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Is the common concept of histoplasmosis one of a disease widespread in certain areas of the country but usually rather innocuous and of importance to public health chiefly because it complicates the reading of chest x-ray films in tuberculosis case-finding surveys? Then this picture of sudden and circumscribed outbreaks will markedly alter that concept. Findings on the method of spread contain much that is new.

The Occurrence of Histoplasmosis in Epidemics—Epidemiological Studies*

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THE occurrence of a series of epidemics of histoplasmosis has offered an opportunity to add to our knowledge of the epidemiology of this disease. In recent years numerous studies employing the histoplasmin skin test have revealed the remarkable geographic distribution of this infection (summarized by Mochi and Edwards¹). The wide clinical spectrum of this disease from benign to fatal cases has been confirmed by careful clinical studies (Christie²

and others), to which the epidemics have contributed.³ A variety of animals have been found to be infected with *Histoplasma capsulatum*,⁴ and the fungus has been cultured from the soil.⁵ Definitive data on the natural reservoir of the fungus and its mode of spread to human beings have been lacking. The purpose here is to report the epidemiological studies of a group of outbreaks of histoplasmosis. Special emphasis will be placed on data which add to our knowledge of the natural reservoir of *Histoplasma* and its transmission to man.

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Two epidemics of histoplasmosis have been previously recorded. The only epidemic in which the etiology was established in the acute phase by isolation of the organisms from a patient was reported by Loosli, Grayston, Alexander, and Tanzi.⁸ White and Hill,⁶ on the basis of follow-up skin tests, serological tests, and chest x-rays, incriminated histoplasmosis in an epidemic which was originally reported by Nauen and Korn.⁷ Several reports of outbreaks of pulmonary disease of undetermined etiology have appeared in the past 10 years. These epidemics have been characterized by febrile illnesses and chest x-ray findings of disseminated pneumonitis. With the cooperation of the original authors, we have carried out studies on six of these epidemics⁷⁻¹² which have helped establish the etiology as histoplasmosis.* In addition, we have studied seven other outbreaks with similar clinical findings and found them to be histoplasmosis. The etiologic studies on this series of epidemics are being reported elsewhere.¹³ To briefly summarize them here: the diagnosis is based on positive histoplasmin skin tests, positive histoplasmosis serological tests, development of miliary calcification, and isolation of *H. capsulatum* from the soil at the point source of the epidemic. All of those individuals involved in the outbreaks who were skin tested with histoplasmin reacted. Some serologic evidence of histoplasmosis was obtained in all the epidemics. In the majority of the epidemics, excellent serologic evidence was obtained on most of the patients. Pulmonary calcification, predominantly of the disseminating miliary type, has been demonstrated in all except the two most recently occurring outbreaks. Details of the soil studies will be discussed below.

* In two epidemics^{7, 10} our contribution was limited to isolation of *Histoplasma* from point source soil samples.

Among the epidemics considered in the companion paper on etiology,^{13b} comprehensive epidemiologic studies were included in the original reports of four.^{7, 9-11} These reported data will be summarized briefly in this paper along with the presentation of the information on nine epidemics on which we have performed epidemiologic studies. Of these, seven are as yet unreported. In three of the unreported epidemics, the studies were made possible by help from physicians caring for the patients. We are indebted to them for some of the data used.¹⁴⁻¹⁶

RESULTS

In each of the 13 epidemics to be considered, it has been possible to find a common place of exposure. A common exposure is supported in many of the epidemics by the close proximity of the dates of onset of illness of all those involved. The time span of onsets and the incubation periods are presented in Table 1. In nine epidemics the span of onsets did not exceed 12 days. At no time did secondary cases appear in family contacts or associates not exposed to the common source. In two epidemics (Gruber, Okla., and Madison, Wis.) where there was a wider span of onset dates, it was possible to show similar incubation periods from exposure to a common source at different times. The incubation period showed some variation but tended to be from one to two weeks.

