INTERPROFESSIONAL SEMINAR ON

DISEASES COMMON TO ANIMALS AND MAN

SEPTEMBER 25 AND 26, 1958
OMAHA, NEBRASKA

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NEBRASKA STATE HEALTH DEPARTMENT
AND
DEPARTMENT OF MICROBIOLOGY

UNIVERSITY OF NEBRASKA
COLLEGE OF MEDICINE
INTRODUCTION

Contained in this manuscript are the abstracts of papers presented at the Interprofessional Seminar on Diseases Common to Animals and Man which was held in Omaha, Nebraska on September 25 and 26, 1958. This seminar was sponsored jointly by the Nebraska State Department of Health and the Department of Microbiology, University of Nebraska, College of Medicine.

The sponsors of this program organized and conducted this program in the hope that it would evolve into an annual regional seminar or conference dealing with diseases common to animals and man. Another desire of the organizing group was that the seminar be conducted on a professional level for scientists working or interested in these diseases rather than as a post-graduate teaching endeavor, although the latter might be an incidental, but important, by-product of the meeting.

The sponsors again wish to thank those who participated in the planning of this meeting as well as those who presented papers or discussions during the seminar.
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COMPARATIVE MEDICAL RESEARCH AND CHRONIC DISEASES OF ANIMALS

James H. Steele

The broad interest which has manifested itself in chronic diseases as public health problems has raised questions in regard to the kind and incidence of these diseases in domestic animals. Veterinarians see many of these diseases in their clinics and practices, in meat inspection and in diagnostic laboratories where pathological examinations are made. Recently studies have been inaugurated in the comparative epidemiology of neoplastic, heart, and degenerative diseases in domestic animals to determine their natural history. It is hoped that these investigations will answer questions that will lead to the elucidation of their epidemiology in animals and eventually man.

Neoplastic diseases

Veterinary medicine has a wealth of raw data which can be adapted by epidemiological methods to the service of mankind. The epidemiological approach to the neoplastic diseases of animals can provide data on the incidence, trends and distribution; describe the natural history and may provide leads as to the cause, and eventually the knowledge necessary to develop a control program.

Little data on the incidence of animal neoplasms has been collected. Small studies in veterinary clinics, schools and abattoirs in Great Britain and USA reveal that the rate among animals varies from 50/1000 in dogs, 10/1000 in horses and cattle, and considerably less in swine and sheep. Collection of data of this type should be co-ordinated in regions and compared with human data.

Veterinary medical investigators are in a fortunate position to study the natural history of neoplastic diseases because of their opportunity to study these infections under experimental conditions. Natural occurring disease can be brought to clinics for further observation and attempts can be made to reproduce the disease. These conditions also lend themselves to therapeutic research programs, which have been inaugurated in a number of hospitals and universities.

The third aspect of the epidemiological approach is the question as to cause and prevention. We have come to understand neoplasia as a particular host response to some inciting agent. The host's response may be controlled by genetic factors or by an "immune response". The inciting agent may be physical, chemical, or infectious. The dog offers an excellent opportunity to test these epidemiological methods in the elucidation of the neoplastic diseases. The dog more than any other animal reflects the environment and habits of man.
A study of canine lymphoma in New Jersey illustrates the problems in setting up such a project. These are:

1. The securing of base line data
2. The establishment of a reporting system
3. The availability of a diagnostic service
4. An evaluation of cases
5. The history of each case and the tabulation of these data

The utilization of these data requires that medical epidemiologists and statisticians participate in such studies so as to determine what epidemiologic clues may develop. Similar investigations are being followed in regard to avian lymphomatosis to determine what the effect of this disease may be as to man. Does exposure to animal lymphomatosis increase resistance or susceptibility? It is difficult to determine where these studies will lead to eventually, but with the wealth of material available, the only limitation will be the imagination of the veterinary and medical epidemiologist.

There are a number of other interesting investigations going on in other parts of the USA and world. Bovine leukemia is being studied in Minnesota and surrounding midwestern states. This disease has also been reported in southern Sweden and more recently in Denmark and Germany. Some investigators state that it is communicable and have been able to reproduce the disease. A condition very similar to lung cancer, pulmonary adenomatosis has been described in sheep in Iceland and Peru. Research on this disease leads one to believe that it may be transmissible, although the incubation may be prolonged extending into years. This may be a pattern of neoplasia in longer lived animals.

Heart disease

During the past decade there has been a growing interest in heart disease of animals which reflects the increased investigations being carried out on human heart disease. The interest of the heart disease specialist in the comparative medical aspects of this major problem has resulted in support that was unknown a few years ago. A recent symposium on heart disease in dogs focused the attention of cardiologists and researchers to the possibilities of investigation of natural occurring disease in a population that can be studied experimentally.

The material presented at the symposium had been collected at an animal hospital during the past decade. This study revealed that primary diseases of the heart are relatively uncommon, e.g. tumors and specific infections, but that secondary lesions appear to be extremely frequent, e.g. inflammation subsequent to bacterial,
viral and metabolic diseases. In a total of 3000 necropsies the following types of heart disease were encountered in 619 cases:

<table>
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<th>Lesions</th>
<th>Incidence</th>
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<tr>
<td>1. Myo (pan-) carditis, myocardial edema, hemorrhage, necrosis, calcification, infarction (Thrombosis and sclerosis)</td>
<td>30%</td>
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<tr>
<td>2. Vascular changes (inflammatory, degenerative, metabolic), periarteritis nodosa, necrotizing arteritis, athero-and arteriosclerosis</td>
<td>25%</td>
</tr>
<tr>
<td>3. Valvular diseases, valvulitis, edema, hemorrhage and fibrosis</td>
<td>25%</td>
</tr>
<tr>
<td>4. Dilation, hypertrophy or atrophy</td>
<td>15%</td>
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<tr>
<td>5. Endocarditis, subendocardial hemorrhage, edema, necrosis, calcification, and fibrosis</td>
<td>10%</td>
</tr>
<tr>
<td>6. Primary and secondary neoplasms</td>
<td>3%</td>
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<tr>
<td>7. Epi- and pericarditis</td>
<td>1%</td>
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<tr>
<td>8. Congential cardiac anomalies</td>
<td>1%</td>
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This tabulation discloses a striking frequency of inflammatory changes as endo-, myo- and pancarditis which may occur either focal, disseminated, diffuse, interstitial, and acute, subacute, chronic, granulomatous and/or sclerosing in type.

The opportunities for various kinds of laboratory investigations are obvious.

Another study at a school of veterinary medicine in the USA has shown that the incidence of cardiovascular disease among dogs is considerably higher than realized. One out of fifteen dogs examined at this institution had some kind of heart abnormality. What the causes of these conditions are is not known - nor what their relative incidence may be in a given population is unknown. To find further information about the disease in this population an epidemiological study is being undertaken to try to ascertain what the external or environment factors may be that contribute to canine heart disease. These studies are being taken under the direction of the National Heart Institute with veterinary epidemiologists. Naturally the data assembled will be studied closely to determine what its value may be in the epidemiology of heart disease in man.

Studies like this should be encouraged in other institutions, countries and continents so as to collect data on the prevalence of canine heart disease and what may be the influences of infectious disease, climate, nutrition and environment.
Another new development in the area of comparative heart disease research is to establish a clinic for the care of various types of canine heart disease. This clinic will provide natural occurring cases of various types to the clinical investigators of various therapeutic, surgical and radiological studies.

