions of killed pathogenic bacteria and their products in physiological salt solution or in oil. Immunization with bacterins against certain diseases, such as hemorrhagic septicemia, blackleg, and other infections, is now an established procedure. Bacterins are standardized to a definite number of dead organisms per cubic centimeter.

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2 This term signifies approximately the same dilution of salt (sodium chloride) that is found in body fluids, usually 0.85 percent.
This procedure involves either the counting of stained organisms in a special counting chamber or the use of a photoelectric apparatus which determines the density of a suspension by measuring the quantity of light refracted or absorbed in passing through the suspension. The latter method has greatly simplified the standardization of such suspensions.

Another biological product used in combating disease is immune blood serum (or immune serum), so-called because of its content of immunizing bodies. When injected into the body, such serum, by reason of the protective nature of the antibodies, does one of two things. It either exerts an inhibitory (stopping) action against the virulent virus or acts as an antitoxin, neutralizing the poisonous products (toxins) of the disease-producing organisms.

For the preparation of immune serum, horses are generally used, principally because their size makes possible the drawing of large volumes of blood. In treating a horse for the production of antitoxin, small quantities of the respective toxin are first injected; for the production of antibacterial serum, suspensions of the bacteria of the specific disease are injected. Periodical tests are made of the potency of the serum, to determine among other things its ability to protect other animals. When a suitable potency is obtained, a quantity of blood is drawn from the jugular vein into sterile containers.
After standing 24 hours, the separated serum is siphoned off, properly preserved, filtered if necessary, and put into final containers.

Immune serum is assimilated most rapidly if administered intravenously (into the veins), especially if therapeutic (healing or curative) action is desired. For prophylactic (preventive) purposes, the injection is made either intramuscularly (into the muscles) or subcutaneously (under the skin).

Toxoids (anatoxins), consisting of detoxified disease-producing toxins, are gaining in importance and are used very extensively for immunization purposes; examples are diphtheria toxoid and tetanus toxoid.

Other products employed for the protection of animals against disease are sensitized vaccines, sensitized bacterins, germ-free extracts, natural and artificial aggressins, and bacterial filtrates. Although the methods of preparation and characteristics of these biologies vary somewhat, the principle of action is essentially the same. It consists in the production of protective substances against corresponding infections.

In the course of their studies bacteriologists propagate bacteria on various kinds of culture media and sometimes produce different strains, comparable to the various strains of plants and animals (fig. 2). For the purpose of immunization, vaccines or bacterins are sometimes prepared from a single strain of an organism, constituting what is called a monovalent vaccine or bacterin. When prepared from two or more strains, the product is known as polyvalent. A polyvalent vaccine or bacterin is not the same as a "mixed" vaccine, or "mixed" bacterin, which is a mixture of different kinds of bacteria.

At times an autogenous (self-generated) vaccine is employed—that is, one prepared for an organism isolated from an animal affected with a disease and used for the protection of the same animal or similar animals in the locality. An autogenous vaccine has the advantage of containing the particular strain of organism that caused the infection.

Although one injection of the vaccine or bacterin induces the production of antibodies, naturally repeated injections produce a higher degree of resistance, which often is hastened by successively larger doses. The correct quantities are established through experimentation.

**BIOLOGICAL PRODUCTS AS DIAGNOSTIC AGENTS**

A highly useful specialized class of biological products is that comprising diagnostic agents. As the name signifies, these are used not for preventing or curing a disease, but rather for indicating its presence. The diagnostic agent tuberculin, used in detecting tuberculosis in cattle, swine, and poultry, is a familiar example.

There are three principal methods of tuberculin testing—the intradermic, subcutaneous, and ophthalmic, of which the first is the method now principally used. It consists in the injection of tuberculin into the dermis, the true skin. If the animal is tuberculous,
a characteristic swelling later occurs at the site of injection. Expert knowledge of the technique of the test is necessary for its proper use and for interpretation of the results.