In many of the epidemics an obviously unusual common activity has pointed to a single place for exposure. This has not been true of all the outbreaks, and cultural study of soil samples from some has aided in the delineation of the sources of the infection. Histories of the activities of those involved in the epidemics have allowed determination of possible modes of transmission. A description of the point source and the suspected mode of transmission in each epidemic follows:

TABLE 1

*The Time Span of Onsets of Illness and the Incubation Periods of 11 * Epidemics of Histoplasmosis*

Place	No. Persons Sick	Onsets-Span in Days	Incubation Periods in Days
Plattsburg, N. Y.	23	7	7-14
Crowder, Mo.	40	10	?
Gruber, Okla.	35	(2 mos.) †	8-18
Williamsburg, Kans.	5	7	6-16
Cincinnati, Ohio	12	9	5-14
Kansas City, Mo.	5	12	7-19
Foreman, Ark.	25	9	4-13
Detroit Lakes, Minn.	6	3	?
Madison, Wis.	12	(3 mos.) †	5-10
Bath, Ill.	2	7	14-21
Mandan, N. D.	5	3	12-16

* This information not available for Bellevue, Ia., and Topeka, Kans., epidemics

† Exposure at different times

Plattsburg, N. Y.—An epidemic of “Acute Miliary Pneumonitis” occurring in a group of WPA workers dismantling an old school building in Plattsburg, N. Y., has been described by Nauen and Korn.⁷ In November, 1938, 19 of 21 men became ill who were intimately associated with what was an extremely dusty job of shoveling large amounts of pigeon droppings and carcasses from the bell tower and ceilings of the building. A picture of the school building many years before its destruction is shown in Figure 1.

Since a new library building and cemented grounds now cover the old site of the school, it was impossible to examine soil from the exact point source of this epidemic. Soil samples obtained from surrounding areas and buildings were cultured. A sample from the dirt basement of a church two doors from the former site of the school building contained *H. capsulatum*.

Camp Crowder, Mo.—In May, 1943, at Camp Crowder, a group of Army trainees suffered a simultaneous respiratory infection characterized by disseminated infiltrations on x-ray. Idstrom and Rosenberg⁸ reported that approximately 40 men in one company were involved. The men had been working as clean-up teams “clearing out dusty abandoned homes, barns, chicken coops,

and other outhouses prior to installation of Signal Corps equipment.” Records have been located indicating that 22 men were hospitalized at the time of the outbreaks. Follow-up studies have been directed at this group.

A fairly well circumscribed area about one-half mile long where the company involved had been training at the time of the epidemic was outlined by investigation on the Crowder reservation. Unfortunately, at this late date it was not possible to determine more precisely the buildings in which the men who became ill had worked. A series of soil samples were obtained from inside and around all the buildings in the designated area. *Histoplasma* was isolated from three of the samples taken from around buildings on both sides of the road over a stretch of approximately 100 yards.

Camp Gruber, Okla.—An epidemic called “Unusual Pulmonary Disease” occurring in some 35 soldiers at Camp Gruber, Okla., in 1944 has been described.⁹ Only men visiting a certain storm cellar were involved. There was no door on the cellar, but the men placed a blanket over the opening and built a fire of rotten boards from the ceiling and strips of bark and chips of wood from the elm supporting logs. In addition to the large original group exposed at the time of building the fire, eight men were