Arteriosclerosis seems to turn up in animals somewhat in proportion to the extent it is sought. Recently a report from Harvard pointed out that the disease was fairly common in South American monkeys - occurring spontaneously. The list of animals in which spontaneous arteriosclerosis occurs is quite extensive. The Philadelphia zoo in a recent report to the National Heart Institute states that 20 percent of the mammals currently being autopsied have arteriosclerosis.

There are some indications that hypertension, the second ranking killer among the human cardiovascular diseases, may be a common natural disease in animal population. Studies in the USA reveal that there is a wide range of natural variation in blood pressure in dogs, some individuals being naturally hypertensive. Certain dogs are much more susceptible to experimental hypertension than others. Other investigators have found that healthy dogs subjected to severe dietary stresses and irregularities over a long period of time will develop sustained diastolic hypertension which may last far after the experimental conditions are terminated.

Aside from dogs it is known that hypertension can be readily produced in rats and rabbits. It is supposed that spontaneous hypertension can occur in these and other wild animals, particularly when one considers the variable rigors of environment imposed by nature on wild animal population.

The incidence of animal congenital abnormalities is largely unknown. One study recently published reported an incidence of 10% among a large group of experimental dogs. Another veterinarian investigating the incidence of congenital abnormalities in stillborn and newborn dead pigs reported 10 malformations of five different types in seven of the 48 pigs examined - 14%. Five of the abnormalities were cardiovascular. This investigator comments that "congenital abnormalities in swine have been so infrequently reported in veterinary literature that it is impossible to estimate their significance".

All of this material is available to the diligent investigator who is willing to seek it out. The opportunities for laboratory, clinical, and epidemiological research are limitless. A collection of data from various geographical areas should be undertaken as soon as possible to elucidate the comparative epidemiology of the various cardiovascular diseases among animals. These data may provide information of great value to the elucidation of the epidemiology of cardiovascular diseases in humans.
Degenerative diseases

Few domestic animals live out their normal life span except animal pets, viz. dogs, cats and birds. But even with these limitations the field of comparative medical studies among domestic and pet animals offers unusual opportunities. Many of the degenerative diseases that are important to human health occur spontaneously in animals that live close to man and are exposed to the same environmental influences. Probably one of the most important from a public health aspect is arthritis. Millions of persons as well as many animals, especially swine, are affected by this malady. Comparative medical studies on this disease are now being carried out in some veterinary and medical research centers. An aspect that needs further exploration is the epidemiology of the disease in both man and animals. It would be very desirable if comparative medical investigations could be established in other parts of the world so as to shed light on the geographical distributions of this universal affliction of man and supposedly animals.

Blindness in some cases is a degenerative disease that affects many humans and a surprising number of certain animal species, viz. horse and dog. Most of these conditions occur in the ageing animal but frequently it is noted in animals that are relatively young. In the horse a recurrent iridocyclitis is not uncommon which leads to permanent loss of vision as the lens becomes opaque. The primary cause of this disease is still to be determined. In the past, the cause has been thought to be genetic transmission, nutritional deficiency (riboflavin) and more recently leptospire infection. Conservative opinion is that it is a degenerative disease of unknown etiology.

Dogs frequently have opacities of the lens that are non-specific as to origin. Some respond to medication, but even in these the condition is re-occurring and eventually causes blindness. When that occurs, only removal of the lens will provide any relief. The natural history of this entity needs investigation as well as the epidemiological pattern. It again is an ideal subject for comparative medical and epidemiological study.

Liver diseases including cirrhosis is found in many species of animals. Many of these have been studied as pathological diseases but again little has been done as to the distribution or incidence.

Metabolic disorders of many types are seen in different animals. One of the more interesting is gout in chickens. Fowls have the ability to excrete large amounts of uric acid which are converted to urates. What occurs to change this and allow the accumulation of these substances in the fowls' tissues is a challenging comparative medical disease problem.

Allergies of all types are seen in some animals. Some are sensitized to therapeutic agents, feeds, and others by endogenoses or autoallergens. The most serious are those due to infective agents resulting in an infectious allergy. The resultant hypersensitivity has primarily vascular localization.
Anemias of many kinds are also frequently encountered. Comparative hematology is an area which is just beginning and should develop rapidly with the extensive interest in blood research.

Diseases of the skin are numerous among domestic animals and pets. Some are metabolic, others are reactions to economic poisons or insecticides, while others are infections. All of these are areas that have received little attention until recent years.

Many animal pets lend themselves to gerontological research - the dog, cat and some birds are being used already. The dog is probably the ideal animal because so much is already known about his physiology, nutritional requirements, and susceptibility to disease. Also large colonies can be readily managed because of the experience that has been accumulated in recent years. Some of these groups that are being used for genetic studies would lend themselves admirably to ageing studies. The dog also has the longest natural life of the smaller animals in close contact with man.

Animal psychoses

It has been long known that animals are susceptible to induced psychotic ills. All degrees of derangement can be created in animals which are susceptible. The circumstances that permit this are not well defined except to say that certain breeds which are highly inbred seem to have the lowest threshold for artificially created mental illness. Animal psychology has advanced rapidly in the laboratory but there is need to carry out field studies to determine if there are epidemiological patterns that may reflect their breeding, environment or human relationship. A world wide survey may provide clues of inestimable epidemiologic value. It is important that this area of comparative medicine receive the recognition and support needed. Scholarships for veterinarians who wish to study animal psychology should be established.
THE FIELD INVESTIGATION OF ZOONOTIC DISEASES

J. L. Braun

Many diseases, once of particular public health importance, are now well controlled and consequently are no longer of paramount public health significance. As a result, other diseases, such as the zoonoses, have assumed positions of relatively greater significance to the public welfare. Necessarily, medical research interests have undergone a similar change. Field investigation is an integral part of the science of epidemiology and, as such, has always constituted an important aspect of medical research. The greater emphasis on diseases such as the zoonoses has resulted in an increased demand for field investigation.

Zoonoses research, by its very nature, necessitates that human medical and veterinary medical talents be coordinated. One of the specific areas demanding such professional cooperation is that of field investigation. Human epidemic diseases are subject to investigation by classical analytical epidemiological methods. Conversely, zoonotic diseases, by their very nature, are not subject to analytical epidemiological methodology. Zoonotic diseases seldom, if ever, occur in epidemic form among human populations; more often, such diseases occur in endemic or sporadic form. Thus, it is necessary that such diseases be investigated utilizing comparative and descriptive epidemiological methods; each case must be investigated, evaluated and compared with other similar episodes. Consequently, the adequate field investigation of zoonotic diseases necessitates on-the-scene investigation. A well trained field investigator can function most productively in this area of professional overlap by insuring rapport between professional disciplines and by collecting necessary epidemiological and epizootiological information. Improved laboratory diagnostic aids require many human and animal blood and tissue specimens; such can be collected by a well trained field investigator.