The accuracy, as diagnostic agents, of tuberculin and of mallein (used to detect glanders in horses) is so great that veterinary officials destroy reacting animals even though they appear healthy. The animals are slaughtered with absolute confidence that in the great majority of instances the post mortem examination will justify the diagnosis, made solely on the findings of the biological test.

Ability to detect latent cases and to verify clinical ones is a valuable aid in eradication measures. Early diagnosis of such diseases also obviates the necessity of long periods of quarantine. For combating dourine in horses the complement-fixation method of diagnosis has given excellent results. This is also the laboratory test used for the diagnosis of glanders; the mallein test—comparable in principle to the tuberculin test—is used chiefly in testing for glanders on farms.

Figure 2.—Examining cultures of \textit{Brucella} organisms at the Animal Disease Station of the Bureau of Animal Industry. Most of the experimental work leading to successful vaccination against brucellosis by means of a selected strain of the organism was conducted here.
The complement-fixation method (12) is based on the phenomenon of hemolysis, or the dissolution of red blood cells. When the cells dissolve, the hemoglobin in them is set free in the surrounding fluid. Research has shown that when the red blood cells of an animal are introduced into another animal of a different species, the latter's blood acquires the ability to dissolve the blood cells of the first animal. The dissolving action is due to the development of antibodies that acquire the power described: and the reaction—hemolysis—takes place readily in laboratory equipment, such as a glass container. The acquired so-called hemolytic property of the blood depends on two substances, one of which, the hemolysin, has been found to resist heating to about 56°–58° C., whereas the other, the complement, is rendered inactive by this degree of heating. When the complement is “fixed” by union with a specific substance in the serum of the animal under test (the substance resulting from the presence of the disease), the red corpuscles are not dissolved but settle to the bottom of the test tube. This represents a positive reaction, indicating disease. In the case of a healthy animal, no fixation of complement occurs; consequently hemolysis takes place, and the test is read as negative. The Wassermann test for syphilis, widely used in human medicine, is a complement-fixation test.

Still other diagnostic tests that have been extensively applied in recent years are the agglutination test for the detection of brucellosis in cattle (7) and the rapid whole-blood test for pullorum disease in chickens (5). In testing for brucellosis, use is made of the production by the body of specific antibodies, previously mentioned, that are believed to assist the animal in resisting the disease. One of these substances, existing in the body of an animal infected with brucellosis, is known as agglutinin. It is present in the blood serum in a quantity that depends on the extent and activity of the infection. When serum from an infected animal is brought into contact with a preparation of Brucella organisms, called antigen, the organisms gather together in clumps and are technically described as agglutinated. This principle is the basis of the agglutination test, which has been found to compare favorably in accuracy with the tuberculin test for tuberculosis. There are two methods of making the agglutination test, one of which involves the use of a tube and the other a plate. The choice depends somewhat on conditions favorable to the use of each. In general they are equally efficient.

In the control of pullorum disease in poultry, which for many years caused extensive losses, the principle of agglutination is likewise employed. The form of test principally used is the rapid whole-blood test, the basis of which is a stained antigen. The discovery through research that a chemical stain added to antigen makes the reaction more easily seen has greatly facilitated the detection of pullorum disease in poultry. With modern equipment for holding and testing the birds, the rate of handling them is very rapid, usually less than 2 minutes each.

Diagnostics are prepared and used in various ways, and the reac-

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Italic numbers in parentheses refer to Literature Cited, p. 153.
tions of animals to them are likewise widely different, requiring specialized training for their proper application and for correct interpretation of the results.

**Biological Products Not to Be Used as Sole Reliance**

The remarkable results often obtained with biological products in combating disease have unfortunately led to a tendency to rely on them solely. A much better course is to give due consideration to the various factors associated with the condition concerned and utilize all measures that will contribute to the desired result. Thus, in treating a case of fistulous withers, it is not enough merely to inject a polyvalent vaccine and then wait for the animal to get well. Supportive treatment, including the possible aid of surgery, should also be considered.