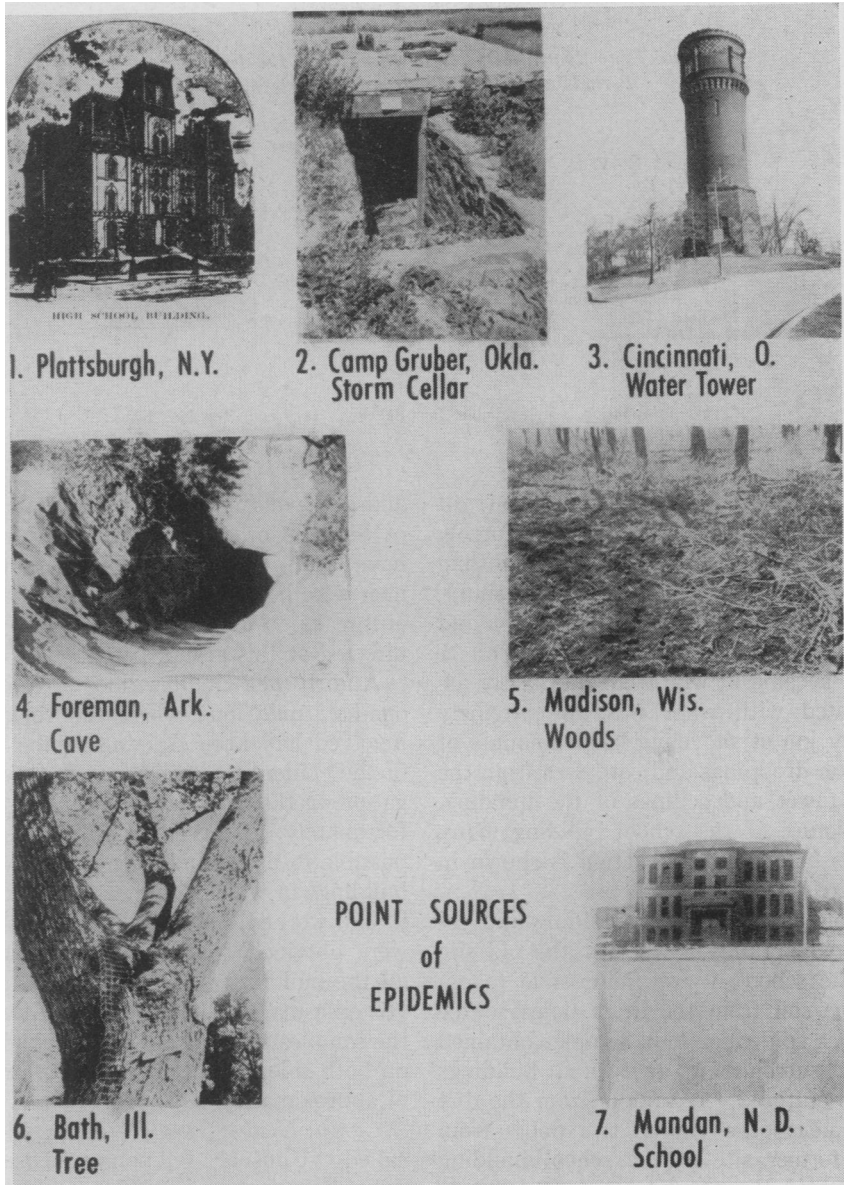


FIGURE 1—Examples of several of the point sources of the epidemics of histoplasmosis

exposed a week later, and two men two months later. All those exposed at a later date had mild disease or no disease at all. The entrance to the cellar is shown in Figure 1. Soil samples have been collected from the cellar and *Histoplasma* isolated from samples collected on four different occasions.

Topeka, Kans.—Study of a 12-year-old boy with disseminated miliary calcification revealed a history of an acute febrile illness with pulmonary symptoms seven years previously in September, 1944, while he was living on a farm 15 miles north of Topeka, Kans. Investigation was carried out on the members

of his family and of two other farm families who had lived on the farm subsequently. In all, 11 persons were examined. Four were found to have disseminated miliary lesions showing early calcification. These four consisted of a young boy in each family, plus a youngster who had visited the farm and came to attention because of a history of illness. Additional findings consisted of single or several pulmonary calcifications in four adult members of the families.

Soil samples from in and about the buildings of this farm were examined. One sample from a small shed immediately in back of the farm house yielded *H. capsulatum*.

Williamsburg, Kans.—On November 15, 1946, a family of nine members moved to a farm near Williamsburg, Kans. Nine days later three of the children had onset of mild febrile illnesses. A week later a fourth child became ill with more severe symptoms. Chest x-rays on the entire family showed that pulmonary infiltrations were present in the four children who had been sick and, in addition, in a 14-month-old infant who had not been noticeably ill. The five children with pulmonary pathology ranged in ages up to 10 years. The parents and the two older children had no findings. Only the child with the more severe illness exhibited numerous widespread miliary infiltrations, the others having one or several localized lesions with hilar adenopathy. It was not possible to incriminate any activity or location as likely source for the infection as the children had investigated all the buildings and grounds in the first few days on the farm. Soil samples were collected from all areas of the farm in 1952, and a strain of fungus which passes through mice and resembles *H. capsulatum* grossly has been secured. It has not been possible as yet to positively identify this strain as *Histoplasma*.