The infectious disease research program at the Institute of Agricultural Medicine is primarily a field investigation program. This approach may be exemplified by a brief review of the human leptospirosis program now under way. All human blood specimens submitted to the Iowa State Hygienic Laboratories for febrile agglutination studies (predominantly brucella serologies) are screen tested for leptospirosis. To date, a total of 12,250 specimens have been tested and 1.4% found to be positive. All specimens found to be positive at a titer of 1:40 or greater are investigated in the field. The submitting physician is contacted and the case reviewed. On the basis of the positive screen test serology and preliminary information secured from the attending physician, the case is evaluated as to its possible leptospira etiology. If indicated, the patient is interviewed, a complete occupational and environmental history obtained, clinical and hospital records abstracted and a
repeat blood specimen secured. In addition, whenever possible, an effort is made to substantiate the suspect exposure source by obtaining blood specimens from suspect infected contact animals. If such cases qualify on the basis of a 4-fold titer rise, compatible clinical symptomatology and documented exposure source, they are accepted as confirmed episodes of human leptospirosis. To date a total of 13 such cases have been documented. Our experience indicates a necessity for personal field investigation of such cases. Only by this method can the necessary information be secured.

Similar field investigation efforts have been successfully applied to Q fever in both man and animals in Iowa. Likewise, psittacosis, ringworm and enteric infections are most successfully investigated by these methods.

A field investigation program of this nature requires adequate and specialized equipment. Weather conditions necessitate use of a dependable field vehicle; commercial station wagons have proven most practical. In addition, equipment must be available for both human and animal investigations. The collection of human blood samples is facilitated by use of the commercial Shepherd blood collecting tubes; experience proves these tubes to be more efficient, dependable and inexpensive than regular syringes. Minimal "animal equipment" consists of rubber boots, coveralls, gloves, boot brushes, buckets, halters, nose tongs, lariats, and suitable blood collecting paraphernalia.

Recent developments in many local, state and federal health organizations serve to point out the feasibility of utilizing lay personnel in the role of medical field investigators. Training in basic epidemiology, the principle of infectious disease, and the mechanics of blood sample collection are prerequisite to the efficient performance of lay individuals in this capacity. Properly oriented, such individuals have proved capable of conducting thorough investigations while dealing with patients, veterinarians, physicians and health officers.
Parasites infecting man are usually closely related to those of domestic animals. The problem of parasites in man and animals differs greatly because of the types of sanitation practiced by these two host groups. Human preventative parasitology has been accepted by those in North America through the adoption of such conveniences and practices as sanitary plumbing, personal hygiene and meat inspection.

Parasites of animals infecting man in the north central states are:

1. *Ascaris lumbricoides* (man) and *Ascaris suum* (pig) - These two helminths are morphologically similar but are biologically different species. Pig ascaris will hatch in man and migrate to the lungs where it is ultimately destroyed. Although it is estimated that about three million human ascaris infections occur in the United States, ascaris in pigs plays no known role in the epidemiology of human ascariasis.

2. *Toxocara canis* (dog) and *Toxocara cati* (cat) - The disease, visceral larval migrans, caused by the migrating larvae of *T. canis* and *T. cati* has been recognized and substantiated during the past five years. The clinical syndrome associated with the migration of the larvae to the extra intestinal viscera of the unnatural host, is characterized by hepatomegaly, intermittent fever, nausea, vomiting, cough, weight loss, anorexia and marked abdominal pain. This infection is usually seen in young children of the "dirt eating age" or under 3 years. The incidence of visceral larva migrans is greater in the southeastern part of the continent although it has been reported in children from the north central states. Keeping pets, dogs and cats, free of this parasite is to be recommended as a preventative measure against human infection.

3. *Trichinella spiralis* - This helminth shows practically no host specificity. The United States has the doubtful distinction of having the highest incidence of trichinosis (about 16%) in the world. Current outbreaks are detected mostly among racial groups who enjoy uncooked sausage made by some local butcher who has a special recipe handed down from generation to generation. In 1952, laws were enacted to cook all commercial garbage fed to swine. At the present time, 46 states cook commercial garbage. In years to come, this should have a considerable effect on lowering the incidence of trichinosis in man and animals.

4. *Trichobilharzia* sp. - Man is accidentally attacked by the schistosome cercariae from flukes of the genus *Trichobilharzia* causing cercarial dermatitis (swimmer's itch). These flukes live in the blood vessels of aquatic birds such as ducks, loons, etc. Cercarial
infection gives rise to intense itching which may last 1-4 days. Swimmer's itch is quite common in many fresh water lake in the north central states. Control is achieved by the application of copper sulfate to the habitat of the intermediate host, the snail. Human infections are minimized by rubbing dry with a rough towel immediately after coming out of infected water.

(5) Diphyllobothrium latum - The broad fish tapeworm, D. latum, occurs in certain lakes areas of Minnesota, Michigan and Florida. Infections are invariably traced to eating raw or insufficiently cooked fish, a custom among various groups of people such as the Scandinavians, Russians, Jews, etc. Human infections may often produce a condition similar to pernicious anemia.

Other parasitic diseases common to animals and man of a greater geographical distribution are discussed. It is emphasized that global travel, concentration of people and animals and indiscriminate shipping and movements of man and animals offers great opportunity for the introduction of new parasites to new geographical regions.
SUSCEPTIBILITY OF VARIOUS SPECIES OF RODENTS NATIVE TO THE NORTHWEST TO EXPERIMENTAL INOCULATION WITH THE PLAGUE BACILLUS

Marion Bacon

At the State College of Washington, wild rodents including 62 meadow mice, Microtus, 72 deermice, Peromyscus maniculatus, 14 pocket mice, Perognathus parvus, and 1 sagebrush vole, Lagurus, were inoculated with graduated dosages of virulent strains of Pasteurella pestis originally isolated from feral sources. These rodents were judged to be the species of mammals most common in eastern and central Washington and among those most apt to come into contact with other species. The Peromyscus, Microtus and Perognathus have closely related species or subspecies resident in the Midwest.

Animals surviving inoculation were sacrificed and tested for the presence of bacteria in their tissues and for agglutinating antibodies in their serums.

Both Microtus and Peromyscus included some plague-resistant and some plague-susceptible individuals. Some of these mice succumbed to dosages of about 10 bacilli each; others survived dosages of over 100,000 bacilli. Perognathus seemed entirely susceptible to fatal infection with virulent P. pestis.

Of the animals surviving the inoculations, two out of 23 Microtus and 2 out of 23 Peromyscus showed positive agglutination titers. P. pestis occurred in the tissues of one survivor among the Microtus and 2 of the surviving Peromyscus. Of the animals dead of plague infection intense bacteremias were found in nearly all of the Microtus and all of the Perognathus; in Peromyscus bacteremias were less intense as a rule, but usually detectable.

The four strains of P. pestis used as inoculums showed differences in their virulences to white mice. All seemed less pathogenic to Microtus and Peromyscus than to white mice.

Of the ten additional Peromyscus fed with plague-infected carcasses, nine developed fatal plague infections.

The one Lagurus was susceptible to plague-infection, but showed a longer survival time than the other species tested and a somewhat different pathology.

