FELINE VIRUS PNEUMONIA AND ITS POSSIBLE RELATION TO SOME CASES OF PRIMARY ATYPICAL PNEUMONIA IN MAN*

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On November 7, 1941, a young farmer from Jewett City, Connecticut, was admitted to the Medical Service of the New Haven Hospital with an illness which resembled primary atypical pneumonia of the type which has been increasingly prevalent since 1934,[1, 5, 6, 10, 19-21, 27, 29, 31-33, 35, 37-42, 44, 46] and is presumed to be of virus etiology.[5, 32, 38, 41, 47, 50] The history revealed not only that two other members of the household had recently had a similar illness and that one was sick at home, but also that eight of twelve cats on the farm had died of a respiratory disease during October and that two of the remaining four were sick with the same illness (Chart 1). The possibility that the afflicted members of the family

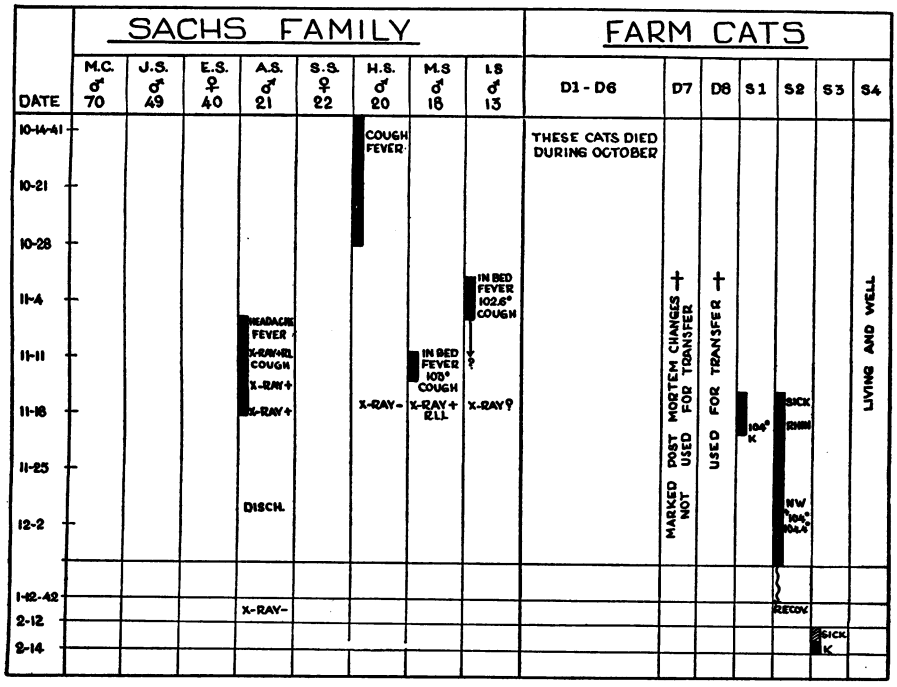

CHART 1 Primary atypical pneumonia in the S. family and in their cats.

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and the cats were infected with the same agent at once suggested itself and an investigation of this possibility was undertaken. In this paper the observations on the patients and on the family cats and attempts to isolate an etiological agent by transmission experiments in cats and mice are described.

Case Reports

A. S., male, age 21, married, farmer, admitted to the New Haven Hospital Nov. 7, 1941, Unit No. B-21,771.

C. C.: Weakness, headache, and fainting spells.

P. I.: About 10 days prior to admission the patient developed a mild sore throat, followed 3 days later by coryza. Two days before entrance a slight non-productive cough began. He felt unusually tired and weak, was feverish and restless at night, and became short-winded. He attributed his illness to the fact that he was kicked in the forehead by a cow 5 weeks before admission. As a result of this trauma he was unconscious for 2 minutes and had subsequently suffered from more or less continuous frontal headache and had had several fainting spells. He was forgetful, dizzy at times, and absent-minded but had had no focal neurological symptoms or convulsions.

P. H.: Appendectomy at 8 years of age, scarlet fever at 9, otherwise well.

F. H.: Irrelevant.

Epidemiology: The family drink unpasteurized milk from their own herd which, however, is free of Bang's disease. There was no contact with rabbits, parrots, or love-birds. There were no pigeons on the farm. A neighbor who lived a quarter of a mile away kept a flock of domestic pigeons, but members of the S. family had no intimate contact with these birds. Subsequent to the establishment of the diagnosis of pneumonitis by roentgenographic examination on November 14, it was learned that 2 younger brothers had recently had an acute illness with fever and cough and that a third was at home in bed with the same disease. It was also learned that an acute respiratory disease had been prevalent in the family cats, of which 8 had died during October, 2 were now sick, and 2 were apparently still well (Chart 1). Whether or not illness appeared in the cats before it occurred in the members of the family could not be determined with certainty.

P. E.: T. 100.2° F.; P. 68; R. 20; B. P. 125/70. The patient appeared moderately ill. No abnormalities were found on physical examination except slight injection of the pharyngeal mucosa and palpable pea-sized cervical lymph nodes.

Lab. Exam.: R. B. C., 5,690,000; Hgb., 16.5 gm.; W. B. C., 9,050; P. 58%, Ly. 32%, L. M. 7%, E. 3%; urine, normal; Kahn, negative; tuberculin and brucellergin tests, negative; blood culture, no growth; agglu-

tinin tests for typhoid, paratyphoid, brucellosis, tularemia, and infectious mononucleosis, negative; throat culture, *Streptococcus viridans*.

Clinical Course: The subsequent course of the patient's illness is shown in Chart 2. Nov. 10: X-ray of the chest showed increased right hilar density with slight infiltration extending from the lower portion of the hilum into the right lower lung field posteriorly (Fig. 1a). Nov. 14: Cough became productive of a moderate amount of mucopurulent sputum which was negative for tubercle bacilli and showed no pathogens on culture; diminished breath sounds and fine moist râles appeared over the right lower lobe posteriorly;

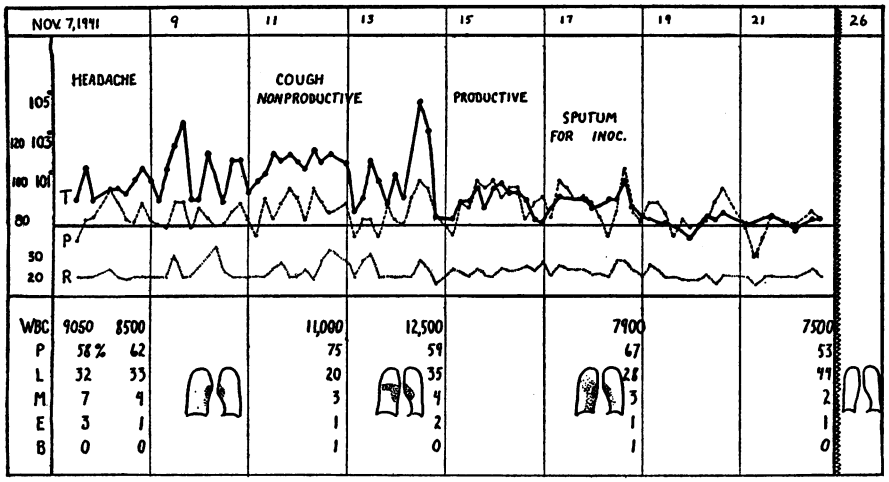

CHART 2

Clinical course of the primary atypical pneumonia in Case A. S.

X-ray of chest showed increase of infiltration in right lower lobe and extension to the right upper and left lower lobes (Fig. 1b). Nov. 17: Sputum was collected for inoculation experiments. Nov. 18: X-ray of chest showed pneumonitis in the right upper, middle, and lower lobes and in the left lower lobe, with right hilar lymph node enlargement (Fig. 1c). Nov. 19: Temperature normal, moist râles over both lower lobes posteriorly. Convalescence uneventful. X-ray of chest, Nov. 26, showed nearly complete resolution of the pneumonitis (Fig. 1d). Discharged Nov. 29. Diagnosis: Primary atypical pneumonia.

H. S., male, age 20, had an acute respiratory illness with fever and cough between Oct. 14 and 28, 1941. He remained at home in bed. The cough was productive. There was no pleural pain. When seen on Nov. 15 he still felt weak and had some cough. Physical examination was negative. X-ray of chest on Nov. 16 showed no abnormalities.

I. S., male, age 13, became sick about Nov. 2 with fever and non-productive cough. There was no coryza or pleural pain. He remained in bed at home for 5 days. When seen on Nov. 15 he felt well but had a slight cough. The lungs were clear. X-ray of chest on Nov. 16 showed questionable slight infiltration of the right lower lobe.

M. S., male, age 18, became sick on Nov. 10 with headache and fever. He developed a productive cough, raising mucopurulent sputum which contained no blood. There was substernal but no pleural pain. He remained at home in bed for 4 days. When seen on Nov. 15 he seemed weak and he coughed. Moist râles were heard over the right lower lobe. X-ray of the chest on Nov. 16 showed moderate infiltration in the paravertebral area of the right lower lobe (Fig. 2).

The 3 older members of the family, M. C., J. S., and E. S., and the daughter-in-law, S. S., had not contracted the disease and were well when seen on Nov. 15 (Chart 1).

The family cats

As stated above, the S. family owned 12 cats. During October and early November, 8 of these cats had become sick and died of an acute respiratory disease characterized by mucopurulent conjunctivitis, rhinitis, sneezing, and coughing. The family could not recall the dates of onset of symptoms and death of these animals. When the farm was visited on November 15, the frozen bodies of the 2 cats which had died most recently (Cats D7 and D8, Chart 1) were collected from a manure pile and brought back to the laboratory for study. At the same time it was noted that 2 of the remaining 4 cats (Cats S1 and S2, Chart 1) were sick with similar respiratory symptoms; they were also brought to the laboratory for observation. Cats S3 and S4 appeared well and were left on the farm. On Feb. 5, 1942, Mrs. S. notified us that Cat S3 appeared to be sick with a similar disease. A visit was paid to the farm on Feb. 12 and the cat was brought back. Cat S4 still appeared well and had apparently escaped the infection up to this time.