Cincinnati, Ohio—An epidemic of disseminated pneumonitis occurred in Cincinnati in July, 1947.¹⁰ Twelve men who were exposed to the cleaning of pigeon excreta from an abandoned water tower became ill. This water tower is in a park not far from downtown Cincinnati. A picture of the tower is shown in Figure 1. The large amount of pigeon excreta was in the basement of the tower. A few of the 12 men just visited the tower at the time of the cleaning and did not actually handle the material. Soil samples from the tower and other surrounding sites have been cultured, but we have been able to isolate *Histoplasma* only from the basement of the water tower.

Kansas City, Mo.—In July, 1947, an elderly couple were preparing to move to a farm just outside Kansas City, Mo. Several of their grandchildren went to the farm with them on different days to help clean it. Four of the children and the grandmother became ill. No illness occurred in the grandfather, but histoplasmin skin test conversion was demonstrated in August. Chest x-rays revealed infiltrations on all these six persons. Numerous miliary lesions appeared in three children with more severe illnesses.

The only time these four children had visited the farm together was on July 7. The major activity on that day was tearing down a chicken coop. This was remembered as a dusty job. Soil samples collected from around the farm in 1952 have shown one positive for *Histoplasma*. This particular sample came from approximately the original site of the chicken coop.

Foreman, Ark.—The epidemic reported by Washburn, Tuohy, and Davis¹¹ as "Cave Sickness" occurred in September, 1947. Twenty-five men and boys became ill with fever and pulmonary manifestations after digging out an old filled in cave near Foreman, Ark. Persons actually involved in the excava-

tion or visiting closely to it were sick. Many of the patients were only mildly ill. Those having more prolonged exposure had the severest illnesses. Although most of those x-rayed showed disseminated infiltrations, there were some with only localized infiltrates.

The cave does not enter into the side of a hill but goes downward into the earth at a 60° angle with the main room off to the right after a 10-foot descent. At first, a bulldozer uncovered the opening to the cave and then the cave was dug out with shovels. A picture of the entrance to the cave as it now appears is shown in Figure 1. Soil samples were collected from inside and around the cave. *H. capsulatum* was isolated from a sample taken from inside the cave.

Detroit Lakes, Minn.—During the last week of January, 1948, all six members of a farm family living near Detroit Lakes, Minn., became ill. Four required hospitalization while two recovered on bed rest at home. Chest x-rays showed disseminated lesions in all. The details of the clinical illnesses have been reported by Rutledge¹² as an unknown pulmonary illness.

Epidemiologic studies carried out in the fall of 1951 failed to reveal a single incident of unusual group activity to which the infection might be attributed. Since a two-foot layer of snow had covered the area for over six weeks, much of the usual movement and activity about the farm was curtailed. The family spent most of their time in the kitchen and dining room of the house where wood warming stoves were present. It was possible to establish by history that the only place all six members of the family had been together during the two months preceding their illness was in the farmhouse. The only material being brought into the house at that time was the firewood for the warming stoves.

Soil samples were collected from about the farm and buildings. The

only one yielding *Histoplasma* on culture was from loose dirt underneath the kitchen of the farmhouse.

Madison, Wis.—During June, July, and August, 1948, a series of cases of disseminated pneumonitis occurred in Madison, Wis. Chest x-rays were available on 10 of the 12 patients and all showed some scattered miliary lesions, although these were frequently fewer in number than in many of the other outbreaks. The cases occurred two and three together in families and among friends. Investigation revealed that a common source existed for the cases in a sparsely wooded area near an outlying manufacturing district. All those who were found with the illness had visited this area to dig angleworms. The wooded area was in low-lying moist land surrounded by high weeds. In the place among the trees where the worms had been dug, there was no growth of foliage on the ground (Figure 1). Several soil samples were obtained from the general area. Samples from the site of digging have yielded *H. capsulatum* on two separate occasions.