It was suggested that Peromyscus and Microtus may play an important role in maintaining plague in an enzootic condition. Perognathus probably cannot maintain intraspecific enzootic plague, but may have enzootic importance where other mammalian species are present. Carnivorous and cannibalistic habits may be important means of transfer of plague infection among some kinds of rodents.
"DISEASE-FREE" SWINE AS HOSTS FOR THE STUDY OF RESPIRATORY DISEASE

G. A. Young, G. W. Kelley, and N. R. Underdahl

Study of chronic respiratory infections of viral origin in experimental animals has as a limitation, the natural occurrence of similar diseases in most species. Experimental respiratory disease imposed upon naturally occurring respiratory infection is simply not interpretable.

One other limitation to experimental animals handled by attendants is possible exposure to human diseases and formation of antibody in inapparent infections. The immunity of such a host may block experimental transmission of the disease with an immunologically related disease agent.

Both of the above problems are eliminated in the use of "disease-free" baby pigs as the experimental host. Pigs are obtained "surgically" before expected birth and delivered in a sterile environment. They are kept under cover and housed in isolation units (modified Hosfall-Bauer). Sterilized and repasteurized cows' milk is fed to these pigs. They do not come in contact with attendants or other animals so are free of pathogens. Since antibody does not pass the swine placenta, immunity in swine is derived entirely from the mother's colostral milk. These pigs receive no colostrum so are immunologically naked.

Use of the above type pig in experimental respiratory infections was discussed. Emphasis was placed on an atypical pneumonia common to swine and possibly related to some of the atypical pneumonias in man.
In spite of the marked reduction in brucellosis in the United States through the controlling of the disease in the bovine and through the pasteurization of milk little attention has been paid to swine brucellosis which is and has been the major source of human brucellosis in Iowa, and other hog raising states. Had some effort been devoted to the control of the disease in swine, human brucellosis today would be at a relatively irreducible level.

Figure 1 shows the reported incidence of human brucellosis in the United States and Iowa for 5 year periods save for the period of 1905-24 and the singular years 1955, 56 and 57.
Figure 2 shows that as brucellosis in the United States as a whole has declined and that the percentage of Iowa cases has increased in proportion to other states. The reason for this percentage increase is that little or nothing has been done to control swine brucellosis. Although bovine brucellosis has been a reportable animal disease in Iowa for years it is indeed surprising that with all the past and present knowledge accumulated in Iowa that swine brucellosis has not been a reportable disease.

In the year 1955, Iowa reported 405 or 28% of those reported for the entire United States while 3 states Iowa, Illinois, and Minnesota reported 661 cases or 46% of those for the United States. Similar findings are recorded for 1956 and 1957.

Figure 2
Table 1 shows that Iowa for years has been among the 10 leading states in the reporting of human brucellosis.

That we are dealing with swine brucellosis is well documented from epidemiologic data, tissue and blood culture studies and the typing of the species of brucella isolated from human, animal and milk sources.

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<td>Texas</td>
<td>Iowa</td>
<td>Texas</td>
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<td>3</td>
<td>Ill.</td>
<td>Texas</td>
<td>Iowa</td>
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<td>4</td>
<td>Ill.</td>
<td>Texas</td>
<td>Iowa</td>
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<td>5</td>
<td>Ill.</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Illinois</td>
<td>Texas</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
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<td>Iowa</td>
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<tr>
<td>6</td>
<td>N.Y.</td>
<td>Mich.</td>
<td>Ill.</td>
<td>Ill.</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
<td>Iowa</td>
</tr>
</tbody>
</table>

Table 2 shows the number and species of brucella isolated and/or typed from individual human cases in Iowa.
Of 533 strains of brucella isolated from individual human cases, Brucella suis was isolated from 335 (60.8%) cases; Brucella abortus from 142 (25.6%) while 76 or 13.6% were Brucella melitensis. Had we not typed all strains of Brucella isolated from human, animal and milk sources, we would not have been aware of the problems in Iowa. Epidemiologic and laboratory studies reveal that all of the melitensis infections had their origin in swine; hence, in the overall, 74.4% of the human infections originated in swine.

The great majority of human cases in Iowa are among male farmers, packing house workers, veterinarians, stock handlers etc. and are traced to direct contact with infected animals, tissues or aborted products. The organism will pass through the unbroken skin but infection is enhanced through the broken skin.

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Brucella suis</th>
<th>Brucella abortus</th>
<th>Brucella melitensis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>306</td>
<td>135</td>
<td>75</td>
</tr>
<tr>
<td>Complicating Lesions</td>
<td>29</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>335</td>
<td>142</td>
<td>76</td>
</tr>
</tbody>
</table>
Figure 3 shows that brucellosis in Iowa is greatest in areas where packing plants processing hogs are located.

Table 3 shows brucella species isolated from milk of individual dairy herds and from swine tissues.

Of 75 strains of brucella isolated from milk of individual dairy herds, 70 were Br. abortus while 5 were Br. suis. Of the 5 Br. suis strains, 3 were associated with epidemics of human brucellosis, traced to the ingestion of unpasteurized milk from
herds allowed to mingle with infected hogs. In one epidemic, 77 cases occurred with multiple cases in several families within three weeks' time. The outbreak promptly ceased following pasteurization of the milk supply. Br. suis was isolated from the milk of 2 of 4 reacting cows in the herd and from 13 blood cultures from the 111 patients.

The virulence of Br. suis strains isolated from cows as judged by pathogenicity in guinea pigs and clinical illness in the patients was considerably less than in cases of Br. suis infections in humans secured by direct contact with infected hogs. From our experience in 3 epidemics of swine brucellosis traced to milk the presumptive evidence is that the strains are reduced in virulence by residence in cattle.

Table 3

<table>
<thead>
<tr>
<th></th>
<th>Brucella suis</th>
<th>Brucella abortus</th>
<th>Brucella melitensis</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILK</td>
<td>5</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>ANIMALS</td>
<td>1</td>
<td>2*</td>
<td>14 **</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>72</td>
<td>14</td>
</tr>
</tbody>
</table>

* 1 from hog tissue
** All from hog tissues
Table 4 shows the complicating lesions of brucellosis in Iowa and the species of brucella isolated from the lesions.

Complications in the course of brucellosis are not unusual particularly in Br. suis infections. Of 37 bacteriologically proven cases, 29 were Br. suis, 7 Br. abortus and 1 Br. melitensis.

Brucella suis infections in man and guinea pigs simulate tuberculosis in many respects.

Brucella may lie latent in the reticulo endothelial cells following apparent clinical recovery. Brucella have been isolated during the primary attack and the same species from lesions following injury two years or more later with apparent well being in the interval. Within 24 hours following injury the patient becomes febrile, complaining as in the primary attack and the same species isolated from the site of injury.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>COMPLICATING LESIONS IN HUMANS VERIFIED BY THE ISOLATION OF BRUCELLA FROM THE LESION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Brucella suis</td>
</tr>
<tr>
<td>Subacute Bacterial Endocarditis</td>
<td>7</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>4</td>
</tr>
<tr>
<td>Meningo-encephalitis</td>
<td>3</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>3</td>
</tr>
<tr>
<td>Cold Abcess</td>
<td>3</td>
</tr>
<tr>
<td>Spondylitis</td>
<td>2</td>
</tr>
<tr>
<td>Pleurisy with Effusion</td>
<td>2</td>
</tr>
<tr>
<td>Cervical Adenitis</td>
<td>2</td>
</tr>
<tr>
<td>Cholecystitis</td>
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<tr>
<td>Hydro-arthritis</td>
<td>0</td>
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<tr>
<td>Ovarian Cyst</td>
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Table 4 Cont'd

<table>
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<th>Condition</th>
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<tbody>
<tr>
<td>Peritonitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver Abcess</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thyroid Abcess</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

Treatment

In our experience with bacteriologically proven Br. suis infections a single antibiotic is insufficient to control the infection. Similar situations are recorded by Herrell and his associates at the Mayo Foundation and by Castaneda in Mexico. Concomitant therapy recommended by Herrell, Castaneda and others consisting of dihydrostreptomycin 1.0 gms. intramuscularly every 12 hours for 12 - 14 days together with simultaneous administration of an oxytetracycline 3 gms. by the oral route every 24 hours in divided doses every six hours is the treatment of choice.