Cat D7. Autopsy showed extensive focal pneumonia. Marked postmortem autolysis of all organs. Discarded.

Cat D8. Autopsy showed focal pneumonia without other gross lesions. Microscopically the lungs show bronchitis, bronchiolitis, and focal interstitial and peribronchiolar pneumonia (Fig. 3). There is considerable necrosis and desquamation of the bronchial and bronchiolar epithelium. The lumina are filled with desquamated epithelial cells and numerous large and small mononuclear cells. There is moderate infiltration of the interstitial tissue with sim-

ilar mononuclear cells. For the most part the alveoli are free of exudate, but small peribronchiolar foci of pneumonitis with a mononuclear cell exudate and occasionally slight hemorrhage in the alveolar spaces are seen. In places there is atelectasis and thickening of the alveolar walls. Only a rare polymorphonuclear leukocyte is seen. There is no fibrin. The pleural surface shows no exudate. Bacteria are seen only in two very small foci, clumps of bacilli in one and cocci in the other. There is no polymorphonuclear exudative response in either focus and it is believed that the bacteria represent postmortem growth. Cultures showed *S. albus* and *B. proteus*. The lungs were frozen and stored in a CO_2-ice cabinet for subsequent transmission experiments (Chart 4).

Cat S1. Nov. 15-18, 1941: appears sick, appetite poor, sneezing and coughing, slight mucopurulent discharge from both nostrils. W. B. C., 10,400 per cmm. Nov. 19: temp. 104° F. Killed. Autopsy showed no gross lesions. Microscopically the lungs show a few small foci of bronchiolitis and bronchopneumonia (Fig. 4). There is some necrosis of the bronchiolar epithelium but no desquamation. The lumina of the affected bronchioles contain an exudate of mononuclear and polymorphonuclear cells. The adjacent alveoli are filled with a similar exudate, predominantly mononuclear cells in some, approximately equivalent numbers of mononuclear and polymorphonuclear cells in others. There is moderate interstitial infiltration with large and small mononuclear cells. There is no exudate on the pleural surface and no bacteria are seen. Cultures on rabbit's blood and cat's blood agar plates remained sterile. The lungs were frozen and stored in a CO_2-ice cabinet for subsequent transmission experiments (Chart 5).

Cat S2. Nov. 15-30, 1941: moderately sick with mucopurulent rhinitis, sneezing frequently, temp. 104° to 104.4° F. on Nov. 26 and 27. Nasal exudate collected Nov. 25 for transmission experiment (Chart 5). Dec. 1 to 22: improving. Dec. 23: appears well and has remained so to date.

Cat S3. Feb. 12, 1942: appears moderately sick with mucopurulent conjunctivitis and rhinitis, respirations shallow and noisy. Feb. 14: killed. At autopsy the turbinates were found to be swollen and injected, the paranasal sinuses and the floor of the left orbit were filled with greenish-yellow purulent exudate, the trachea contained thick tenacious mucus and its mucosa appeared edematous, the lungs appeared normal except for the right anterior lobe which showed a considerable area of gray, firm consolidation (Fig. 5). On cut section the smaller bronchi of this lobe appeared prominent and exuded a small amount of thick, glairy material. There was no pleural exudate. The other organs were not remarkable. Cultures of the turbinates showed *S. albus*, of the trachea, *B. proteus*, and of the lungs, *S. albus* and diphtheroids. Microscopically the turbinates and the trachea show moderate edema and large mononuclear cell infiltration of the mucosa and an exudate of polymorphonuclear and mononuclear cells on the epithelial

surface. Sections of the right anterior lobe of the lung show focal areas of bronchiolitis, and interstitial and peribronchiolar pneumonia. The cellular exudate in the alveoli and interstitial tissues is predominantly large mononuclear in character, that in the lumina of the bronchioles a mixture of large and small mononuclear cells, desquamated epithelial cells, and polymorphonuclear leukocytes. No bacteria are seen. The pleural surface shows no exudate.

A 20 per cent emulsion of the right anterior lobe was prepared for immediate transfer to Cat 28 (Chart 5).

Transmission experiments in cats

The transmission experiments in cats fall into 3 groups: those attempted with the patient's sputum (Chart 3); those from Cat D8, one of the dead cats brought in from the farm (Chart 4); and those from the sick cats S1, S2, and S3 (Chart 5). The respective charts present the serial passages and the clinical picture in the inoculated animals. The temperature, clinical symptoms, weight of the animal, strength of the emulsion, amount of inoculum, and route of inoculation are shown for each cat. The gross and microscopic pathology of the lungs of those animals which succumbed or were sacrificed is described in the text.

Methods.—Nembutal anesthesia was used in all transmission experiments from the patient's sputum (Chart 3, Cats 3, 4, and 12 to 15 inclusive), from Cat D8 (Chart 4, Cats 6, 7, 8, and 49 to 59 inclusive), and from Cats S2 and S3 (Chart 5, Cats 11 and 28). Veterinary Nembutal (Pentobarbital sodium, Abbott), each cubic centimeter of which contains 1 grain of Nembutal in an aqueous solution containing alcohol 10 per cent, was employed, the dose administered intraperitoneally being 0.6 cc./K for animals weighing over 800 gms., 0.5 cc./K for those weighing 800 gms. or less. Complete relaxation, with suppression of the cough reflex in most instances, was usually obtained within 20 minutes. A change to ether anesthesia was instituted in October, 1942, and was employed for all passages from Cat S1 (Chart 5, Cats 84 to 99 inclusive).

Moribund animals and those sacrificed were killed by the intraperitoneal injection of from 1 cc. to 2 cc. of Nembutal, depending upon the weight of the animal. Fifteen to 20 minutes after injection 20 cc. to 30 cc. of blood were collected by cardiac puncture. Autopsies were performed immediately after death and the organs were examined grossly and microscopically. Portions not used immediately were stored in a CO_2-ice cabinet.

Emulsions of organs were prepared for inoculation by mincing the tissue with scissors, followed by grinding with sterile sand. Normal saline was used as the diluent in the transmission experiments originating from the patient's

sputum and from Cats D8, S2, and S3; beef-heart infusion broth containing 3 per cent p-aminobenzoic acid and buffered to pH 7.3 was used in the transmission experiment from Cat S1. In the earlier experiments a 10 per cent emulsion was used. Subsequently a 20 per cent emulsion was usually employed, exceptions being noted on the charts. Inoculations were made by the intranasal, intratracheal, or combined intranasal and intratracheal routes, usually in doses of 1 cc. or 2 cc., in the experiments originating from the patient's sputum and from Cats D8, S2, and S3. In the transmission from Cat S1 the intranasal route and 2 cc. amounts of emulsion were used throughout.

Transmission from sputum of patient A.S. (*Chart 3*).—Sputum, mucopurulent in character, was collected from the patient on Nov. 17, 1941, and stored in a CO_2-ice cabinet for 2 days. Cultures of the sputum showed *Staphylococcus albus, Streptococcus viridans,* diphtheroids, and a few pneumococci. On Nov. 19 the blob of sputum was thawed and emulsified with 2 cc. of saline. Under Nembutal anesthesia 0.35 cc. of this emulsion was injected intratracheally into Cat 3 and 1 cc. intranasally in Cat 4.

Cat. 3.—Fever developed and rose to 105° on the 5th day. Lacrimation, rhinitis, and shivering were present early. The fever

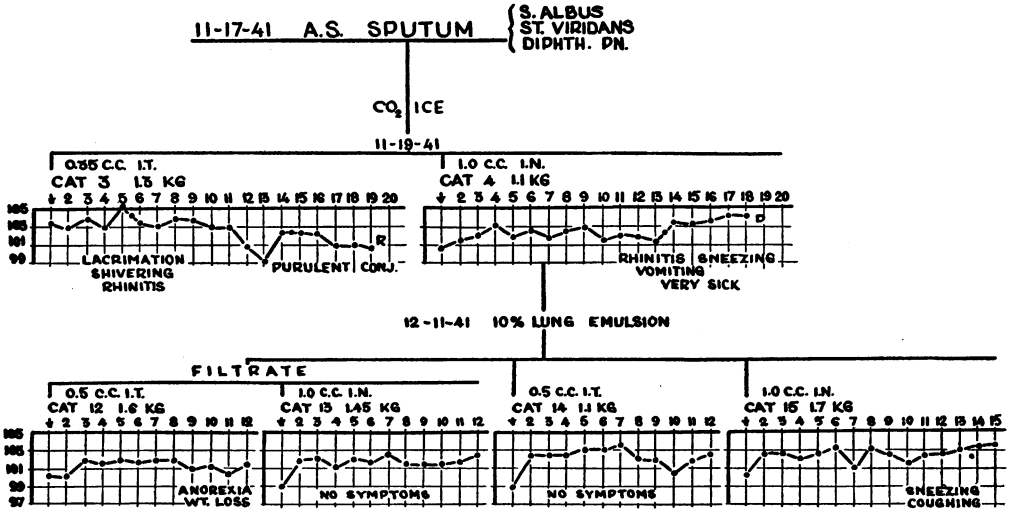

CHART 3

Transmission experiments in cats, from the sputum of Case A. S.

slowly subsided and purulent conjunctivitis replaced the more watery discharge noted earlier. The animal at times ate poorly and showed some weight loss, but eventually recovered.

