ANIMALS AND DISEASE

TABLE I
Death Rates for Certain Diseases
U.S. Registration Area
(Deaths per 100,000 Population)

<table>
<thead>
<tr>
<th>Disease</th>
<th>1900</th>
<th>1925</th>
<th>1950</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>40.3</td>
<td>7.8</td>
<td>0.3</td>
</tr>
<tr>
<td>Malaria</td>
<td>6.2</td>
<td>2.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Measles</td>
<td>13.3</td>
<td>2.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Pneumonia and influenza</td>
<td>402.4</td>
<td>141.7</td>
<td>47.0</td>
</tr>
<tr>
<td>Scarlet fever</td>
<td>0.6</td>
<td>2.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>194.4</td>
<td>84.8</td>
<td>22.6</td>
</tr>
<tr>
<td>Typhoid fever</td>
<td>31.3</td>
<td>7.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Whooping cough</td>
<td>12.2</td>
<td>6.7</td>
<td>0.7</td>
</tr>
</tbody>
</table>

tularemia is sectional in incidence and, because of present control measures, is largely an accidental infection contracted as the result of contact with wild rabbits. Trichinosis has decreased as the result of fewer garbage-fed hogs going to market and greater emphasis on the consumption of adequately preserved or cooked pork products. Salmonelloses, excluding typhoid and the paratyphoid fevers, largely manifest themselves as minor gastrointestinal upsets. Articles on toxoplasmosis and rabies have recently appeared in Pediatrics.

In choosing topics for discussion under the title "Animals and Diseases" the infections cited in the paragraph immediately above were considered and eliminated for the reasons given, and many other conditions have not been included because they are not frequently encountered in childhood. An attempt was made to include problems such as the fungus and parasitic diseases raised along with relatively new infections such as the rickettsial diseases, cat scratch fever and leptospirosis.

REFERENCE

CAT SCRATCH DISEASE

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Since the first report by Debré1 in 1950 of a syndrome of regional lymphadenopathy after a cat scratch, a number of publications reporting several hundred cases have firmly established cat scratch disease as a clinical entity. The role of the cat in the natural history of the disease is not clearly understood, but the available evidence suggests the cat acts as a vehicle of transmission of an infectious agent although its role as a reservoir of infection has not been completely ruled out. The usual method of transmission appears to be inoculation of the agent at the site of a cat scratch, but other possible methods of transmission such as inhalation of the agent are substantiated by the several reported cases with a history of contact with cats but with no definite history of a scratch.

Daniels and MacMurray2 in 1954 reported an analysis of 160 cases, and in 1955 Kalter and associates3 summarized 250 cases which had come under their observation. Both of these reports gave excellent de-
criptions of the clinical features of the illness and this paper has drawn heavily upon their observations.

The primary feature of the clinical syndrome of cat scratch disease is lymphadenopathy which is usually regional and restricted to the drainage area of the site of the inoculation. Involvement of the lymph nodes of the upper extremity after inoculation on the hand or arm is most frequently observed. Cervical or inguinal involvement is not uncommon and occasionally generalized lymphadenopathy has been reported. The nodes are usually quite large, ranging up to several centimeters in diameter. They may be elastic, movable and painless but usually there is some tenderness associated with redness, heat and swelling of the overlying skin. Suppuration of the nodes is very common but the formation of cutaneous sinus tracts is a rare complication. Spontaneous regression of the nodes when they are left undisturbed usually occurs in 2 weeks to 2 months after the onset.

In most cases constitutional symptoms of some type accompany the lymphadenopathy. The general symptoms of infection including feverishness, chilliness, headache, generalized aching and general malaise tend to predominate. Fever of variable range and duration is present at some time in most cases but normal temperature is usually maintained after the first week or two of the illness.

In about one-half of the cases a primary lesion located at the site of a scratch has been reported. The primary lesion may precede the lymph node enlargement by a few days or may appear after the onset of the lymphadenopathy. The most common form of lesion is a papule which may or may not be surmounted by a vesicle or pustule. In some instances it appears as a scratch which is locally or diffusely inflamed and which heals with scar formation.

The incubation period of the disease appears to be quite variable. In the cases described by Daniels and MacMurray it was most commonly 3 to 14 days from the date of contact to the onset of the primary lesion and 7 to 21 days to the onset of lymphadenopathy. Occasional cases have been reported with much longer incubation periods but it is obviously difficult to date the contact responsible for transmission especially when cat contact is continuous and there is no history of a scratch. There is a great variability in the age distribution in reported cases but in most reports the disease occurred predominantly in younger patients. Over one-third of the cases studied by Daniels and MacMurray occurred in patients less than 10 years of age and two-thirds were in patients less than 30 years of age. Cases among much older individuals, however, have been repeatedly reported. No sex predilection has been observed. Most reports appear to be of isolated cases but Daniels and MacMurray observed 12 household epidemics centering about the family cat. The precise distribution of the disease is unknown, but it appears to be widespread in this country and Europe.

Most reports stress the generally benign character of the disease, its association with spontaneous regression and an excellent prognosis. Several reports of neurologic manifestations accompanying the disease have appeared, however, and Paxson and McKay recently summarized the findings in the 12 previously reported cases and in two reported by them. Ten of the fourteen patients had signs and symptoms of encephalitis, two of encephalomyelitis, and one each of myelitis and radiculitis. The neurologic symptoms became apparent 1 to 5 weeks after the onset of the disease and the duration ranged from 2 days to 4 months, the signs disappearing in most cases within 2 weeks. The onset in some was sudden and severe but most patients recovered without residual effect. These authors have suggested that cat scratch disease be entertained as an etiologic factor in cases of encephalitis associated with unexplained lymphadenopathy.