In the presence of complicating lesions, therapy should be continued for 28 days as noted except that dihydrostreptomycin is reduced to 0.5 gms. twice daily.

Summary

1. Brucella infections of swine origin predominate in Iowa and other areas of the midwest, thus infection in the human will not be eliminated until the disease is also controlled in swine.

2. From animal inoculation studies of cultures and clinical evaluation of patients in Iowa, Brucella suis infections are far more serious and more complications are encountered than from infections due to Brucella melitensis or Brucella abortus.

3. There is evidence that Brucella suis isolated from infected cattle is of lower virulence than strains isolated from humans infected by direct contact with swine.

4. Concomitant therapy with dihydrostreptomycin and a broad spectrum antibiotic is essential to adequately terminate infections in the human due to Brucella suis.

5. Recurrent brucellosis is usually the result of inadequate therapy or failure of the drug to penetrate recitculo-endothelial cells containing viable, intact brucella.
VIBRIO FETUS IN DOMESTIC ANIMALS AND MAN

S. M. Morrison and V. A. Miller

Vibrio fetus is the causative agent of a very widespread contagious abortion, usually called vibriosis, of sheep (and goats) and of cattle (and buffalo). Eighteen documented cases of human infection with this organism have been reported from France and the U. S. The organisms from each of these species are homogeneous morphologically and biochemically but heterogeneous immunologically. Similar organisms, some non-pathogenic and some causing other disease conditions are known.

In cattle the disease is transmitted by the bull which harbors the organism in the genital organs. The cow aborts before the sixth month of pregnancy, experiences difficulty in reconceiving and, it is believed, transmits the disease to its female offspring. Outbreaks involving 20 per cent of the herd are known. In sheep the outbreaks of vibronic abortion are more explosive, involving as high as 60 per cent of a flock, with abortions late in pregnancy. The disease is transmitted by the oral route probably by contact with expelled fetal material in feeding. The ram seems unimportant. After abortion the ewe has a normal breeding year.

The pathology in both sheep and cattle is similar, the most striking lesions being in the cotyledons of the placenta. Uterine damage is characterized by edema and hemorrhage in the caruncles and the intercaruncular areas. In the fetus, edema of the umbilical region with sanguinous fluid in the body cavities is present.

In the human, no definite conclusions can be drawn from the few studied cases. Three cases were in pregnant women, two ending in abortion. The other cases (13) were in adult males, five of whom worked with animals. The disease was often diagnosed as brucellosis and even malaria. The most consistent symptom was undulating fever and many patients showed chills, headache, respiratory difficulty, weakness and anorexia. The bacteremia was followed by paralysis and heart damage in some cases, but the true relationship is not known.

Improved isolation and diagnostic procedures are necessary to determine the extent of this disease in humans.
STUDIES ON TRICHINIASIS IN IOWA*

W. J. Zimmerman, E. D. Hubbard, and L. H. Schwarte

Studies during 1944-46 showed the presence of Trichinella spiralis in about 12 percent of 904 samples of commercial pork sausage. Similar studies during 1953-58 revealed only 1.4 percent of 6,115 samples of non-processed pork sausage to be positive. During the past year the incidence of T. spiralis has been about 0.3 per cent. This decrease may reflect the effect of garbage cooking regulations as well as better swine management methods. The examination of diaphragms from 3,592 grain-fed swine revealed an incidence of only 0.17 percent. The incidence of T. spiralis in dogs and cats is 9.8 and 5.7 percent, respectively.

The examination of 4,697 specimens from 44 species of Iowa wildlife has thus far shown nine species to be reservoirs of T. spiralis. These species are: rat, fox, mink, raccoon, opossum, striped skunk, spotted skunk, coyote, and badger. In order to determine the possible role of wildlife in perpetuating trichiniasis in grain-fed swine, two modes of transmission have been considered: (1) direct consumption of infected carcasses by swine, and (2) fecal transmission from infected animals to swine. Experimental results indicate both modes of transmitting the parasite may be important.

*This investigation was supported in part by a research grant E606 (04), from the National Institute of Health, U. S. Public Health Service.
THE CURRENT STATUS OF LEPTOSPIROSIS IN THE UNITED STATES

A. H. Quin

On a world-wide basis, some forty species of pathogenic leptospires with additional subtypes, as yet, not too clearly identified serologically, are responsible for disease in a wide range of animal hosts including man.

These microorganisms, essentially saprophytic and aquaphilic in nature, are transmitted to other mammalian hosts by a long list of rodents. Several species of rats are primary reservoirs of Leptospira icterohemorrhagiae, the specific pathogen of Weil's disease.

Specific diagnosis of clinical leptospirosis has proved difficult for it requires special microscopic and staining approaches and the septicemic phase is transient. A rising blood titer as indicated by accepted serological technics with selective antigens is a specific indication of active infection in cases where isolation of the micro-organism in culture or laboratory animal inoculations have not been accomplished.

Broad scale serological surveys indicate that L. Pomona is the predominant pathogen responsible for livestock leptospirosis in the United States, while L. canicola and icterohemorrhagiae are the etiological factors of canine leptospirosis. Low dilution titers indicate that L. sejroe, ballum autunnalis and gripotrophosa may also carry as yet undetermined epizootic significance for livestock as well as human hosts. However, so far as livestock is concerned the epizootic significance of species other than L. pomona must await more data based on (serological diagnosis coupled with isolation and specific identification of involved serotypes.

Whether in rodent hosts, domestic animals or man, leptospirosis may range from inapparent infection to a highly fatal febrile illness. For this reason, it is probable that a great majority of cases involving domestic animals or man are not diagnosed. The current availability of selective rapid type, formalin killed diagnostic antigens should contribute materially to solving this problem.