Further, in attempting to control a disease, it is not sufficient to limit activities to vaccination of the exposed and susceptible animals; it is equally essential to inaugurate the necessary sanitary measures, and if possible the source of infection should be looked for and eliminated.

Animals suffering from infectious diseases may be thought of as living factories that produce and distribute vast numbers of disease germs. Thus they are more or less directly a menace to others, and the healthy animals should be segregated from the sick. This is best accomplished by removing the healthy animals immediately to a disease-free environment. In some cases destruction of the infected animals is the wisest course. Thorough disinfection (see Disinfection and Disinfectants, p. 179) and efforts to minimize the danger of exposure to possible subsequent infection should also be a part of the disease-control plan.

As already indicated, the passive form of immunity, conferred on animals as an immediate protective measure, is of short duration, lasting at times not more than a month. Therefore, when the danger of infection is still believed to exist, steps must be taken to guard against losses when the temporary immunity expires. In such instances the passive immunization should be followed with the active form, which renders the animal safe for a much longer time.

**Importance of Proper Administration and Care of Biologics**

The technique of administration must be given careful attention if best results are to be obtained. The animal to be treated should be properly prepared; the site of inoculation should be carefully cleansed and disinfected; and all instruments and utensils coming in contact with the product to be administered should be thoroughly sterilized. Bacterial suspensions should be shaken vigorously to insure an even mixture, and great care should be taken to see that the dose administered is accurate. When dealing with such products as anthrax vaccine and hog cholera virus, it is important that the
empty containers and unused portions of such products be disposed of properly. If they should be carelessly thrown aside, there is a possibility that they might be a factor in causing future outbreaks of the disease. It is always essential that the products intended for use in vaccinating should be pure, potent, and used with proper skill. In accordance with the provisions of the Virus-Serum-Toxin Act, a Federal statute, most biological products for the prevention and cure of infections in animals are prepared under license of the United States Department of Agriculture. The products should preferably be administered by a trained veterinarian.

Most biological products are sensitive to light and heat, and directions for their proper storage should be strictly followed to prevent deterioration. Practitioners have no ready means of recognizing changes that may have taken place in a product. If its previous handling or storage has been faulty, a biologic may have become inert. This phase of biological treatment is especially important in connection with highly infectious diseases. When an inert vaccine is used in such cases, both the veterinarian and the stock owner are often unable to explain the subsequent appearance of the disease. Unfortunately, such cases are rather numerous, and from the writer's personal experience in testing vaccines from various sources he can state that the failure to keep the vaccines under proper conditions is responsible for many such disappointing results. The importance of using dependable biologies and having them properly stored and competently administered can scarcely be overemphasized.

Although many different products are prepared for the prevention and treatment of disease, some stand out prominently over others in their specific action and rank among the triumphs of modern medicine. Diphtheria antitoxin, tetanus antitoxin, rabies vaccine, anthrax vaccine, blackleg aggressin, and calf scours serum have given results absolutely unattainable by any other means. Yet it must be remembered that a biological remedy is not specific in the sense that it will always prevent or cure. Neither do the diagnostic agents always detect disease. To the trained mind, these limitations are not unexpected; they exist because the ever-varying individual factor is involved.

Each year of research and experience extends the usefulness of biologic therapeutics. Increasing knowledge also continues to emphasize these basic points: (1) Biologic remedies should be used early, in full dosage; (2) they must be potent at the time of use; (3) antisepsis must be thorough; and (4) supplementary treatment that tends to ameliorate symptoms or conserve vital powers is a valuable adjunct to the use of biologies.

**PROTECTIVE MECHANISMS AGAINST PARASITES**

Until a few years ago it was considered improbable that there is any protective mechanism or immunity against animal parasites. The few reactions observed in parasitic infections were believed to be fundamentally different from those in other types of infection. It is now well established, however, that many animals do manifest
both natural and acquired protective mechanisms against parasites and that these are basically similar to those observed in virus and bacterial infections. The occurrence of immunity and its effectiveness varies greatly in different host animals and against different parasites.