The variability of the clinical picture of cat scratch disease allows rather easy confusion with a wide variety of lymphadenopathies including tularemia, infectious
mononucleosis, tuberculous adenitis and benign and malignant tumors. The only truly reliable diagnostic aid is the skin test performed with antigen prepared from lymph node material obtained from proved cases. Kalter and associates studied the reactor rates among 250 patients with lymphadenopathy and 94 well controls. The results suggest specificity of a high order with only 3% of the controls showing a definitely positive reaction. If the 25 patients subsequently proved to have other diseases are removed from consideration in the group with lymphadenopathy, definitely positive reactions were recorded in 92% of the remaining lymphadenopathies. If further restricted to those with a history of cat contact the sensitivity would appear to be greater than 95%. There is no readily available supply of skin test antigen but suitable material may be rather simply prepared from aspirated pus or from macerated lymph node material by the personnel of most clinical laboratories.

The usually employed laboratory tests are within normal limits in most cases although a moderate leukocytosis has been reported in some and a mild eosinophilia has been seen in others. The skin test with Frei antigen is invariably negative but the complement fixation test with Lygranum complement fixation antigen is frequently positive at the time the case is first seen and a significant rise in titer during convalescence has been reported occasionally. Armstrong and associates recently compared the percentage of reactors among patients with lymphadenopathy with positive skin tests and well controls. The results suggest that the reactivity is probably more closely associated with the age of the patient than it is with cat scratch disease, and the authors conclude that the test is without diagnostic value in individual cases of the disease. These findings also cast doubt on the significance of the frequently postulated relationship of the agent of cat scratch disease to the lymphogranuloma-psittacosis group of viruses.

The microscopic appearance of involved lymph nodes is one of granulomatous adenitis frequently associated with suppuration and necrosis. This pattern is suggestive but not diagnostic of cat scratch disease and the removal of lymph nodes as an aid to diagnosis is of little value except to rule out other suspected diagnoses. The removal of pus from suppurating nodes for the preparation of skin test antigen is undoubtedly justified. The usual bacteriologic and mycologic examinations of suppurative material are invariably negative.

A number of chemotherapeutic and antibiotic agents have been used in therapy but there is no convincing evidence of their effectiveness. It is the impression of some authors without the assistance of controlled observations that the tetracyclines and chloramphenicol may be beneficial but others under similar circumstances have failed to find them effective.

Whereas much progress has been made in delineating the clinical course of cat scratch disease, its etiology and epidemiology are still uncertain. The disease has apparently been successfully transmitted to human volunteers and to monkeys by Mollaret and his associates by the inoculation of lymph node material from patients, but several authors have reported failure to isolate an agent in laboratory animals or in tissue culture. In April, 1957, Graber and his associates presented to the Ohio Branch of the Society of American Bacteriologists an interesting paper which has as yet not been published. These authors, working with material obtained from patients whom we have investigated, were able to demonstrate what appeared to be viral type hemagglutination of rabbit erythrocytes by a saline suspension of aspirated pus from patients with cat scratch disease. No agglutination of human, sheep or guinea pig cells was observed and the agglutination of the rabbit cells was significantly inhibited by the diluted serum of a patient with cat scratch disease and by rabbit antisera prepared by the inoculation of rabbits with the agglutinated cells. Some hemagglutination activity was observed with antigen prepared...
from macerated normal lymph nodes but similar activity occurred with human, sheep and guinea pig cells and the agglutination was not inhibited by the human serum or the specifically prepared rabbit antisera. If this report should be confirmed it would suggest the presence of a virus or virus-like agent in the aspirated material and might well provide the basis for a specific hemagglutination-inhibition test.

Observations on cats associated with cases in humans have invariably found them to be apparently well with a negative skin test and without significant pathologic changes at necropsy. Repeated attempts by several authors to isolate an agent from cat organs have also been negative. Anderson* of our department has attempted rather extensive isolation procedures using material from five cats associated with the patients we have studied. The inoculation of macerated organs, nasopharyngeal washings and stool into adult mice, suckling mice, guinea pigs, monkey kidney cells and HeLa cells produced no recognizable activity nor the presence of a passable agent. Skin test of the cats using antigen of human origin was negative in all five instances. One attempt to transmit the disease to a human volunteer using a saline suspension of claw scrapings was unsuccessful.

These repeated failures to demonstrate illness or lesions in cats have led several authors to hypothesize that the cat plays the role of a passive vehicle of transmission of the disease agent and that the reservoir of infection is elsewhere in nature, possibly being small rodents, birds, plants or soil. A real understanding of the epidemiology of the disease will probably depend upon the isolation of the disease-producing agent from humans and the application of suitable tests for its presence in a variety of likely reservoirs.

In summary it may be stated that cat scratch disease, a self-limited illness with regional lymphadenopathy, has been firmly established as a clinical entity and that the association of the disease with contact with cats has also been repeatedly confirmed. The only presently reliable diagnostic aid is the skin test performed with antigen prepared from aspirated pus or macerated lymph nodes from humans. No etiologic agent has to date been isolated from patients or from cats associated with patients, but the recent report of Graber and associates,7 if confirmed, would suggest the presence of a viral agent in aspirated pus. The role of the cat in the natural history of cat scratch disease is uncertain, but the most likely possibility at present appears to be that of a passive vehicle of transmission of the causative agent.

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REFERENCES

CAT SCRATCH DISEASE
Frederick H. Wentworth
Pediatrics 1958;22;376

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/22/2/376