Control of L. pomona leptospirosis of livestock as well as L. canicola and icterohemorrhagiae leptospirosis of dogs has been expedited by development of specific bacterial vaccines which confer an adequate measure of protection against field exposure.
ANTIGENIC VARIABILITY OF LEPTOSPIRAL SEROTYPES

Robert M. Pike

As a possible means of obtaining serologic variants of leptospiras, cultures were repeatedly transferred in medium containing homologous immune rabbit serum. In high concentrations of immune serum growth was inhibited but in lower concentrations, although many of the organisms agglutinated, some remained free and motile. Subcultures of the unagglutinated leptospiras at first showed the same serologic characteristics as the parent cultures. After ten or more transfers at intervals of about a month reduced agglutinability became apparent. After 37 transfers L. grippotyphosa agglutinated to a titer of 40 as compared to a titer of 40,960 for the parent strain. Evidence that the altered strain had also acquired new antigenic components was provided by its ability to induce the production of antibodies which were not absorbed by the parent strain. L. pomona and, to a lesser extent, L. canicola also showed reduced agglutinability after prolonged growth in the presence of homologous immune serum. The altered strain of L. grippotyphosa has showed no tendency to revert to the original parent type over a period of 15 months in the absence of immune serum. It is suggested that comparable antigenic changes may occur under natural conditions.
Increased interest in leptospirosis has directed attention to the need for a safe genus-specific serologic test, that could be readily performed by the usual diagnostic or public health laboratory. In 1955 a report from this laboratory described a hemolytic (HL) reaction, which involved the ability of leptospiral extracts to sensitize sheep erythrocytes to hemolysis in the presence of leptospiral antiserum and complement. These extracts were similar in preparation to those previously reported by Chang and McComb in 1954, who described their use in a hemagglutination test with human erythrocytes. The HL procedure was shown to be broadly specific, in sharp contrast to the high degree of type-specificity seen in conventional agglutination or agglutination-lysis (AL tests). Subsequent reports last year described the preparation, standardization, and stabilization of the antigen from the so-called non-pathogenic L. biflexa.

Data are presented which describes the evaluation of the HL reaction with serotype specific rabbit antisera, with sera from 190 proved human cases of leptospirosis, with sera from pre- and post-infected dogs and cattle, and with sera from randomly selected cattle. The HL reaction would seem to warrant serious consideration as a routine serologic procedure in the diagnosis and epidemiology of human leptospirosis. The evidence indicates that it may also prove to be of value in serodiagnosis of caninc and bovine leptospirosis; at least further studies of its possible use would seem to be justified.
A SEROLOGIC SURVEY OF LEPTOSPIROSIS IN A NON-SELECT GROUP OF HOSPITAL PATIENTS AND IN PACKINGHOUSE WORKERS

N. G. Miller
J. J. Bence

A total of 761 serum samples were examined for leptospiral antibodies. Five hundred and twenty-eight samples were obtained from patients in various Omaha hospitals representing both an urban and a rural population. These patients were referred here as the non-select group since serums were submitted for various serologic examinations other than leptospiral. In addition, serums from 233 packinghouse workers representing a specific occupational group were obtained.

Leptospira icterohaemorrhagiae, Leptospira canicola and Leptospira pomona were used as antigens throughout this study. These particular serotypes were selected because they are still considered the primary infecting type strains in the United States. The serotypes were grown in a fluid medium slightly modified from that originally described by Stuart. The serologic examination of all serum samples was carried out by means of the agglutination-lysis test using darkfield illumination.

Seven, or 1.3%, of the 528 serums from the non-select group of hospital patients demonstrated a titer for leptospiral antibodies. Four were positive for L. pomona and three for L. icterohaemorrhagiae. No reaction was seen with the L. canicola antigen and none of the titers in this groups were greater than 1:100.

Of the serums from the 233 packinghouse workers, 15, or 6.4%, were positive at a titer of 1:30 or greater. It is of particular interest that all of the 15 serums were positive for L. pomona. Two serum samples demonstrated titers of an active infection. Successive serum samples from one of the two samples demonstrated a definite increase of L. pomona antibodies. This patient also showed clinical symptoms characteristic of L. pomona infection.

These results indicate a rather low incidence of infection with the three more common leptospires in a general population represented here by the non-select group of hospital patients. This is particularly true when this group is compared with a specific occupational group such as the packinghouse workers. Since both cattle and hogs may become healthy carriers of L. pomona, an increase of positive reactors to this serotype in packinghouse workers is not too surprising. Again, the obvious conclusion must be reached that the majority of leptospiral infections are the result of occupational hazards.
THE PLATE AGGLUTINATION TEST FOR THE SERODIAGNOSIS OF LEPTOSPIROSIS*

A. H. Killinger, M. B. Hays, and M. F. Coria

The plate agglutination test for the serodiagnosis of leptospirosis was developed by Dr. H. G. Stoenner. Antigen used in the test is a chemically-killed, stable, refined, concentrated and standardized suspension of leptospira.

In the preliminary screen test one loopful (0.005ml) of serum is mixed with one drop of antigen on a glass plate. After incubation and rotation, agglutination is visible around the margin of the drop. In positive samples the titer of the serum should be determined by a rapid plate dilution test.

The general interpretation of the results of the test is as follows:

1. Negative plate screen -- negative.

2. Positive plate screen. Positive rapid plate in dilutions of 1:10 to 1:40 --
   a) Low level of antibody against leptospira
   b) Cross reaction with another serotype of leptospira
   c) Non-specific reaction
   d) Vaccination

3. Positive plate screen. Positive rapid plate in dilutions of 1:160 or higher. -- Possible present or past infection with specific leptospira.

*For a complete discussion of this technique, reference is made to the Fort Dodge Bio-Chemio Review, 26:3 (1956) entitled "Leptospirosis Diagnosis, A Single Macroscopic Agglutination Test."
Leptospirosis of the domestic animals in the United States has been recognized as a serious problem within the last decade. Various serological surveys have adequately demonstrated the importance of this disease in both large and small animals. The principal leptospires producing the disease in the United States are *L. icterohemorrhagiae*, *L. canicola* and *L. pomona*. Recent surveys have revealed significant evidence of other serotypes.

Infected animals shedding the leptospires via the urine serve as the primary source of infection to susceptible animals.

The clinical manifestations of leptospirosis in animals are extremely variable even within a specific species. Typical cases develop symptoms after an incubation period of 5-18 days. During the early stages of the disease, the leptospiremia will be characterized by fever, lassitude, anorexia and tissue damage, particularly hemorrhage, and associated symptoms.

The septicemia may last from 2-7 days and upon the appearance of leptospiral antibodies the organisms tend to disappear from the blood stream and localize in the kidney tissue where they multiply and are excreted in the urine.

Various forms of the disease are noted and may be divided into sub-clinical, hemorrhagic, icteric, classical, and chronic depending on the subjective symptoms.

Among cattle hemoglobinuria, atypical noninflammatory mastitis and abortions are suggestive of leptospirosis.

The disease in swine may be relatively benign except for its effects on pregnant sows where abortions and high incidence of mortality of the newborn are characteristic. In the horse there is evidence that leptospirosis might be associated with recurrent iridocyclitis.

Broom very aptly described leptospirosis of the canine when he stated that the clinical manifestations might be absent, latent, sub-clinical, typical, mild or severe. The most frequent sequel to leptospirosis in the dog is chronic interstitial nephritis and subsequent uremia which appear months or even years after the acute infection.
THE CONTROL OF LEPTOSPIROSIS IN DOMESTIC ANIMALS

A. L. Brown

The control of leptospirosis begins with an understanding of how it is spread. At some time during the course of any leptospiral infection, a leptospiremia exists and leptospira may be isolated from any organ. This stage ends when antibodies are formed and if by this time the leptospira are not located within the kidney tubules, the disease is self limiting. While it is customarily stated that leptospiral infections are accompanied by the development of chronic interstitial nephritis, the leptospira are not located within the kidney tissue. The organisms form tangled masses within the secondary convoluted tubules which might be considered as bacterial colonies. From these masses, leptospira are shed into the urine for a period of from several weeks to a lifetime. During their presence in the tubules, the leptospira stimulate a low grade inflammatory reaction in the interstitial tissues which results in a comparatively slow but progressive chronic nephritis.