Natural and acquired immunity is now generally considered to play an important part in reducing the damage done by parasites. Since it does not afford complete protection, however, and adequate methods of artificial immunization are lacking, it would seem safest and wisest for the livestock producer not to depend on it for prevention of parasitic losses. Instead it would seem highly advisable for him to attempt to prevent and remove parasitic infection wherever possible through sanitation and treatment and to foster the good health of his animals in all possible ways. He would thus not only greatly lessen the necessity for protective reactions but would insure their having the highest effectiveness when mobilized to combat the comparatively small amount of parasitic infection which he may be unable otherwise to control.

The great importance of protective mechanisms in the control of parasitic disease can perhaps be best illustrated by outlining what usually happens under natural conditions when susceptible animals are placed in contact with parasitized ones. The new arrivals will, in general, be protected against the parasites of other unrelated kinds of animals by what is known as natural immunity. For example, hogs will not become infected, even though exposed to infection, with the parasites of horses, and vice versa. Older stock not previously exposed to infection may also be protected by what is known as age immunity. This form of natural immunity is of widespread occurrence. It is especially marked in dogs and cats against hookworms and in chickens against gapeworms. Some of the animals will also be innately more immune than others because of the possession of an inherited individual, species, or breed immunity. For example, Rhode Island Red and Plymouth Rock chickens have been found to be more resistant to certain experimental infections than Leghorns, Buff Orpingtons, and Minorcas (1), and in mixed flocks of sheep Cheviots were found more tolerant of parasitism than Leicesters (6).

Susceptible animals introduced into an infected environment may be expected to acquire infection and suffer from parasitic injury. As a result their natural mechanisms of defense are stimulated to repair the damage and to counteract the presence of the parasites. Multiplication of the parasites in the blood or tissues or their increase through continual exposure to new infection forces the animals to react more vigorously to the increasing number of parasites. If the number of parasites increases more rapidly than the activity of the protective reactions, the animals suffer and perhaps die from the effects of severe parasitism. If the number of parasites is small or increases slowly, the defense forces of the animals have time to become mobilized and may produce an acquired immunity.

* Readers interested in a more extensive or more technical discussion of immunity to parasites than that given here are referred to the extensive literature reviewed in citations 6, 11, 19, 21.
This type of immunity has been shown to develop in many different kinds of animals and with many parasitic infections under both experimental and natural conditions. Especially interesting studies have been made of acquired immunity in cattle against cattle tick fever \( (16) \); in birds, against malaria \( (20) \); in sheep, against stomach worms \( (18) \); and in laboratory animals, against ticks.

The maintenance of a high level of general health is regarded as important in promoting immunity to parasitism. Such factors as the presence of bacterial disease, multiple parasitic infection, hemorrhage, and the extra demands of breeding, gestation, and lactation have all been cited as detrimental. Inadequate and deficient diets have also been shown to lessen immunity. For example, it has been shown that both natural and acquired immunity to hookworm infection breaks down when immune dogs are fed a generally deficient diet \( (8) \); that chickens on diets deficient in vitamins A, B, and D become more susceptible to infection with the common intestinal roundworm \( (2, 3, 4) \); and that whereas a diet deficient in vitamin A increases susceptibility to infestation with lice, a diet containing an abundance of this vitamin will prevent or cure such infestation \( (15) \).

When the parasites and the injuries they cause are localized in one particular part of the body, blood cells and circulating antibodies are mobilized at that point by the process of inflammation. Although this process occurs in all animals during the course of the primary infection, it is much more rapid and more marked in an immune animal. The harmful products of the parasites are precipitated, neutralized, and destroyed by the cells and fluid of the inflammatory exudate (material discharged), such as pus. The larger, many-celled parasites may also ingest the exudate and be subjected to its action internally as well as externally. Evidence of such action may be seen in the formation of precipitates in the intestine and on the outside of parasites immobilized in the tissues of immune animals.