Bath, Ill.—In April, 1951, two nine-year-old cousins became ill within a week of each other. Chest x-rays showed numerous disseminated infiltration in both. History revealed that approximately three weeks prior to onset of the illnesses the two cousins had played together. It was well remembered that the boys had climbed up into a tree and let themselves down into the hollow trunk (Figure 1). They were in this very cramped situation for over an hour. Because of the narrow opening the boys were trapped in the tree, and one of their fathers had to come with a ladder and extricate them from the hole. The tree is located in the schoolyard near the center of Bath, Ill., a small town lying along the Illinois River.

Soil samples were collected from inside the tree and the surrounding areas.

A considerable amount of loose material could be scooped out of the bottom of the hole in the tree trunk. It consisted of dried powdery wood chips and flakes intermixed with sandy soil. Histoplasma has been isolated on two occasions from samples taken from inside the tree.

Bellevue, Ia.—In September, 1951, our attention was drawn to a culturally proven fatal case of histoplasmosis in a five-month-old infant in Iowa.* The case was of interest as it appeared that the infection must have occurred during the first six weeks of the baby's life. She had been taken to California, which is out of the known histoplasmosis area, at 6 weeks of age and returned to Iowa only three days before hospitalization. Prior to leaving for California the baby had lived with her mother on the maternal grandparents' farm outside Bellevue, Ia. Other persons living on the farm during these six weeks were the grandparents and their two sons. Each member of the household was examined. The two boys (17 and 19 years) were found to have disseminated fine infiltrations on chest x-ray. The grandfather exhibited well healed multiple pulmonary calcifications. He had lived on the farm for 30 years. During the early summer just after the infant had been on the farm, both of the boys had mild "flu-like" illnesses.

The infant had not been on the ground outside the farmhouse or in any of the other buildings. During the spring of the year, the wood burning heating stove in the living room of the farmhouse was used frequently to keep the baby warm. This seemed to be the main contact the baby had with material from outside the house. Cultural examination of samples of wood and soil from all areas around the farm resulted in finding one positive for *H. capsulatum*. This one was from soil collected from along the outside of the house below the living room.

Mandan, N. D.—An epidemic occurred in Mandan, N. D., during February, 1952, involving four men. The story is very reminiscent of the Plattsburg, N. Y., outbreak, as these men were engaged in tearing down an old abandoned school house (Figure 1). A considerable amount of pigeon and, possibly, bat droppings was removed from rafters and window casings of the building approximately two weeks prior to the onset of severe pneumonic illnesses. This activity raised such a high concentration of dust that, despite the bitter cold weather, the windows were opened in order to breathe. Although each man had numerous widely disseminated lesions on x-ray, it was apparent that two of the men suffered a more severe illness than the others. The men worked in pairs on days off from their regular railroad jobs. The two with the severest illness had been more intimately involved with the removal of the droppings.

When visited five months after onset of the illness, the building had been completely leveled. The building site is within the city and less than 100 yards from the municipal swimming pool. Soil samples were obtained from about the foundation of the building and from surrounding areas. Laboratory examination of these samples is not yet completed.

Table 2 summarizes the activities associated with infection and the common sources of the epidemics.

Other Epidemics—The proven epidemic reported by Loosli and associates³ involved the members of a farm family who were infected from sawdust material in an abandoned silo. Other outbreaks of disseminated pneumonitis have occurred. In three of these, excellent serological evidence supporting the diagnosis of histoplasmosis has been obtained. One which was referred to by Sabin^{10b} involved seven men who had shoveled pigeon manure from a church

* By Dr. I. H. Borts.