Leptospira shed in the urine are the most usual source of new infections. New infections may be derived both through direct contact with animals shedding leptospira or indirectly through contaminated environment. Leptospirosis spread by direct contact may spread slowly through a group of animals thereby making diagnosis difficult. Under conditions where the number of leptospira in surface water is able to build up, explosive outbreaks of leptospirosis are noted.

There has been an increased incidence of leptospirosis due to L. pomona in cattle and swine in this state during the past 18 months, particularly in northeast and southeast sections where there has been flooding in 1957 and 1958. Information obtained from plate agglutination tests show an increase in reactor herds during this period since the end of the drought in 1957. This increase may be roughly correlated with rainfall and flooding. There is no evidence that wildlife play an important part in the transmission of Leptospira pomona in this state.

The use of Leptospira pomona Bacterin is the most reliable method for controlling infection in swine and cattle. The bacterin is effective because it may be used on any age animal, produce rapid and long lasting immunity and is stable in the liquid form. Some suggested uses for this product are as follows: To check the spread of leptospirosis in a herd or drove following diagnosis, to protect animals in herds adjoining infected herds or along a common water shed, to protect susceptible animals before introduction into herds or areas which are contaminated, to protect animals taken to shows and returned to herd, and to protect cattle in feeder lots especially when pigs and cattle are fed together.
Antiserum for the protection of dogs against *L. canicola* is available in combination with anti-canine distemper serum and anti-canine hepatitis serum. It is very effective in the usual dosage of 0.5 ml per pound of body weight if given previous to exposure. An experiment was presented to emphasize its effectiveness.

Antibiotics have been found reasonably effective in eliminating the carrier state but are of dubious value in modifying the course of disease. The antibiotics that have been found most effective are those eliminated through the kidneys in a high concentration over an extended period of time. Included in this group of antibiotics are the tetracyclines and streptomycin.

The author wishes to thank Dr. Daniel Waring, Dr. Milo Johnson and Mr. Robert Cumings of the State and Federal Brucellosis Laboratory, Lincoln, Nebraska for use of their data on the incidence of leptospirosis in Nebraska.
DIAGNOSIS, EPIDEMIOLOGY AND TREATMENT OF HUMAN STAPHYLOCOCCAL DISEASE WITH SOME CONSIDERATION OF THE DISEASE IN ANIMALS

I. M. Smith, M. E. Godfrey, and A. P. Wilson

Although staphylococci can be differentiated by their pigment or coagulase production, this does not allow a precise enough diagnosis for epidemiological purposes. Strain differences and similarities are best studied by phage typing with 24 or more standard phages. The virulence of staphylococci is at present difficult to assess. One of the reasons for this is that the same number of cocci injected into experimental animals by different routes will kill rapidly in one case and will merely result in temporary indisposition in a second.

In hospital nasal carriers of staphylococci are more common than in the general population. Phage typing studies show that 29% of the total hospital staphylococcal infections are caused by one type, namely type 81. Twenty-seven per cent of the staff carry this strain but more importantly 57% of staphylococcal skin sepsis in the staff is caused by this strain.

In the family a virtual plague of boils may make the rounds over a period of months or years. Approximately 50% of the members of such families are nasal carriers of the strain causing these furuncles. In some cases the strain was introduced from a hospital by a physician or nurse member of the family.

The types of infection caused in man range from boils and carbuncles to necrotizing hemorrhagic pneumonia and septicemia. Many of these diseases are acquired in the hospital, frequently when the patient is debilitated from other causes.

Control of the disease consists in breaking the chain of infection. Patients dripping pus must be isolated. Physicians and nurses must return to reasonable standards of asepsis and staphylococcal diseases must be treated early and adequately.

These organisms are known to cause a variety of skin diseases, mastitis, enteritis and septicemia in a number of animal species. In birds, dermatitis and staphylococcosis occur. It is not known whether a closed circuit of staphylococcal infection is present in animals or whether, in truth, these are diseases of man transmissible to animals.

Treatment is unfortunately not predictable but there is a group of suitable drugs from which a choice can be made. If the organism is susceptible the drugs of choice are in order of preference: penicillin, streptomycin, erythromycin, novobiocin, chloramphenicol, oleandomycin or the tetracyclines. Vancomycin and ristocetin are reserved for severe infections and bacitracin, neomycin, tyrocidin or the furacins for local treatment.
RABIES - THE EPIDEMIOLOGIC PATTERN

Stanley L. Hendricks and I. H. Borts

The reported incidence of rabies in dogs in the United States has decreased in the last decade but the disease in other animals, principally wildlife, has remained at a high level. In a group of selected states (Minnesota, Iowa, Missouri, Kansas, Nebraska, South Dakota and North Dakota) this trend is more marked. In these states about one-half of all rabies cases reported are wild animals. Skunks constitute 84% of the wild animal cases. In contrast 65% of the wild animal rabies reported in the United States is among the fox population. Of 5,698 animal heads examined at the State Hygienic Laboratory over a 20 year period 1,558 or 27.3% were positive for rabies. The per cent of positives varied considerably among different species of animals. Of all the heads that were positive 17.1% were Negri negative but mouse positive. This too, varied greatly with species. There were 4,184 microscopic negatives of which 267 or 6.3% were positive by mouse inoculation.
THE PATHOGENESIS OF RABIES IN INSECTIVOROUS BATS

S. Edward Sulkin

Preliminary experiments (Sulkin et al, Proc. Soc. Exper. Biol. Med. 96:461, 1957) have indicated that the interscapular brown fat of the Mexican free-tailed bat may constitute a target organ in which virus may persist for long periods of time. These experiments have now been extended to include experiences with the little brown bat, Myotis lucifugus, a true hibernator, in addition to the Mexican free-tailed bat, Tadarida mexicana, a quasi hibernator. Hibernation delays significantly multiplication of the virus inoculated intramuscularly or into the surgically exposed interscapular brown fat and provides a means for "cold storage" of the rabies virus under natural circumstances. The study would seem to support the proposition that brown fat which provides food reserve during the inactive state may also provide means for storage of the virus during the period of latency. Environmental temperature has a profound effect on the progress of experimental rabies in bats. Both the virus and the host remain quiescent when maintained in the cold and both are activated when the animal is transferred to a warm environment.
AVIAN TUBERCLE BACILLUS INFECTION IN MAN

Alfred G. Karlson

In the United States the greatest incidence of avian tuberculosis in the North Central area, where in some localities half of the chicken flocks harbor the disease. The infection rate may vary from 10 to 25 per cent in flocks of hens 2 years of age and older.

*Mycobacterium avium* grows in 10 to 14 days on egg-medium to form small, moist, smooth, rounded, buff-colored colonies. They are relatively resistant in vitro to streptomycin, to para-aminosalicylic acid and to isoniazid. Avian tubercle bacilli are identified by their ability to cause progressive disease in rabbits and chickens and by their failure to do so in guinea pigs. There is partial cross-sensitivity with mammalian tubercle bacilli, with *Mycobacterium paratuberculosis*, with some unidentified acid-fast bacteria.