After the parasites have become inactive and their development has been checked, they are gradually hemmed in by densely packed cells, which form nodules or cysts that become fibrous by the gradual formation of scar tissue around them. The parasite is imprisoned until it dies and is either gradually dissolved by the surrounding macrophages or persists as a calcified, or hardened, remnant. Meanwhile, the tissues injured by the parasite are being repaired by the replacement of destroyed cells and by scar-tissue formation.

The general mechanism of immunity outlined in this brief description is probably of wide occurrence since it has been observed with such diverse parasites as fly maggots, tapeworm larvae, and the larvae of roundworms. The basic phenomenon involved—interference with the normal feeding and development of the parasite by a protective substance in the animal—is probably also operative in immunity against parasites which are essentially outside the tissues. This has been demonstrated in the case of ticks and intestinal worms. Antibodies are evidently of primary importance in these cases of acquired immunity to metazoan parasites, since it has been shown that the immunity can be transferred to a normal animal by the injection of immune serum.
NUTRITION AND DISEASE RESISTANCE

Generally speaking, poor nutrition tends to break down the natural barriers of the animal organism against the ravages of the infecting agents of disease. The whole question of how this is accomplished is an exceedingly complex one. Infections vary widely in their nature, they involve various parts of the body, the many structures are affected differently, and their proper nutrition or repair calls for different food elements. Determining the specific functions of the food constituents has challenged the skill of many investigators. In recent years the vitamins have received major attention, but the various essential mineral elements, the proteins, and the energy intake have also been the subject of research, especially with a view to correcting deficiencies.

Much of the experimental work on the relation of nutrition to resistance has been done on laboratory animals such as the rat, guinea pig, and pigeon. Relatively little attention has been given to farm animals. Because of species differences in the need for several vitamin factors, generalizations from the results with laboratory animals are not necessarily applicable to cattle, sheep, swine, and horses.

The need of the higher animals for vitamin A and the early work which showed a close association of bacterial infection with xerophthalmia, a serious nutritional disease due to lack of vitamin A, have naturally focused attention on this factor. Vitamin A has been properly termed the "anti-infective factor." It has been suggested that the underlying cause for the increased susceptibility of vitamin-A-deficient animals resides in the changes produced in the epithelial tissues (those of the skin and lining membranes) through the substitution of keratinized, or horny, tissue for normal tissue. This change occurs in the respiratory, alimentary, and genitourinary tracts, the eye, and the glands of the throat and ear. If this is the case, the change in epithelial tissues brought about by lack of vitamin A increases the susceptibility to invasion by disease-producing organisms, but there is not necessarily a decrease of immunity in the strictly medical sense. Certain experiments in which the disease organisms were artificially injected into the animal have demonstrated that the decrease in resistance is due to more than the mere break-down of epithelial tissue. Animals that received an adequate supply of vitamin A in their food were much less susceptible to the disease produced by the injection of the infecting agent than were the deficient animals.

All farm animals require vitamin A, and a number of reports are available on experimental work on the association of the deficiency and disease resistance. There is considerable evidence that the incidence of white scours in calves is associated with vitamin A; thus Stewart and McCallum (17) found that a lowered vitamin A content in the colostrum of the cow was associated with an increased number of deaths among calves infected with Bacillus coli. It does not necessarily follow that all cases of white scours will respond to vitamin A therapy. Some persons have suspected that increased resistance to tuberculosis was associated with adequate vitamin A intake, but a limited amount of work with pigs has not brought out such a
Cattle maintained on a vitamin-A-deficient diet have appeared to be more susceptible to infections and have shown a relatively high mortality rate as compared with animals fed on adequate rations.