Cat. 4.—Following questionable slight fever between the 4th and 9th days, definite fever, rhinitis, and sneezing developed on the 14th day. The animal appeared ill and vomited on several occasions. It was found dead on the morning of the 19th day, having lost 285 grams in the last 5 days of life. Autopsy showed translucent, deep red consolidation of both anterior lobes with hyperemia and congestion of the rest of the lungs. Cultures of the right anterior lobe showed *B. proteus.*

The lungs of Cat 4 were stored in CO_2-ice for 4 days. A 10 per cent saline emulsion was then prepared from the left anterior lobe. Part of this emulsion was passed through an L_3 Pasteur-Chamberland filter. Four cats were inoculated under Nembutal anesthesia, as follows: Cat 12 with 0.5 cc. of the filtrate intratracheally; Cat 13 with 1 cc. of the filtrate intranasally; Cat 14 with 0.5 cc. of the 10 per cent lung emulsion intratracheally, and Cat 15 with 1 cc. intranasally.

Cat 12.—No febrile response was elicited in this animal, though anorexia and loss of 410 grams in weight occurred between the 9th and 18th days following intratracheal inoculation. The cat recovered and was discarded 8 months later.

Cat 13.—Intranasal instillation of the filtrate of the lung emulsion prepared from Cat 4 failed to produce fever or symptoms in this animal. It was discarded after 8 months of observation.

Cat 14.—No clinical symptoms and very little fever followed the intratracheal inoculation of Cat 4 lung emulsion into this animal, nor was there any weight loss. An autopsy performed 53 days after inoculation revealed scattered throughout the lungs tiny pin-point areas of grey translucent consolidation, which microscopically appeared to be an old and resolving process.

Cat 15.—Inoculation intranasally of the lung emulsion of Cat 4 caused only slight fever at the end of the first week, followed during the second week by sneezing and coughing. Recovery was prompt. The cat remained well until it was sacrificed 53 days after inoculation. Autopsy revealed that the lungs were dotted with tiny grey, glassy spots, which on section were shown to be focal areas of organizing pneumonitis.

The patient's sputum, collected 3 weeks after the onset of his illness, seemed capable of producing symptoms of an upper respiratory infection when introduced into cats, and in one of the two inoculated pneumonitis was evident at autopsy. Attempted passage to other cats was equivocal as judged by clinical symptoms, although autopsy in Cats 14 and 15, which were sacrificed 53 days after inoculation, indicated the possibility that a clinically unrecognizable focal pneumonitis had occurred. No further transfers have been attempted from this line.

Transmission from Cat D8 (Chart 4).—The lungs of Cat D8, which was brought in dead from the S. family farm in Jewett City on Nov. 15, 1941, (Chart 1) and autopsied Nov. 16 (Fig. 3) were stored in a CO_2-ice cabinet for 5 days. On Nov. 21, a 10 per cent saline lung emulsion was prepared and a small portion of it was filtered through an L_3 Pasteur-Chamberland filter. Three cats were inoculated under Nembutal anesthesia, as follows: Cat 6 with 0.5 cc. of the emulsion intratracheally; Cat 7 with 1 cc. intranasally; and Cat 8 with 0.6 cc. of the filtrate intranasally.

Cat 6.—Fever, associated with lacrimation and sneezing, appeared suddenly 5 days after inoculation. Fever continued for about 5 days. The lacrimation and sneezing persisted for two weeks. The animal recovered, remained asymptomatic, and was used for re-inoculation more than 6 months later (Chart 4). At the moment it appears healthy and without signs of any disease.

Cat 7.—This animal developed fever 8 days following the nasal instillation of 1 cc. of the lung emulsion of Cat D8. For 2 days it refused all food and appeared sick. It was sacrificed on the 11th day. Grossly no consolidation was found on examination of the lungs. In some of the microscopic sections tiny areas of bronchiolitis and peribronchiolar pneumonia were found (Fig. 7). The organs were stored in a CO_2-ice chest.

Cat 8.—Symptoms of lacrimation, sneezing, and coughing appeared 12 days after intranasal inoculation with 0.6 cc. of the filtrate prepared from Cat D8 lung emulsion. Fever was slight at this time and lasted for 2 days only. Weight loss of 200 grams occurred. The upper respiratory symptoms persisted for 2 weeks, followed by complete recovery. The animal was sacrificed 72 days after inoculation. At autopsy a thin margin of pinkish-grey noncrepitant lung was discovered at the extreme periphery of the left

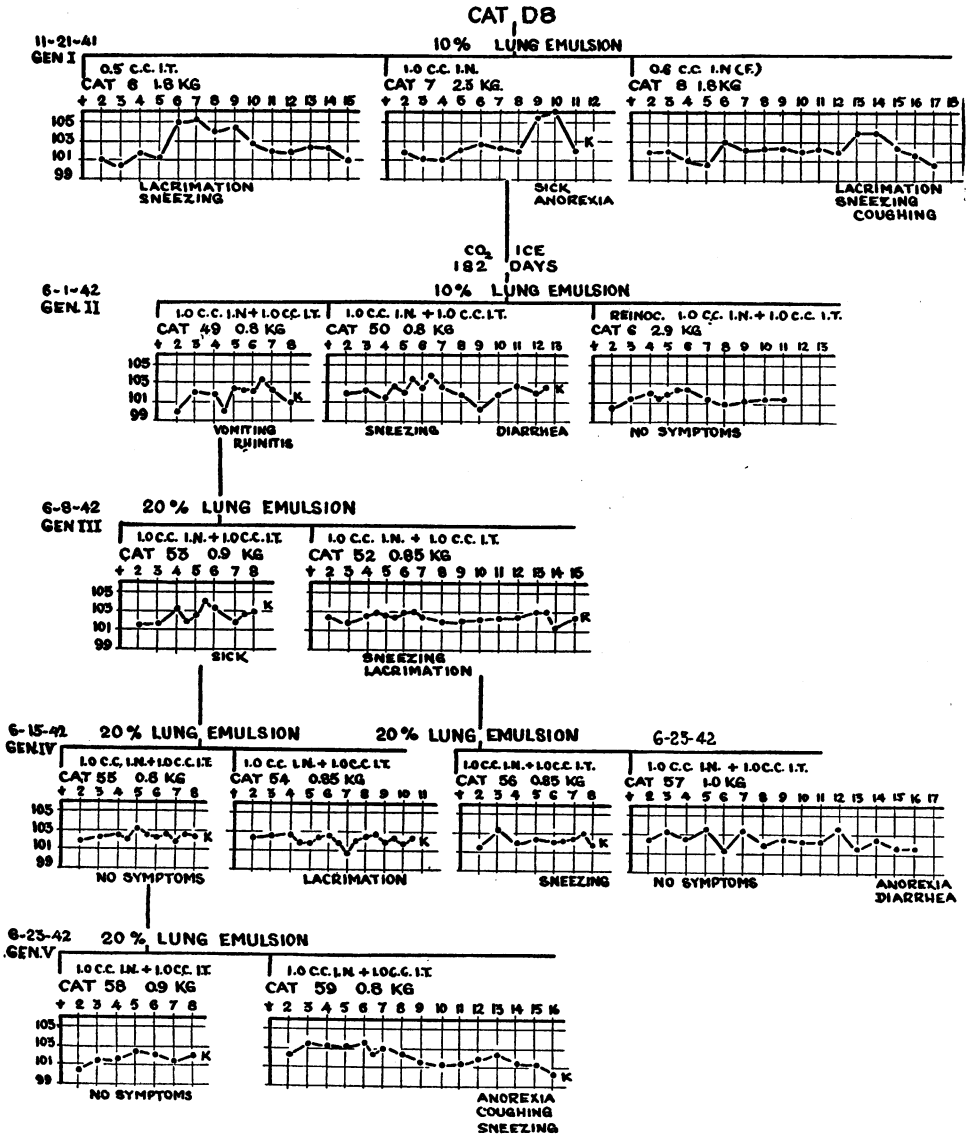

CHART 4

Transmission experiments in cats, from Cat D8.

anterior lobe. Although bronchitis was demonstrable in the sections, no definite areas of pneumonitis were found.

Other work intervened and no further passages were made from this line until June of 1942, when a further attempt at transmission was made using the lungs of Cat 7, which had been stored in CO_2-ice during the interval. From the experiments recorded above it was obvious that there were great variations in the time of appearance and in the severity of the clinical symptoms; detection of the presence of a pneumonitis without sacrifice of the animal was also uncertain. It seemed possible that these difficulties might be obviated if younger cats, which would perhaps prove to be more susceptible, were used. Furthermore, it seemed not unlikely that a virus, if present, might be more readily transmitted early in the course of the infection than would be the case later when enough neutralizing antibody might be present to inhibit successful passage. It also appeared desirable to increase the strength of the lung emulsion and the amount of the inoculum employed. Accordingly, the following plan was adopted: kittens not exceeding 1 kilogram in weight were used; a 20 per cent lung emulsion was employed; the amount of inoculum was increased by combining the intratracheal and intranasal routes; two cats were inoculated at each passage, the sicker animal of each pair being sacrificed after 7 days for transfer at regular weekly intervals, the other cat being sacrificed after approximately 2 weeks to determine what later lesions, if any, might have occurred. Nembutal was again used as the anesthetic and the emulsions were prepared in normal saline as in the previous experiments. The results of this attempt at further passage from Cat 7 are shown in Chart 4 and briefly summarized below.

Cats 49 and 50.—Each was inoculated on June 1, 1942, with 1 cc. intranasally and 1 cc. intratracheally of a 10 per cent saline lung emulsion from Cat 7. These lungs had been stored in CO_2-ice for 182 days and were quite desiccated, so that a 20 per cent emulsion was too thick to pass through a 27-gauge needle. It was, therefore, necessary in this instance to dilute with saline to a 10 per cent emulsion.