Avian tuberculosis is found in many kinds of domestic fowl, in wild birds, and in exotic avian species in zoological parks. Naturally occurring infection is found in swine, cattle, sheep, mink, rabbits, and--rarely--horses and goats. Guinea pigs are highly resistant and dogs and cats apparently are immune. In this country almost all tuberculosis in swine is of avian origin. In 1956 approximately 5 per cent of all swine slaughtered in the United States had tuberculous lesions. Cattle with avian tuberculosis may react to the routine test for bovine tuberculosis.

It is apparent that man is relatively resistant to infection with *Mycobacterium avium*. In only about 30 recorded cases of infection in man has the microorganism been identified adequately. Four cases will be described here. In each, the acid-fast bacilli were of interest originally because they did not appear to be human or bovine tubercle bacilli. They were found to have the cultural and pathogenic properties of avian tubercle bacilli. They were agglutinated by serum from tuberculous chickens and they induced sensitivity to avian tuberculin in guinea pigs.

Case 1.--A 22-month old child with a low-grade respiratory illness of a few months' duration was found to have diffuse infiltration of the right upper pulmonary lobe. Bronchoscopic washings contained acid-fast bacilli. One culture of gastric washings presented colonies of acid-fast bacilli which proved to be avian tubercle bacilli. The patient's reaction to avian tuberculin was more pronounced than her reaction to PPD. She remained free of symptoms through 9 months of hospital care, during which time the pulmonary infiltrate gradually cleared. The child came from a Minnesota farm where 50 per cent of 400 chickens were found to react to avian tuberculin.
Case 2.—A 57-year old Iowa farm woman came to the clinic for other reasons but incidentally complained of a fluctuating swelling of the right index finger which had persisted for a year. This was incised and granulomatous tissue was removed. A pathologic diagnosis of tuberculous synovitis was made. Avian tubercle bacilli were cultured from the material. Treatment with isoniazid and para-aminosalicylic acid was given for 8 weeks but was discontinued when the micro-organism was identified. An uneventful recovery and complete return of function of the hand was achieved.

Case 3.—A 59-year old man with severe cardiac and pulmonary embarrassment had a history compatible with silicosis and had been a tool grinder in a rural town in Ohio. Thoracic roentgenograms revealed extensive bilateral fibrosis. Avian tubercle bacilli were isolated in cultures of three specimens of sputum and one of gastric washing. The patient died of cardiac failure. Sections of lung presented fibrosis with birefringent crystals. One section showed a small focus of necrosis with acid-fast bacilli.

Case 4.—A 64-year old granite worker, a lifelong resident of Minnesota, gave a history of "having lung trouble for a long time." Thoracic roentgenograms revealed pulmonary fibrosis compatible with silicosis. Repeated cultures of gastric washings and of sputum contained acid-fast bacilli identified as avian tubercle bacilli. This patient gave a pronounced reaction to avian tuberculin as well as PPD. His serum agglutinated his own as well as other strains of avian tubercle bacilli.

It is of special interest that the last two patients had silicosis, in view of the well-known observation that certain avirulent strains of tubercle bacilli such as BCG and H37Rv can cause progressive disease in silicotic but not in normal guinea pigs.

It is likely that infection with avian tubercle bacilli is more common in man than reports indicate. Failure to disclose such infections may be due to the relatively high resistance of guinea pigs, which are the animals commonly used in the diagnosis of tuberculosis. Also, it is possible that in some laboratories workers are not acquainted with the cultural characters and methods of identifying Mycobacterium avium.
A procedure was developed for investigating modifications of virulent mycobacteria with enzymes without marked reduction of cell numbers. Routine indexes for cellular alterations included; rapid reduction of methylene blue dye (Thunberg technique); failure to bind the neutral red dye and cell dispersement as observed microscopically. Other manifestations of alteration observed included change in growth and staining characteristics and ability to absorb mercuric ions.

Mycobacteria fulfilling the above indexes were used first for physiological studies. It was shown that with enzyme treated washed cells oxygen consumption was considerably greater when the substrates lactate, pyruvic acid, glucose and acetic acid were compared with non-treated cells. Similar results were shown with substrates isocitric, malic and fumaric acid. Less marked, but nevertheless increased stimulation was observed with cisaconitic, citric and succinic acid. Warburg studies with sonorated cell-free extracts with various coenzymes confirmed the presence of the above enzymes. Potentiation of antibiotic activity in the presence of trypsin was shown. Trypsin was observed to have an opsonic effect on virulent tubercle cells when tested with rabbit macrophages.

To identify some of the cellular components removed by enzyme action, amino acid analysis was completed chromatographically. A total of 17 amino acids were identified in the supernatents of enzyme treated cells: Alanine, arginine, aspartic acid, cystine, glycine, histidine, isoleucine, leucine, lysine, methionine, proline, phenylalanine, threonine, tyrosine, valine, tryptophane and serine. Fourteen of these, all except arginine, lysine and tyrosine, were shared in lesser amounts with the enzyme itself. Quantative work to uncover these is necessary. For confirmation of above cell wall amino acids fairly pure cell wall preparation was necessary. Heat treatment, sonoration and Miele disintegration were used. Limited observations of electron micrographs revealed sonoration provided the most satisfactory cell wall preparations.
Although the major factors in the natural histories of western equine encephalomyelitis (WEE) and St. Louis encephalitis (SLE) have been known since the early 1940's, there is considerable need for continued research. This need exists because adequate methods for preventing spread of the infections to man have not yet been devised.

Indispensable to control of encephalitis is the specific identification of important vectors and hosts. It is known that both WEE and SLE viruses in rural areas of the west are transmitted chiefly by the mosquito Culex tarsalis. In urban areas of the east, SLE virus is transmitted mainly by the Culex pipiens complex. The relative importance of different bird species as hosts of the viruses is unknown. Certain leads, however, have been obtained. Theoretically, the species should be abundantly distributed in affected areas; they should be available in a quiescent state during the period of peak biting activity for the vectors; and their breeding season should extend well into the summer since nestling birds are more vulnerable than adults to attack by mosquitoes.

Environmental factors that are important in the transmission of WEE and SLE viruses include climatic factors which are favorable to the production and longevity of birds and mosquitoes. Also of importance are certain man-made factors, such as agricultural practices and the urbanization of communities, which influence favorably the breeding of mosquitoes. Large numbers of cattle or other dead-end hosts may compete with birds as sources of blood for the vectors and thereby exert a suppressing effect on virus transmission.

Evidence has been obtained that WEE virus may survive the winter in California in adult mosquitoes and/or as latent infections in birds. No evidence has been obtained that the viruses are brought into the country by birds migrating from more southern areas.

Important advances in laboratory methodology include the development of a hemagglutination inhibition test for detecting serum antibodies and a tissue culture procedure for virus isolation attempts.

Trends for future studies should be directed toward devising better methods of control. It is believed that the following possibilities should be investigated: (a) Is pre-epizootic control of
encephalitis areas a practicable concept? (b) Can a satisfactory vaccine be developed for use in man and, if so, would it receive acceptance by the public? (c) Can more effective insecticides be developed? (d) Which species of birds or other vertebrates are essential to survival of the viruses? and (e) Can encephalitis epidemics be predicted sufficiently in advance of onset to permit their prevention through prompt action by public health officials?
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