TABLE 2

Tabulation of the Activities Associated with Infection and the Common Sources of 13 Epidemics of Histoplasmosis

Place	Activity	Common Source	<i>Histoplasma</i> Soil Isolation
Plattsburg, N. Y.	Shoveling pigeon excreta	Schoolhouse	Nearby church basement
Camp Crowder, Mo.	Cleaning	Farm buildings	Shed, cellar, and barn
Camp Gruber, Okla.	Building fire	Storm cellar	Storm cellar
Topeka, Kans.	Playing	Farm	Shed
Williamsburg, Kans.	Playing	Farm	..
Cincinnati, Ohio	Shoveling pigeon excreta	Water tower	Water tower
Kansas City, Mo.	Tearing down	Chicken coop	Site of chicken coop
Foreman, Ark.	Digging earth out	Cave	Cave
Detroit Lakes, Minn.	Wood fire (?)	Farmhouse	Underneath kitchen
Madison, Wis.	Digging fishing worms	Area in woods	Area in woods
Bath, Ill.	Playing	Hollow tree	Hollow tree
Bellevue, Ia.	Wood fire (?)	Farmhouse	Edge of house
Mandan, N. D.	Shoveling pigeon excreta	Schoolhouse	..

TABLE 3

Attack Rates in Seven Epidemics of Histoplasmosis Among Those Persons Intimately Associated with the Activity at the Point Source Incriminated As Being the Mode of Infection

Place	No. with Signs or Symptoms	No. Intimately Exposed	Attack Rate Per cent
Plattsburg, N. Y.	19	21	90
Gruber, Okla.	29	30	97
Kansas City, Mo.	6	6	100
Foreman, Ark.	25	25	100
Detroit Lakes, Minn.	6	6	100
Bath, Ill.	2	2	100
Mandan, N. D.	4	4	100

belfry in Warrenton, N. C.; another, to be reported by Woodward,¹⁷ involved four brothers in a farm family who had recently cleaned manure out of a barn on a farm near Taneytown, Md.; and the third which has been studied by Englert¹⁸ involved three men who scraped bat dung from a bridge in Maryland.

Although attention is much less likely to be attracted, single cases of disseminated *Histoplasma pneumonitis* occur with stories of infection similar to the epidemics. We have studied two such cases: one in which a farmer became ill following cleaning pig manure from a barn, and the other in which a soldier was infected while cleaning debris from a chicken coop. *Histoplasma* was isolated from the chicken coop.

Attack Rates—The calculation of attack rates is possible in seven of the

epidemics where the number of persons exposed to a definitely incriminated common source is known. If only the persons intimately associated with the activity at the point source are considered, the attack rate in each of these epidemics is 90 per cent or above (Table 3).

Severity of Disease and Extent of Exposure—Although there was a remarkable similarity in the type of clinical and x-ray picture observed in all the epidemics, considerable variation was found in the severity of disease among the individual patients. It was possible to show in many of the epidemics that both the severity of symptoms and the number of lung lesions had a direct relation to the length or intensity of exposure to the point source.

On the basis of all-over severity the epidemics can be divided into more

TABLE 4

Comparison of the All-Over Severity of Each Epidemic of Histoplasmosis with the Extent of Enclosure of the Point Source of the Epidemic

<i>More Severe Epidemics</i>		<i>Less Severe Epidemics</i>	
Plattsburg, N. Y.	Enclosed	Crowder, Mo.	?
Gruber, Okla.	"	Topeka, Kans.	Partially open
Cincinnati, Ohio	"	Williamsburg, Kans.	?
Detroit Lakes, Minn.	"	Kansas City, Mo.	Open
Bath, Ill.	"	Foreman, Ark.	Mostly open
Mandan, N. D.	"	Madison, Wis.	Open
		Bellevue, Ia.	?

severe and less severe groups. These groups can be seen in Table 4, along with an evaluation of the extent of enclosure of the point sources. A correlation between the intensity of exposure and the severity of the epidemic is suggested by the finding that infection in the more severe epidemics occurred in closed places.