Cat 49 developed vomiting and rhinitis 3 days after inoculation, the latter persisting up to the time the animal was sacrificed, 7 days after inoculation. Grossly the lungs showed pale pink translucent spots, none greater than 7 to 8 mm. in diameter, the largest number

and the most prominent ones being in the middle lobes, although they were present throughout the lungs. They appeared to be related to the bronchioles and this was confirmed by microscopic examination which showed focal peribronchiolar pneumonitis.

Cat 50 was observed for two weeks and then killed. Sneezing was prominent the first few days following inoculation. A watery diarrhea was present the last 2 days of life. The pathology of the lungs was similar to that found in Cat 49, though somewhat more extensive, particularly in the lower third of the anterior lobes. The microscopic sections disclosed an extensive bronchitis, bronchiolitis, and focal pneumonitis which tended to be confluent in some places.

Cats 52 and 53.—This pair of animals was subjected to intratracheal and intranasal instillation of a freshly prepared 20 per cent saline emulsion of the lungs from Cat 49, 1 cc. intratracheally and 1 cc. intranasally.

Cat 52, within 3 days of inoculation, developed symptoms of sneezing and lacrimation which persisted for the experimental period of 2 weeks. It was killed on the 15th day. The lungs showed the most extensive involvement encountered up to this time. The lower halves of both anterior lobes, and the upper halves of the posterior lobes were the seat of a deep cherry-red consolidation. The microscopic picture was similar to that seen in Cats 49 and 50, though much more extensive.

Cat 53 showed no upper respiratory symptoms, although its temperature reached 104° F. on the 5th day. It became sluggish, ate little or nothing, and was killed at the end of a week. The amount of pulmonary involvement seen at autopsy was equivalent to that found in Cats 49 and 50, and the microscopic picture was similar.

Although the two foregoing passages suggested that transmission at weekly intervals might be satisfactory, it nevertheless seemed desirable to determine whether a longer interval might not be equally satisfactory, since Cat 52, held under observation for 2 weeks, had shown such extensive pulmonary consolidation. Consequently 20 per cent saline emulsions were prepared from both Cat 53 and Cat 52 for the next passage.

Cats 54 and 55.—This pair of cats received the routine dose of 1 cc. intratracheally and 1 cc. intranasally of the 20 per cent saline emulsion of the lungs of Cat 53.

Cat 54 was observed for ten days, during which time it seemed

sluggish and exhibited lacrimation. The lungs at autopsy on the 11th day showed some congestion but no grossly obvious pneumonitis similar to that found in Cats 49 to 53. The microscopic sections, however, disclosed a moderate amount of bronchitis, bronchiolitis, and pneumonitis.

Cat 55 showed no symptoms following inoculation. The lungs on post-mortem examination showed a few small, red, translucent spots of consolidation, but the involvement was definitely less than had been found in the other cats of this series sacrificed 7 days after inoculation.

Cats 56 and 57.—These animals were given the usual doses of 1 cc. intratracheally and 1 cc. intranasally of a 20 per cent lung emulsion prepared from Cat 52, which had been held for 2 weeks before sacrifice.

Cat 56 showed little in the way of clinical symptoms. From the 6th to the 8th day there was mild sneezing. There was slight nasal discharge and a weight loss of 165 grams. When the animal was killed a few small patches, suggesting consolidation, were seen close to the hilum of the lung. These findings were definitely less than those noted in the previous generations in animals held for a comparable period of time. The microscopic picture showed only slight bronchitis and bronchiolitis with thickening of alveolar walls and a few foci of peribronchiolar infiltration.

Cat 57, the companion to Cat 56, was observed for a week longer. It showed no symptoms except anorexia and diarrhea, which developed 48 hours before the experiment was terminated. Again the gross and microscopic findings were meager.

Cats 58 and 59.—The inoculation of these animals completed the third serial passage at weekly intervals in this group. A 20 per cent lung emulsion prepared from Cat 55 was injected in the usual manner and in the same dosage.

Cat 58 showed no clinical symptoms. Sacrificed at the end of 7 days, there was nothing to be seen grossly in the lungs at autopsy. A few small areas of bronchiolitis and peribronchial infiltration were found microscopically.

Cat 59 developed anorexia, coughing, and sneezing on the 11th post-inoculation day. These symptoms were present at the time the animal was sacrificed. Grossly there was a pale, greyish-pink, translucent consolidation of the lower halves of the anterior lobes and of

the upper portions of the posterior lobes. Microscopically bronchiolitis was fairly prominent and pneumonitis was found to be present.

Although it seems possible from the foregoing experiments that an agent capable of producing a respiratory disease in cats was transmitted from the lungs of Cat D8 through 5 generations, it is clear that this hypothetical agent, if present, was not sufficiently enhanced in virulence by the methods used to produce a constant, easily recognizable clinical picture or fatal illness suitable for immunological investigation. On the contrary the infection, if anything, appeared to become less marked with repeated passage. While the histological characteristics of the pneumonitis encountered appeared to be consistent with those to be expected in a virus infection, cultures of the lungs from cat to cat showed a variety of contaminating bacteria, usually in small number, which, nevertheless, served to introduce an element of doubt. Cultures of the lungs of Cat D8, for example, showed *S. albus* and *B. proteus*; of Cat 7, staphylococci; and of Cat 8, *Strep. viridans*. Pure cultures of the *B. proteus* and the *Strep. viridans* strains injected intratracheally and intranasally in cats were without effect, indicating that these organisms may be regarded as incidental contaminants or secondary invaders. Furthermore, both aerobic and anaerobic cultures of the lungs of Cats 49 and 50 remained sterile. On the other hand, cultures from the lungs of Cats 52, 53, 54, 55, 56, 57, and 59 all showed moderate growth of *B. bronchisepticus*, reported by McGowan[34] to be associated with the pneumonia of cat distemper. In view of the difficulties outlined above, further passage of the D8 strain was abandoned.

Transmission from Cats S1, S2, and S3 (Chart 5).—For convenience of presentation, as only one transfer each was attempted from Cats S2 and S3, these will be described before the many passages from Cat S1.

Cat S2, after being brought from the farm to the laboratory on Nov. 15, 1941, continued to drain a thick, tenacious, mucopurulent material from the nose for many weeks. The nose was washed with saline on Dec. 1, 1941, more than 2 weeks after the onset of the respiratory infection, and the secretions obtained were injected intratracheally into Cat 11 anesthetized with Nembutal. Cat 11 showed no symptoms and at the end of 3 weeks escaped through an open window. Cat S2 has completely recovered and is now alive and well.

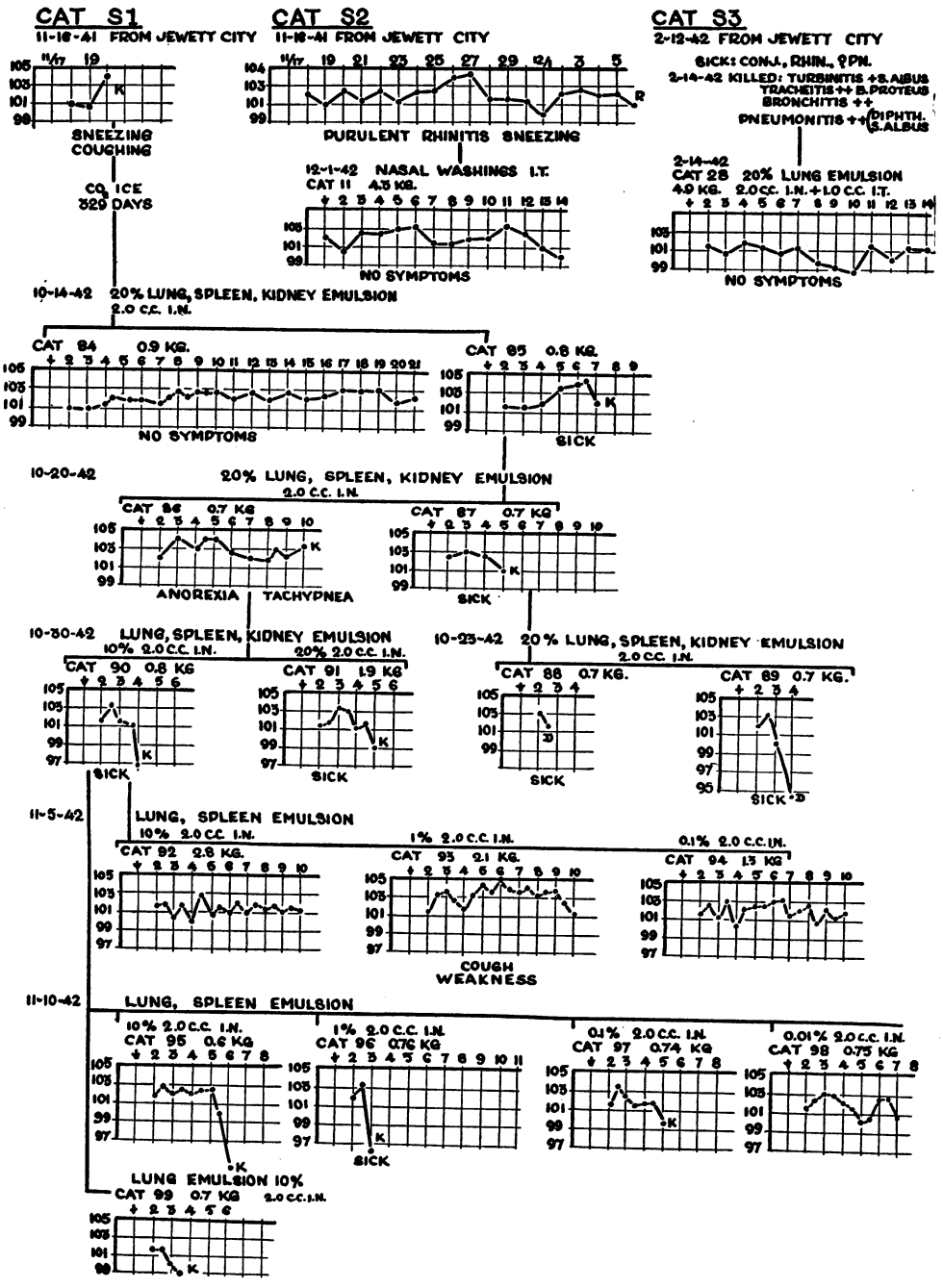

CHART 5

Transmission experiments in cats, from Cats S1, S2, and S3.