The evidence on the influence of vitamin D on infection is conflicting. Experimental findings with laboratory animals fed on diets that produced rickets have indicated a decreased resistance to certain micro-organisms and no change in resistance to other organisms.

It has been established that the needs of herbivores for the factors of the vitamin B complex are or can be met for the most part through synthesis of the vitamin factors by micro-organisms residing in the alimentary tract. Swine and poultry, however, depend upon the diet for these factors. Experimental work on vitamin B₁ deficiency has shown that animals so affected are generally less resistant to infection and succumb more readily to the ravages of disease than normal animals. It is believed that the lowered body temperature and possibly the loss of appetite resulting from a prolonged intake of the vitamin-B₁-deficient diet is largely responsible. The pronounced fall in body temperature that may occur is well illustrated in studies on pigs (22), in which a drop of as much as 8° F. was recorded. From the standpoint of loss of appetite, a decrease in the power of the blood to promote the formation of phagocytes (devouring cells), which occurs in starvation, as established by the work of Gellhorn and Dunn (9), may well account for the decreased resistance.

Evidence is accumulating that necrotic enteritis in swine, a disease produced by Salmonella suipestifer and possibly other related organisms, can be alleviated by the use of nicotinic acid. The fact that liver and certain other natural feedstuffs are more effective than nicotinic acid in effecting cures or in preventing the disease suggests that other factors besides nicotinic acid are involved. The mode of action is not understood, but there appears to be an increase in the building of scar tissue over the lesions of dead tissue in the intestine.

The quality and quantity of protein in the diet are thought to bear a close relation to the resistance of human beings to certain infective diseases. The unusual food habits of certain primitive tribes or of groups of people on restricted diets in wartime have been cited to show that a decreased protein intake was associated with an increase in the occurrence and severity of infectious diseases such as tuberculosis. Lowered protein intake apparently reduced the resistance to certain infections in dogs and in suckling pigs. On the other hand McCay and others (11) have reported that moderate restriction in the food intake of rats, sufficient to retard their growth and development but prolonging their span of life, lessened their susceptibility to lung disease at approximately 1 year of age, when normal rats suffered severely. Well-founded evidence is available to show that lowered incidence of middle-ear and lung disorders is found among retarded animals.

A lowered intake of protein and calcium by sheep kept on poor pasture has been suspected of contributing to a decrease, below the normal levels, in the amounts of the normal lysins (substances capable of dissolving bacteria) of Bacillus coli and B. suipestifer, and of the
agglutinins (substances capable of causing the clumping of bacteria) of *Brucella abortus* and *B. paratyphosus*.

On the other hand, studies on the relation of diet to infectious abortion by Hart, Hadley, and Humphrey (10) showed that a good ration well fortified with protein, fat, calcium, phosphorus, and iodine did not increase resistance to inoculation with *Brucella abortus* over that shown by heifers fed a so-called poor ration. The authors observed that vitamin A was an important cause of failure in reproduction. Where the restriction is so severe that it approaches starvation conditions, there seems to be little doubt that the resistance of the body to infection is decreased. The Colorado Agricultural Experiment Station (13) has found that sheep deprived of feed for short periods are subject to paratyphoid dysentery. It appears that the organism *Salmonella aertrycke* is a normal resident of the intestinal tract and develops added virulence under certain conditions, among which deprivation of feed is one.

The general belief is that both the normal antibodies of the serum and the power to form antibodies are not affected by dietary deficiencies. Even this premise may be contradicted, however, as evidence accumulates on the corrective and stimulative action of food factors in the formation of antibodies.

The examples presented on the relationship of nutrition and disease resistance in farm animals are intended to show, on the one hand, the nature of the relationship and, on the other, the scarcity of conclusive data. In spite of the latter, there can be little doubt that nutritive well-being in general is essential for the animal body to combat and counteract the action of disease-producing organisms. The fact that a certain nutritive essential does not appear to bear a direct relation to resistance to a particular infectious disease should not be taken as proof of a lack of relationship.

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