Animal Illness—In all the epidemics investigated an effort was made to obtain information regarding any illnesses in animals. There had been occasional disease in the animals of the various farms involved but nothing suggestive of being histoplasmosis. Skin testing of the animals on two of the farms shown to be sources of human infections was carried out. Two cows of 10 tested on the Williamsburg, Kans., farm were positive to histoplasmin. In addition, one of two dogs reacted. The three reacting animals were autopsied but showed no findings of active histoplasmosis. At the Bellevue, Ia., farm seven of 19 cattle reacted positively to histoplasmin. Only one other reactor was found in the same county out of 187 cows tested.

Approximately half of the common sources of the epidemics were definitely noted to be associated with animal excreta. Careful search in the other cases, where an exact source was known, failed to reveal evidence of animal contamination; however, the possibility of such could not be ruled out, since in many cases the point sources were examined a number of years after the occurrence of the epidemic.

Environmental Observations—Studies have shown that *H. capsulatum* requires very high humidity for growth in soil under laboratory conditions.¹⁹ Measurements of temperature and humidity in one open and one closed point source have been made. Humidity recordings obtained from inside the Camp Gruber storm cellar showed readings of over 95 per cent at least once a day for five consecutive days. The temperature ranged between 70° and 80° F. on those days. Records were taken over a 14-day period in the wooded area outside Madison, Wis. The humidity was above 95 per cent at some time during all 14 days, and for five consecutive days remained above 95 per cent for all but 15 hours. The temperature ranged from 47° to 76° F. during the two-week period.

General observation of the other known exact point sources revealed evidence of frankly moist areas with the suggestion of the possibility of high humidity.

Attempts to show consistent association of the common sources with various climates or vegetation have been unsuccessful. The finding of rough wooded areas on the farms and Army camps involved and near the Arkansas cave deserves mention.

Location of Epidemics and Endemic Areas of Histoplasmosis—The location of the epidemics of histoplasmosis in relationship to histoplasmin sensitivity areas appears in Figure 2. Only three of the epidemics occurred in the area of greatest endemicity of histoplasmosis as shown by histoplasmin sensitivity. Some

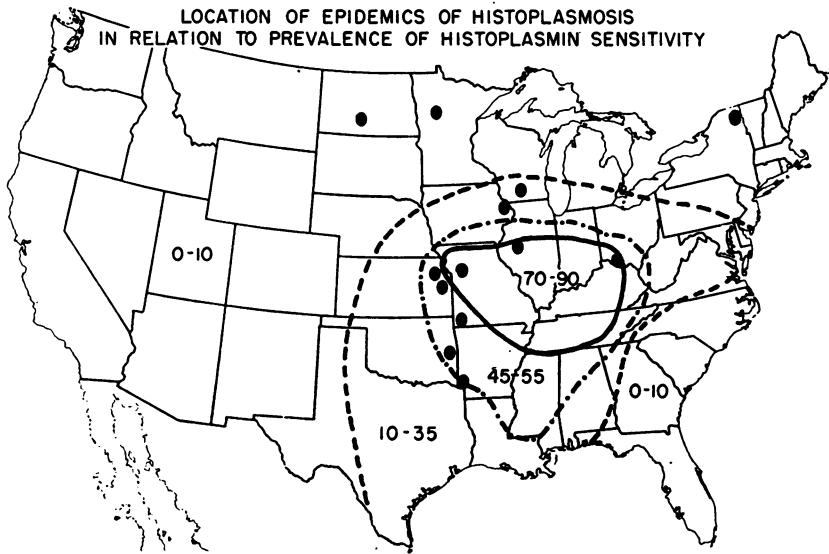


FIGURE 2—The areas of histoplasmin sensitivity are shown schematically by the approximate per cent of young adults reacting to histoplasmin

of the epidemics occurred in areas of low histoplasmin sensitivity. In addition, it was found that all the soldiers involved in the two Army camp epidemics came from states with low prevalence of histoplasmin reactors.