Cat S3, which became sick in Jan., 1942, was brought to the laboratory on February 12, nearly 3 months after Cats S1 and S2. It was obviously sick on arrival and presented a purulent rhinitis, conjunctivitis, and signs of a left periorbital abscess. The animal was killed 48 hours after arrival and autopsy showed an area of greyish consolidation occupying part of the right anterior lobe (Fig. 5). A 20 per cent emulsion in saline of this lobe was prepared. Two cubic centimeters were instilled intranasally and 1 cc. was injected intratracheally in Cat 28 anesthetized with Nembutal. No clinical symptoms resulted in Cat 28 during the 2 weeks following inoculation. When killed and autopsied 2 months later, a few minute foci of organized peribronchiolar pneumonitis were found.

Cat S1, which served as the source for the following transmission experiments, had been brought to the laboratory acutely ill with a respiratory infection on Nov. 15, 1941. It was killed on Nov. 19 and its organs were stored in CO_2-ice for 329 days before use. As pointed out above, ether anesthesia was substituted for Nembutal, and beef-heart infusion broth for saline as a diluent in transfers from Cat S1, with the hope that these procedures might yield more satisfactory and uniform results. Lung had been the only tissue used in previous emulsions, but since the potency of the organs of Cat S1 was in doubt, particularly because there had been only microscopic evidence of pneumonitis, it was decided to use a 20 per cent emulsion of lung, spleen, and kidney and this was done as shown in Chart 5. When available, kittens of less than 1 kilogram in weight were employed.

First passage, Cats 84 and 85.—Oct. 14, 1942, these 2 cats under ether anesthesia were each given 2 cc. intranasally of the 20 per cent emulsion prepared from the lungs, spleen, and kidneys of Cat S1.

Cat 84 failed to show any symptoms and had only a questionable slight fever beginning on the 8th day. It remains alive and well.

Cat 85 developed fever 4 days after inoculation, appeared sick, refused all food, and was sacrificed on the 7th day. Post-mortem examination showed scattered large and small areas of pinkish-grey consolidation throughout all lobes. Aerobic and anaerobic cultures of the lungs remained sterile. The abdominal viscera appeared grossly normal. A 20 per cent emulsion containing equal parts of lung, spleen, and kidney in broth was promptly prepared and passed to two other kittens, 86 and 87, under ether anesthesia.

Second passage, Cats 86 and 87.—Cat 86 quickly developed fever and anorexia following the intranasal instillation of 2 cc. of the pooled organ emulsion of Cat 85. Rapid, shallow breathing was marked at the end of a week and the animal, obviously sick, was killed on the 10th day. An extensive pneumonia involving all lobes was present. Cultures of the lungs showed a sparse growth of large Gram-negative bacilli and small cocci. Liver, spleen, and kidneys were not unusual in appearance. A 20 per cent pooled organ emulsion of lung, spleen, and kidney in broth was prepared for passage into Cats 90 and 91.

Cat 87 showed less fever than Cat 86, but it was obviously sick. It was sacrificed on the 5th day. The pulmonary involvement present is shown in Fig. 6. Aerobic and anaerobic cultures of the lungs showed no growth on blood-agar plates; non-hemolytic streptococci developed anaerobically in broth. No gross abnormality of the liver, spleen, or kidneys was discernible. A 20 per cent emulsion was prepared in broth from equal parts of lung, liver, and spleen and transfers to Cats 88 and 89 were made.

Third passage, Cats 88, 89, 90, and 91.—Cat 88 was found to be sick the morning following the intranasal inoculation of 2 cc. of the 20 per cent emulsion of organs of Cat 87. It was sluggish and did not eat. By afternoon the temperature was falling and respirations were labored. It was found dead the next morning, less than 48 hours after inoculation. The lungs were almost completely consolidated, a tiny fringe of crepitant lung tissue being present only at the periphery. Cultures showed a moderate growth of a large Gram-negative bacillus and a few diplococci.

Cat 89 followed a course similar to that of Cat 88. The morning of the 3rd day after intranasal inoculation the temperature was 94.4° F., respirations were shallow and rapid, and it died within an hour. With the exception of the left posterior lobe which was emphysematous but otherwise normal, all lobes were the seat of a purplish red consolidation. Cultures showed α' streptococci and a large Gram-negative bacillus. There was a small amount of blood-tinged fluid in each pleural cavity. The spleen seemed larger than normal, was deep purple in color, and the pulp tended to bulge on cut section. Liver and kidneys were pale but otherwise normal.

The rapid demise of Cats 88 and 89 made it appear advisable to reduce the strength of the inoculum for kittens. Consequently,

when transfers from Cat 86 were made, 2 cc. of a 10 per cent lung, spleen, and kidney emulsion were given intranasally to Cat 90, while Cat 91, which was full grown and weighed 1.9 kilos, received 2 cc. of a 20 per cent emulsion.

Cat 90, despite the reduction in the strength of the inoculum, ran a course similar to that of Cats 88 and 89. When the temperature was found to be 97° F. on the third morning after the inoculation, the animal, which had had respiratory difficulty for 36 hours, was sacrificed. There was a small amount of clear straw-colored fluid in both pleural cavities. The lungs showed almost complete purplish-red consolidation. Aerobic and anaerobic cultures remained sterile. The spleen was not enlarged, though it appeared darker than normal. Liver and kidneys were grossly normal.

Cat 91 survived a day longer than did Cat 90, though the symptoms and temperature curves were similar. A small amount of clear pleural fluid in both pleural cavities and extensive purplish-red consolidation throughout the lungs were found at autopsy. Aerobic and anaerobic cultures remained sterile. The other organs seemed normal.

Fourth passage, Cats 92 to 99.—An attempt to titrate what appeared to be a potent virus seemed advisable at this point. This was carried out in full-grown cats as well as in young kittens in order to determine possible differences in infectivity in the two groups. As a sufficient number of kittens was not immediately available, the first titration was performed in full-grown cats, the second titration in kittens 5 days later. Consequently, the emulsion used was not the same preparation in both series, though it was derived in each instance from the same organs of Cat 90. On Nov. 5th, a 10 per cent broth emulsion was prepared using equal parts by weight of lung and spleen. Ten-fold dilutions of this emulsion were made with broth for intranasal inoculation. Cat 92, the heaviest, received 2 cc. of the 10 per cent emulsion; Cat 93, 2 cc. of the 1 per cent dilution; Cat 94, 2 cc. of the 0.1 per cent dilution. Cats 92 and 94 have shown no symptoms nor fever, have maintained a good appetite, and appear generally healthy. Cat 93, receiving the 1 per cent emulsion, developed fever with cough and weakness 4 days after inoculation. At the height of the fever, 105° F. on the 6th day, respirations were wheezing in character. The animal recovered fairly promptly and with its mates is being held for re-inoculation.

In contrast with the response in the full-grown cats, the titration

carried out in young kittens on Nov. 10 resulted in a uniformly severe infection for all dilutions, Cats 95, 96, 97, and 99 being moribund with terminal hypothermia when killed. A 10 per cent broth emulsion of lung and spleen from Cat 90 was prepared and 10-fold dilutions to 10^{-4} with broth were made. Each cat received 2 cc. of a given dilution by nasal instillation. Cat 96, inoculated with the 1 per cent emulsion, was the first to show symptoms and succumbed in little more than 48 hours after inoculation. The lungs on autopsy were purplish and rather edematous. Cat 97, which received 2 cc. of the 0.1 per cent dilution, developed fever, anorexia, and rapid respirations within 36 hours. When the temperature had fallen to 99.5° F. on the 4th day after inoculation and the animal was in extremis, it was killed and the lungs were found to be almost completely consolidated. Cat 95, although the smallest animal in the group and receiving the largest dose, 2 cc. of the 10 per cent emulsion, showed no fever though respiratory symptoms were present 48 hours after inoculation. The animal was killed the morning of the 5th post-inoculation day when the temperature was found to be 93° F. The autopsy findings were similar and as extensive as in Cats 96 and 97. Cat 98 was inoculated with the smallest dose, 2 cc. of the 0.01 per cent emulsion. It appeared perfectly well for 4 days. From the 5th to the 9th days, the appetite was capricious, the respiratory rate increased, the animal appeared sluggish, and its coat was dull and rough. It was killed on the morning of the 10th day following inoculation because of respiratory distress. The autopsy findings of an extensive pneumonia confirmed the clinical impression. Three-fourths of the lungs were involved. The pneumonic consolidation was pale and grey instead of the bright purplish or cherry-red seen in the other cats.

Cat 99 was inoculated intranasally with 2 cc. of a 10 per cent broth emulsion of the lung of Cat 90 in order to determine the infectivity of lung tissue alone. The animal failed to show any febrile rise. Respiratory difficulty was severe toward the end of the 2nd day after inoculation and the animal was killed. There were 4 cc. of a somewhat cloudy fluid in the left pleural cavity. Pneumonia was present and involved the anterior lobes most extensively. Large patches were seen in the posterior lobes, but about half of these were normal in appearance.