In attempting to determine the probability of previous *Histoplasma* infection in those persons involved in the epidemics on the basis of the distribution of histoplasmin sensitivity, it is necessary to consider the ages of the individuals as well as their residences. The prevalence of histoplasmin reactions in children may be much lower than adults in the same area. The involvement of children in many of the epidemics occurring in areas of relatively high histoplasmin sensitivity would, therefore, add to the impression that persons involved in epidemics of histoplasmosis tend not to have had previous exposure to the fungus. This impression gains support from the data available in the Kansas City, Mo., epidemic. Skin test conversion was demon-

strated on one of the adults, and, in addition, due to routine skin testing of school children it was known that three of the children involved in this epidemic failed to react to the histoplasmin skin test two months prior to their illnesses. A major exception exists to this conclusion regarding previous exposure in the Cincinnati, Ohio, epidemic. Cincinnati is an area of extremely high prevalence of histoplasmin reactors. Some of the 12 adult men involved in this epidemic most certainly had previous histoplasmosis infections.

DISCUSSION

With the exception of the generalized variety, histoplasmosis is predominantly a pulmonary infection. It has been speculated that the usual mode of infection is by inhalation of the organism. This theory gains powerful support from the nature of the disease and apparent mode of infection in the series of epidemics herein discussed. The recurring story was found of exposure to dust

created by agitation of material proved to contain *Histoplasma* spores, resulting after from one to three weeks in illness associated with numerous discrete pulmonary infiltrations. A correlation between the number of the lesions and the severity of the illness on the one hand and the length and intensity of the dusty exposure on the other was established both between epidemics and within a given epidemic. The x-ray picture of numerous discrete pulmonary infiltrations would appear to represent numerous primary lesions caused by inhalation of a large number of spores with their deposition in many alveoli. The possibility of such deposition has been supported by the finding that the size of the majority of the *Histoplasma* spores is under 5 microns.²⁰

Age, sex, and possibly immunity seemed to exert much less effect on the immediate disease picture than did extent of exposure. However, these factors apparently played a role in the development of complications and of generalized disease. The only fatality in the entire group occurred in an infant, and the only other cases exhibiting the generalized form of the disease were two older men.

Environmental studies fail to reveal complete consistency in the nature of the point sources of the epidemics or in the type of material containing the organisms. The frequent association with animal excreta is of interest. However, no evidence of animal contamination of the source material could be found in nearly one-half of the outbreaks. It seems likely that the excreta may merely have contributed to a good growth condition for the organism rather than indicating an animal carrier. The involvement of wood as a vehicle of infection in four of the epidemics further emphasizes its position as possibly important to the growth of *Histoplasma* in nature. It is recalled that sawdust was prominently incriminated

in the previously reported Lowell, Ind., epidemic.³ The requirement of the organism for high humidity for growth in nature was apparently met at the point sources without precluding sufficient drying of the material to permit it to become air-borne when agitated.

Information gathered from laboratory histoplasmosis infections²¹ has shown that although infection continues to occur among newly introduced histoplasmin-negative individuals, previously infected persons have not had second illnesses. This would indicate that infection with *Histoplasma* whether of clinical significance or not, provides resistance to reinfection. The findings in 12 of the 13 epidemics are consistent with this view. On the basis of place of residence and age of the persons involved in 12 of the epidemics there seems little chance that they had had previous histoplasmosis infections. The Cincinnati, Ohio, epidemic was an exception. It seemed most likely that many of those involved in this epidemic had previous infection. It would appear that although the usual epidemic would involve susceptible histoplasmin-negative persons, heavy exposure in persons with previous infection is capable of causing illness. In this connection it is of interest that the pulmonary x-ray picture of the Cincinnati patients exhibited a possible difference from that seen in most of the other epidemics in that the individual discrete lesions were smaller and there was an absence of hilar reaction.^{10c}

SUMMARY

The epidemiologic features of 13 epidemics of histoplasmosis are presented. The common source nature of each outbreak is established. Description of the activities at the point sources and the clinical features of the illnesses lead to the conclusion that infection occurred through the inhalation of air-borne organisms. The presence of *Histoplasma*

in the soil material at the point sources of most of the epidemics was demonstrated. Environmental studies, including animal illnesses, failed to establish any consistent factors at all the common sources of infection. Evidence of the role of previous infection as indicated by histoplasmin sensitivity in creating immunity to further histoplasmosis is discussed.

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