Aerobic and anaerobic blood-agar plate cultures of the lungs of the cats of the foregoing fourth-passage series were either sterile

(Cats 95 and 98) or showed a few colonies of nonhemolytic streptococci or an unidentified large Gram-negative bacillus. Similarly, aerobic and anaerobic cultures in broth of bits of lung tissue either remained sterile (Cats 98 and 99) or showed variously a growth of streptococci, a large Gram-positive coccus, Gram-negative bacilli, or *B. subtilis*. The absence of bacteria in some instances in the serial passages from Cat S1, the scanty growth in others, and the inconstancy of any particular organism indicate that the bacteria encountered were incidental contaminants of the pulmonary tissues.

The microscopic pathology of the lungs in the passage series originating from Cat S1 is consistent throughout with a pneumonitis of virus etiology and need not be described in detail for each animal. In the cats killed from the 3rd to 5th days there is conspicuous edema of the perivascular and peribronchial interstitial tissue with sparse large mononuclear cell infiltration; the bronchi and bronchioles show beginning necrosis of the epithelial cells with some desquamation; their lumina contain a serous exudate with variable numbers of large and small mononuclear cells and occasional polymorphonuclear leukocytes; in focal peribronchiolar areas the alveoli show variable degrees of atelectasis, their walls are thickened, the alveolar lining cells show signs of necrosis, and the alveolar spaces are filled with a serous exudate containing variable numbers of cells, conspicuously and predominantly large mononuclear in character, though some small mononuclear and sparse polymorphonuclear leukocytes are present (Fig. 9); there is little or no fibrin, no hemorrhage, and the pleural surface shows no exudate. No bacteria are seen in the sections of those cats which were sacrificed and autopsied immediately after death. By the 7th day after inoculation the cellular component of the exudate in the interstitial tissue, bronchioles, and alveolar spaces is much more marked and is again conspicuously large mononuclear in character (Fig. 8). By the 10th day the edema of the interstitial tissue has largely disappeared and the serous component of the pneumonic exudate has been largely replaced by large mononuclear cells. The bronchiolar epithelium is regenerating and the thickened alveolar walls are in many places lined with large cuboidal cells.

Transmission experiments in mice

Although preliminary attempts to transmit the infection from Cats S1, 4, and 7 to mice had met with failure, it nevertheless seemed

desirable to make a further attempt to determine whether mice were susceptible to the virus-like agent derived from Cat S1, particularly in view of the recent report by Baker[3] that a psittacosis-like agent obtained by him from a pneumonia of cats is readily transmissible to mice. The source material consisted of tissue emulsions from Cats S1, 85, 86, 87, 90, and 91 (Chart 5). Groups of mice under ether anesthesia were inoculated by the intracerebral, intranasal, and intraperitoneal routes with 10 or 20 per cent emulsions prepared, with beef-heart infusion broth as a diluent, from the lungs, spleen, and kidneys of the infected cats. Several different breeds of mice were used in an effort to find one that might prove susceptible. As controls for a possible latent infection in the stock mice broth was injected by similar routes. The mice were held under observation for at least two weeks; in many instances for longer periods of time. At intervals of 7 to 11 days selected mice were killed for pathological examination and for attempted passage of a possible latent infection. Selected 2nd generation mice were similarly killed and passage to a 3rd generation carried out. The results are presented in detail in Table 1. Among the 105 mice inoculated with cat tissue emulsions there were only 10 deaths, all of which were attributable to intercurrent bacterial infections. None of the remaining 95 showed any symptoms nor did any of those sacrificed for passage exhibit any gross lesions in the brain, lungs, or abdominal viscera. Similarly negative results occurred in the 2nd and 3rd generation mice and in the controls.

It would appear from these experiments that the virus-like agent obtained from Cat S1 and capable of being transferred in cats is not easily transmissible to mice, if at all, since the cat-organ emulsions or passage material from mice receiving them failed to produce evidence indicative of virus infection in 207 mice. Ten of 12 deaths which occurred were obviously due to bacterial contaminants. No latent mouse virus was encountered in the stocks used.

Discussion

The epidemiological implication of the concurrent outbreak of an acute respiratory infection in 4 of the 8 members of the S. family and in 10 of their 12 cats during October and November, 1941, is clear, namely, that the same infection may have been present in both groups, irrespective of whether it appeared first in the cats or in one of the members of the family, Case H. S.

TABLE 1

MOUSE TRANSFERS

Generation I						Generation II		
Date	*Source*	*Inoculum*	*Route of inoc.*	*Breed of mice*	*No. Inoc. / No. Dead*	*Date*	*Source*	*Inoculum*
10-14-42	Cat S 1	20% emulsion of lung, spleen, kidney	i.c.	Yonkers	5/1[1]	10-21-42	i.n. Gen. I mouse	10% lung emuls.
			i.n.	Yonkers	5/1[2]		i.p. Gen. I mouse	10% spleen, kidney emuls.
			i.p.	Yonkers	5/0			
			i.c.	C.B.A.	2/0			
			i.n.	C.B.A.	2/1[3]			
			i.p.	C.B.A.	2/0			
			i.c.	A.	2/1[4]			
			i.n.	A.	2/0			
			i.p.	A.	2/0			
			i.c.	C_3H.	2/1[5]			
			i.n.	C_3H.	2/0			
			i.p.	C_3H.	2/0			
			i.c.	J.K.	2/0			
			i.n.	J.K.	2/0			
			i.p	J.K.	2/0			
10-20-42	Cat 85	20% emulsion of lung, spleen, kidney	i.c.	Yonkers	5/0	10-29-42	i.n. mice Gen. I	20% emuls. lung, spleen
			i.n.	Yonkers	5/0		i.p. mice Gen. I	20% emuls. lung, spleen
			i.p.	Yonkers	5/0			
10-29-42	Cat 86	20% emulsion of lung, spleen, kidney	i.c.	N.H.H.	3/0	11-5-42	i.n. mice Gen. I	10% emuls. lung, spleen
			i.n.	N.H.H.	3/0			
			i.p.	N.H.H.	3/3[7]			
10-30-42	Cat 86	10% emulsion of lung, spleen, kidney	i.n.	N.H.H.	2/0			
			i.p.	N.H.H.	2/2[8]			
10-24-42	Cat 87	20% emulsion of lung, spleen, kidney	i.c.	Yonkers	3/0	10-31-42	i.n. mice Gen. I	10% emuls. lung, spleen
			i.n.	Yonkers	3/0		i.p. mice Gen. I	10% emuls. lung, spleen, liver
			i.p.	Yonkers	3/0			
11-2-42	Cat 90	10% emulsion lung	i.c.	C.F.W.	3/0	11-9-42	i.c. mouse Gen. I	10% emuls. Pool of i.c. brain, i.n. lung & i.p. spleen&liver
			i.n.	C.F.W.	3/0		i.n. mouse Gen. I	
			i.p.	C.F.W.	3/0		i.p. mouse Gen. I	
		kidney	i.p.	C.F.W.	3/0	11-13-42	i.n. mice Gen. I	10% emuls. of lung
		spleen	i.p.	C.F.W.	3/0			
11-3-42	Cat 91	20% emulsion lung	i.n.	N.H.H.	3/0	11-11-42	i.n. and i.p. mice Gen. I	10% emuls. Pool of lungs from i.n. 20& 10% emuls., liver&spleen from i.p. 10% emuls.
			i.p.	N.H.H.	3/0			
		10% emulsion lung	i.n.	N.H.H.	3/0			
			i.p.	N.H.H.	5/0			
10-13-42	Controls	Broth	i.c.	N.H.H.	3/0	10-18-42	i.c., i.n., i.p. mice Gen. I	10% emuls. Pool of i.c. brain, i.n. lung, & i.p. spleen and liver
			i.n.	N.H.H.	3/0			
			i.p.	N.H.H.	3/0			
10-14-42	Controls	Broth	i.c	Yonkers	3/0	11-2-42	i.c., i.n., i.p. mice Gen. I	20% emuls. Pool of i.c. brain, i.n. lung, i.p. spleen
			i.n.	Yonkers	3/0			
			i.p.	Yonkers	3/0			

[1] Dead 7 days after inoculation. Culture of brain: few degraded streptococci.
[2] Dead day following inoculation. Culture of lungs: large Gram-negative rods: α streptococci.
[3] Dead day following inoculation. Culture of lungs: staphylococci.
[4] Sick and killed 5 days following inoculation. Culture of brain: α streptococci.
[5] Dead day following inoculation. Culture of lungs and brain: staphylococci.

TABLE 1

MOUSE TRANSFERS

Generation II			Generation III					
Route of inoc.	*Breed of mice*	*No. Inoc. / No. Dead*	*Date*	*Source*	*Inoculum*	*Route of inoc.*	*Breed of mice*	*No. Inoc. / No. Dead*
i.n.	Yonkers	3/0	10-29-42	i.n & i.p. mice Gen. II	20% emuls. lungs, spleen	i.n.	N.H.H.	3/0
i.p.	Yonkers	3/0				i.p.	N.H.H.	3/0
i.n.	Yonkers	3/0		i.n & i.p. mice Gen. II	20% emuls. lungs, spleen	i.n.	N.H.H.	3/0
i.p.	Yonkers	3/0				i.p.	N.H.H.	3/0
i.n.	N.H.H.	3/0	11-5-42	i.n. & i.p. mice Gen. II	10% emuls. lungs, liver, spleen	i.n.	N.H.H.	3/0
i.p.	N.H.H.	3/0				i.p.	N.H.H.	3/0
i.n.	N.H.H.	3/0		i.n. & i.p. mice Gen. II	10% emuls. lungs, liver, spleen	i.n.	N.H.H.	3/0
i.p.	N.H.H.	3/1[6]				i.p.	N.H.H.	3/0
i.n.	N.H.H.	3/0	11-13-42	i.n. & i.p. mice Gen. II	10% emuls. lungs, liver, spleen	i.n.	N.H.H.	3/0
i.p.	N.H.H.	3/0				i.p.	N.H.H.	3/0
i.n.	C.F.W.	3/0	11-7-42	i.n. & i.p. mice Gen. II	10% emuls. lungs, liver, spleen	i.n.	C.F.W.	3/0
i.p.	C.F.W.	3/0				i.p.	C.F.W.	3/0
i.n.	C.F.W.	3/0		i.n. & i.p. mice Gen. II	10% emuls. lungs, liver, spleen	i.n.	C.F.W.	3/0
i.p.	C.F.W.	3/0				i.p.	C.F.W.	3/0
i.c.	C.F.W.	3/0						
i.n.	C.F.W.	3/1[9]						
i.p.	C.F.W.	3/0						
i.n.	C.F.W.	3/0						
i.n.	N.H.H.	3/0						
i.p.	N.H.H.	3/0						
i.c.	N.H.H.	3/0						
i.n.	N.H.H.	3/0						
i.p.	N.H.H.	3/0						
i.c.	C.F.W.	2/0	11-9-42	i.c., i.n., i.p. mice Gen. II	10% emuls. Pool of i.c. brain, i.n. lungs, i.p. liver and spleen	i.c.	C.F.W.	1/0
i.n.	C.F.W.	2/0				i.n.	C.F.W.	1/0
i.p.	C.F.W.	2/0				i.p.	C.F.W.	1/0

[6] Dead 5 days following inoculation: marked postmortem change. Discarded.
[7] Dead day following inoculation. Smear of peritoneal exudate loaded with Gram-negative rods and with cocci.
[8] Dead day following inoculation. Smear of peritoneal exudate loaded with bacteria.
[9] Dead 2 days following inoculation. Lungs negative except for postmortem decomposition. Discarded.

The clinical picture of the disease in Case A. S., which has been described above, was consistent with that of primary atypical pneumonia and there would appear to be little doubt that the 3 other patients had the same infection. This clinical picture or syndrome in our present state of knowledge[13, 17] apparently embraces several specific entities of established etiology and a larger group of atypical pneumonias of unknown cause, the differentiation of which may be suggested by epidemiological evidence but can be established only by the recovery and identification of the infectious agent or the demonstration of a significant increase in specific antibodies in the blood following recovery. The first group may be considered to include psittacosis,[48] ornithosis,[15, 36] Q fever,[11, 14, 22, 24] and possibly rare cases of atypical pneumonia due to infection with the virus of lymphocytic choriomeningitis.[45] Some cases of pulmonary coccidioidomycosis[12] and of tularemic pneumonia[4] might also present a picture difficult to distinguish on clinical grounds alone. Whether the second or larger group, as yet of unknown though presumptive virus etiology, is homogeneous or likewise includes several specific entities remains to be determined. In the case of the S. family, coccidioidomycosis may be excluded for geographical reasons, tularemia on bacteriological and immunological grounds. Furthermore, the epidemiological data, though not conclusive, militate against a diagnosis of psittacosis, ornithosis, or Q fever. For these reasons the infection in the S. family may tentatively, at least, be placed in the second group of primary atypical pneumonias of undetermined etiology.

The nature of the acute respiratory infection which occurred in the family cats is more difficult to relate to known feline diseases. Feline distemper, according to Kirk,[26] appears to be a diagnostic term rather loosely employed to include (1) catarrhal distemper characterized by sneezing and discharge from the eyes and nose and probably the same disease as the "feline influenza" of Buxton;[8] (2) an abdominal type of feline distemper, which is a severe and often rapidly fatal epidemic disease characterized primarily by vomiting and profuse diarrhea with catarrhal inflammation of the small intestine but not infrequently exhibiting upper respiratory symptoms in the more chronic cases of the disease; and (3) a specific feline enteritis, particularly affecting kittens and characterized by anorexia, vomiting, marked constipation, brief fever, and sudden collapse with death in 24 to 48 hours. Similarly Köbe,[28] in Gildemeister, Haagen,

and Waldmann's *Handbuch der Viruskrankheiten*, supports the view of Dalling[9] that so-called feline distemper includes at least two diseases, namely, infectious gastro-enteritis and a definite respiratory infection characterized by rhinitis, tracheitis, laryngitis, and bronchopneumonia. To these two, Köbe[28] adds an infectious laryngo-enteritis described by Krembs and Seifried.[30] Of these diseases only the abdominal form of "feline distemper" (infectious gastro-enteritis) appears to have an established etiology, namely, a filterable virus, as suggested by the experiments of Verge and Christoforoni[49] and established by the studies of Hindle and Findlay.[23] With respect to the etiology of the respiratory disease, variously called catarrhal distemper or feline influenza, little is known. In 1911, McGowan[34] recovered an organism, which appears to have been *B. bronchisepticus*, from the lungs of cats dead of this disease with sufficient frequency to have led him to attribute etiological significance to it, although today it would probably be regarded as a secondary invader. The recent report of Baker[3] concerning the recovery of a psittacosis-like agent from a highly infectious respiratory disease of cats may serve to define at least one specific entity now included in feline catarrhal distemper.

Despite the obvious difficulties in differentiation, the infection in the S. family cats, characterized clinically and anatomically by conjunctivitis, rhinitis, tracheitis, bronchitis, and pneumonia, without diarrhea or lesions in the intestines, would appear to fall within the category of those feline infections commonly called catarrhal distemper and not to have been the abdominal form of feline distemper or infectious gastro-enteritis.

Investigation of the etiology of the pneumonia found at autopsy in these cats has furnished evidence that the disease is due to a virus. Although the limited attempts at transmission with nasal washings from Cat S2 and with the lung tissue of Cat S3 were unsuccessful and the serial passages from Cat D8 only suggestive, the result obtained in the serial passages from Cat S1 appears sufficiently clear-cut to warrant this interpretation. Possibly the substitution of ether for Nembutal as an anesthetic and the use of broth instead of normal saline as a diluent were factors which contributed to the successful outcome in this case, though other variables may of course have played a part.

While a few bacteria were cultured from the lungs of Cats D8 and S3, none were found in the lungs of Cat S1 from which the

virus was successfully recovered. Furthermore, cultures of the lungs of Cats 49 and 50 in the Cat D8 passage series, and of Cats 85, 90, 91, 95, and 98 in the Cat S1 passage series remained sterile. The bacteria recovered in cultures of the lungs of the other passage cats were variable and may be regarded as having no pathogenic significance with the possible exception of *B. bronchisepticus*, which appeared as a probable secondary invader in the 3rd, 4th, and 5th passages of the Cat D8 line, but was not encountered in the Cat S1 line. It is, perhaps, noteworthy that the passage cats of the Cat S1 line, though inoculated intranasally, did not exhibit the upper respiratory symptoms shown by the family cats and some of those in the Cat D8 line. While the explanation for this difference is not clear and requires further study, it seems possible that the purulent conjunctivitis and rhinitis may have been due to secondary bacterial infection rather than to the primary virus.

As pointed out above, further evidence in support of the virus etiology of the feline pneumonia described in this paper is to be found in the histological characteristics of the pulmonary lesions, particularly the necrosis of the bronchiolar and alveolar epithelium, the predominant large mononuclear cell reaction *early* in the disease, and the absence of pleural inflammation.

While additional studies now in progress and to be reported later are required to define the characteristics of the Cat S1 virus and its immunological relationship to other viruses known to induce pneumonia, it would appear from the observations reported above that the virus survives in an active state in tissues frozen with CO_2-ice for at least 329 days, that it can induce a severe and rapidly fatal pneumonia in kittens by intranasal inoculation, and that it is not readily, if at all, transmissible to mice, a fact which would seem to distinguish it from the viruses of psittacosis,[43] lymphocytic choriomeningitis,[2] meningopneumonitis,[18] the pneumonia virus of mice,[25] the cat virus reported by Baker,[3] and possibly those of ornithosis[16, 36] and Q fever.[7, 14]

Whether the concurrent respiratory infections in the members of the S. family and their cats were identical in etiology as yet remains uncertain. Obviously the one attempt to recover a virus readily transmissible in cats from the sputum of Case A. S. was not successful, even though the initial inoculations in Cats 3 and 4 were suggestive. Several factors may have contributed to this failure. The sputum

was not collected until approximately 3 weeks after the onset of the disease; ether anesthesia and broth as a diluent were not used; full-grown cats were employed. A preliminary neutralization test, recently performed, with acute and convalescent sera from Case A. S. with the Cat S1 virus is suggestive but not sufficiently conclusive. Further work on this problem is in progress and will form the subject of a later communication.

Summary

The occurrence within a brief period of an acute respiratory disease resembling primary atypical pneumonia in 4 members of a family and in 11 of their cats on a farm in Jewett City, Connecticut, is recorded.

A virus capable of producing a similar pneumonia in cats was recovered from the lungs of one of the family cats.

Kittens appear to be more susceptible to the virus than do full-grown cats.

The virus has failed to infect mice and for this reason appears to differ from most viruses known to cause infections of the respiratory tract.

The evidence so far obtained suggests, but does not establish, the fact that the respiratory infections in the members of the family may have been caused by the same virus.

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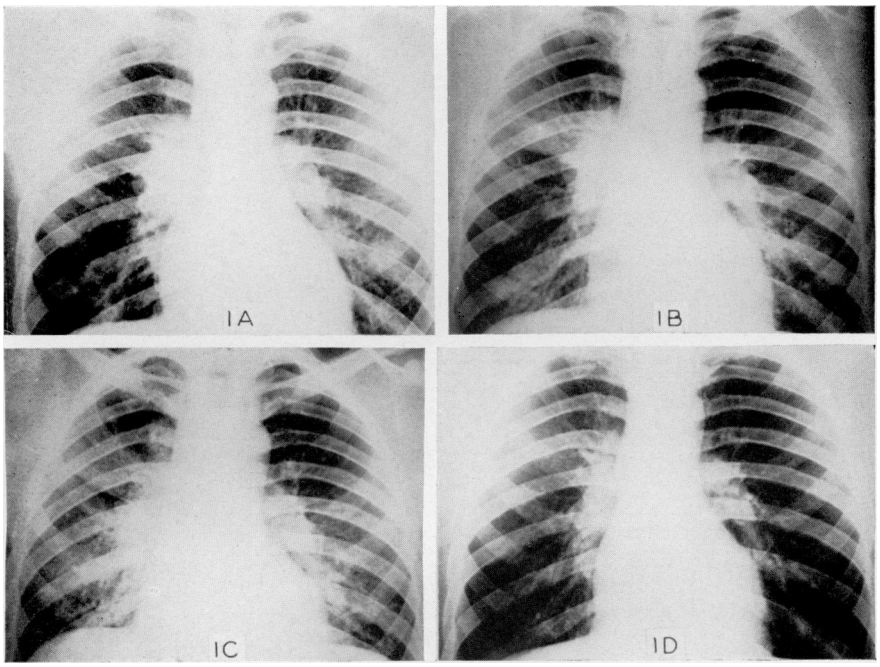


FIG. 1. Roentgenograms of Case A. S. 1A on Nov. 10th; 1B on Nov. 14th; 1C on Nov. 18th; 1D on Nov. 26th.

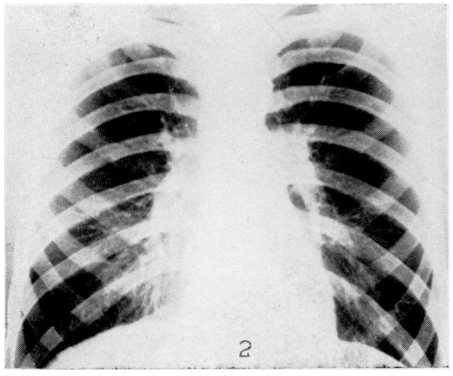
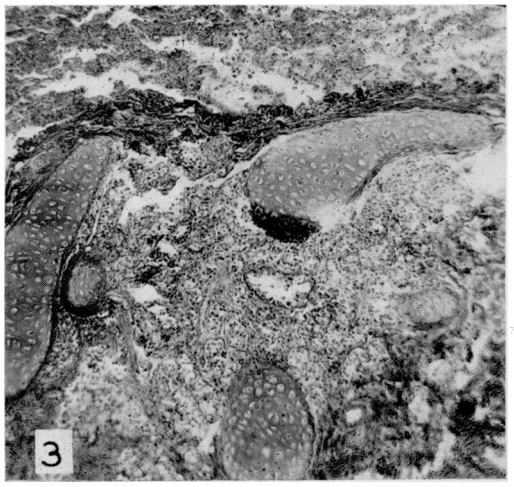


FIG. 2. Roentgenogram of Case M. S.; Nov. 16th.



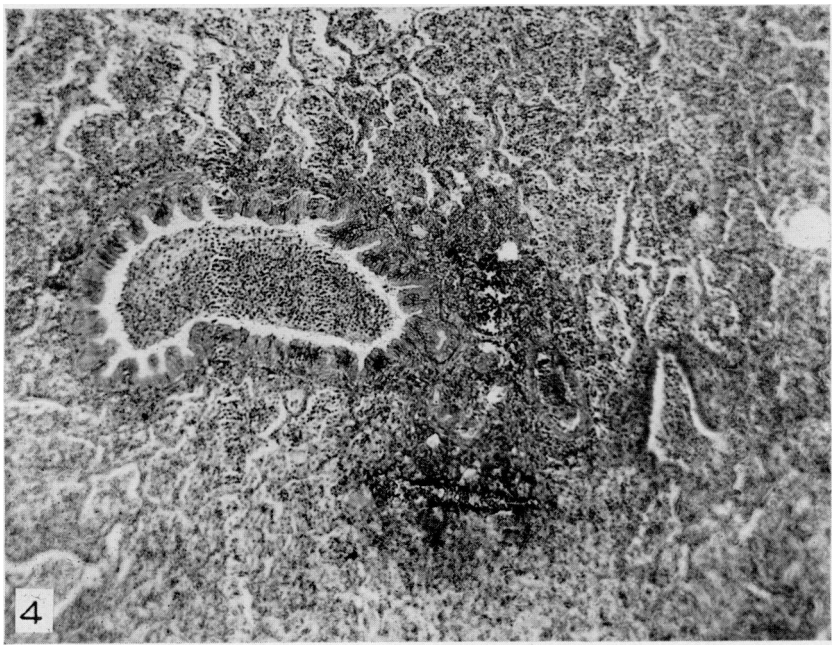


FIG. 3. Cat D8. Lung.
FIG. 4. Cat S1. Lung.
FIG. 5. Cat S3. Right anterior lobe.

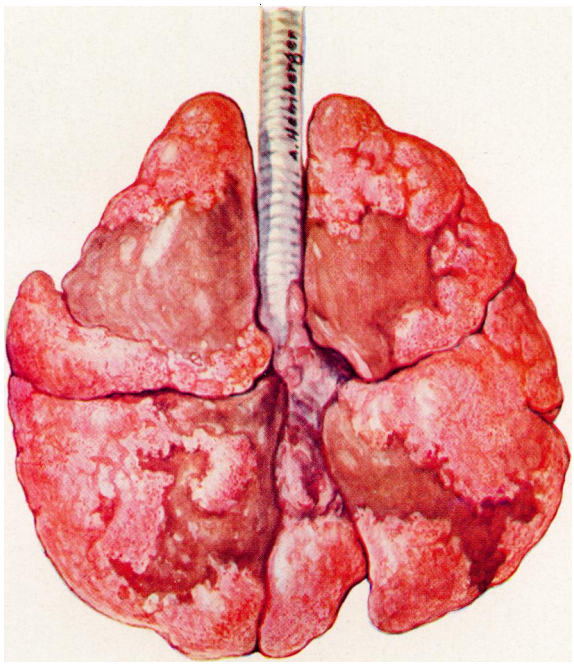
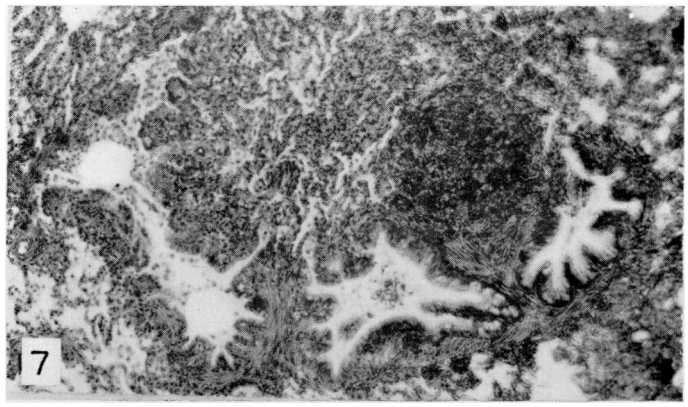
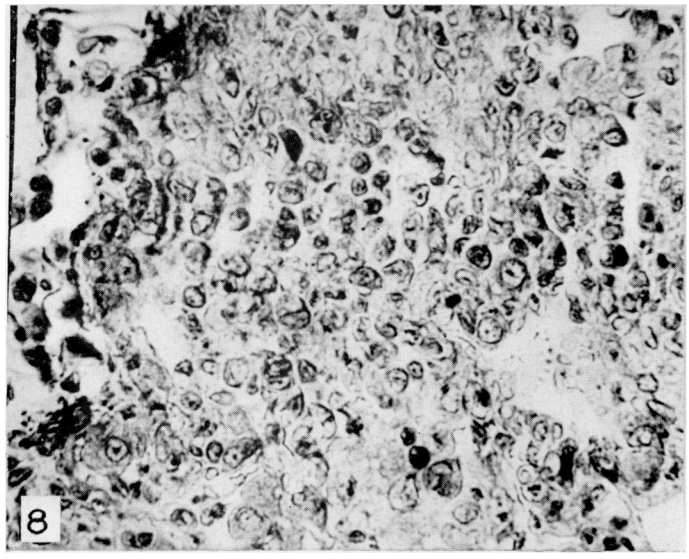


FIG. 6. Cat 87. Lungs, 5th day.





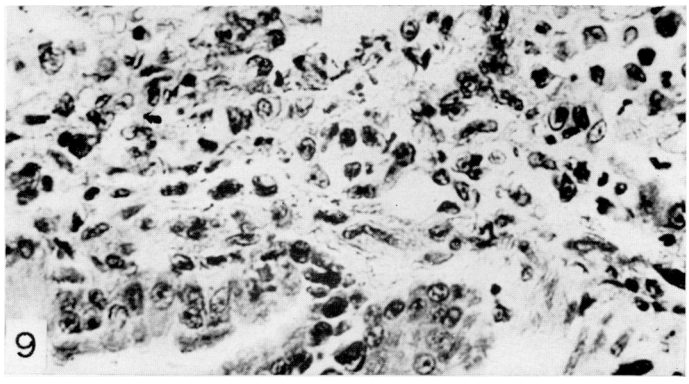


FIG. 7. Cat 7. Lung, 11th day.
FIG. 8. Cat 85. Lung, 7th day.
FIG. 9. Cat 90. Lung, 4th day.