## CENTER FOR DISEASE CONTROL



## SURVEILLANCE

Report No. 2 July 1971



# PREFACE .

The information presented here is intended primarily for use by those responsible for disease control activities. Much of the information is preliminary. Anyone desiring to quote this report should verify the information at its original source for confirmation and interpretation.

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#### I. INTRODUCTION

During 1970, human plague was detected in 13 persons from three western states. All but one survived the infection, although two were not diagnosed until after the acute phase of their illness. The single fatality (case 13, Table 1) did not seek medical help until the fifth day of illness, six hours before he expired. One of the two persons who survived without a specific diagnosis (case 10, Table 1) had received specific antibiotic therapy for plague with a clinical diagnosis of tularemia. The other (case 4) received only penicillin and recovered without benefit of specifically effective antimicrobial therapy. Both of these cases were detected retrospectively by screening suspect tularemia cases for evidence of serum antibodies to Yersinia pestis and are discussed in detail below.

The 1970 plague cases constitute the largest annual number of reported human infections contracted from wild animal sources, as well as the largest number of human cases since the urban rat-borne epidemics prior to 1925. The past year concludes a decade of unprecedented numbers of human infections in the United States (Figure 1). Human plague cases by decade beginning in 1931 numbered 11, 11, 9, and 41; fatalities in these four decades were 5 (45 percent), 6 (55 percent), 4 (44 percent), and 8 (20 percent), respectively. Figure 1 also reveals that, whereas 80 percent of human cases were reported from the Pacific States from 1925 to 1950, the Mountain States have accounted for 90 percent of human infections in the past two decades. California and New Mexico have reported the majority of cases.

## **II. SURVEILLANCE**

#### A. Human Plague

The listing of human cases reported in 1970 (Table 1) reveals that the age, sex, season, and source of infection is comparable with previous years (see *Plague Surveillance Report* Number 1, July 1970). One notable exception was a 2½-month-old infant, one of the youngest reported patients with bubonic plague in this country. In the past, plague infection has been

associated with small wild mammal sources contacted during recreational or occupational activities in rural or natural areas. In 1970 the probable or known source of infection in eight of 13 cases was associated with the immediate home environment and day-to-day activities. There appears to be an increasing trend in many western states to develop housing areas with little disturbance of the native habitat. Retention of native habitat results in the maintenance of at least some of the native small mammal populations and their fleas, which together serve as sources for plague infections. This trend in building is notable in north-central New Mexico and California areas.

#### **B.** Animal Plague

In addition to the 13 humans discussed above, evidence of Y. pestis infection was detected in 16 specimens from rodent, rabbit, and carnivore tissues, 112 pools of fleas, and 101 sera from rodents and carnivores (Tables 2 and 3). Evidence of plague activity was discovered in 6 western states (Figure 2). Among rodents collected in the Rocky Mountain region, deer mice (Peromyscus maniculatus) most frequently displayed evidence of plague infection; in coastal California, meadow mice (Microtus californicus) were most frequently involved; and in montane California, chipmunks (Eutamias sp.) were the most common rodents infected.

Human plague cases in the Sierra-Cascade region of California and in northern Oregon heralded the reappearance of rodent plague in these areas. The northern Oregon case was the first such occurrence in that state since 1934. The first evidence of plague in west Texas since 1949 was discovered in July 1969 when prairie dog carcasses submitted by the Division of Wildlife Services, U.S. Fish and Wildlife Service, were found positive by fluorescent antibody staining. A die-off of prairie dogs in an adjacent area was reported in 1970 by the Division of Wildlife Services and confirmed by isolation of Y. pestis from five flea pools. Early in 1971, plague infection in two pools of rat fleas was detected in Tacoma, Washington, after a lapse of 17

years. The increased incidence of human plague as well as the evidence for renewed geographic expansion of wild rodent plague marks 1970 as the year of most intense plague activity since 1925.

Rodents, primarily *Rattus* sp. arriving in United States ports on ships and aircraft originating from actually or potentially plague-infected areas were intercepted by Foreign Quarantine, U.S. Navy, and U.S. Air Force and were tested for plague at the Fort Collins Laboratories. All were negative for *Y. pestis.* 

# III. RESEARCH, INVESTIGATIONS, AND TECHNIQUES

#### A. Surveillance Brochure

A brochure has been developed for use by interested observers including not only local and State health agencies, but wildlife personnel, ranchers, and others who may be in a position to note and report unusual phenomena among small mammal populations suggestive of plague or other disease activity. The brochure briefly describes the problem and need for such surveillance, including background information on plague in the United States and methods for submitting suspect materials to be tested for *Y*. *pestis* infection. This brochure is available to state agencies and is intended for use primarily in the western states where plague is enzootic.

#### B. Carnivore Sentinels of Plague

One aspect of the nature of plague which needs to be defined concerns its temporal and spatial manifestations among wild mammal populations. Further knowledge concerning ecologic factors and geographic distribution, especially a reexamination of the eastern boundary of known plague occurrence, is highly desirable.

Serologic methods provide the most efficient survey tool available for this purpose because such methods, when properly utilized and interpreted, provide a recent history of plague in any given area. However, the extensive surveys necessary to gain substantive ecogeographic information require prohibitive field and laboratory work loads to trap, bleed, and test the sera of rodent reservoirs of plague. In 1970, 2,311 rodent sera were tested; 3 percent were positive. The total rodent sample was biased toward positive results by the inclusion of many samples from areas suspected of recent plague activity. Of 143 carnivorous mammals tested from similar areas during the same period, 24 percent were positive for *Y pestis* antibodies.

In a pilot study by the Zoonoses Section carried out in Larimer and Weld Counties, Colorado, the sera of wild carnivores produced ten positives from 39 animals. Seropositive species included five raccoons, one weasel, two feral housecats, one coyote, and one bobcat. Titers ranged from 1:32 to 1:4096. Thus, although the trapping and bleeding of individual wild carnivores requires far greater effort than with rodents, the likelihood of finding evidence of *Y. pestis* infection in their sera is considerably greater than with rodents. This preliminary investigation demonstrates the potential value of wild carnivores as sentinels of plague activity.

Efforts are being made to enlist the aid of agencies and investigators working with wild carnivores in the western states in carrying out more widespread and comprehensive serologic surveys of plague ecogeography. In order to reduce the time and effort necessary to collect blood samples from carnivores collected by personnel of cooperating agencies, the filter paper collection technique has been tested and found successful for plague antibody detection. Blood samples are taken on Nabuto's filter paper strips, air-dried, and mailed with data to the laboratory. This technique eliminates the need for syringes, tubes or vials, and the process of serum separation. Agencies interested in collaborating on such studies should contact the Zoonoses Section, Ecological Investigations Program, Post Office Box 551, Fort Collins, Colorado 80521.

## C. Temperature Effect on Plague Transmission by *Xenopsylla cheopis*

Experimental work done by Dr. Dan C.

Cavanaugh, Walter Reed Army Institute of Research, concerning the influence of temperature of the oriental rat flea (Xenopsylla cheopis) on its ability to transmit plague (1) was reported at the Fort Collins plague seminar (See IV below). At lower temperatures, enzymes in the flea's gut, produced by the plague organism as well as by the flea's stomach, act as fibrinforming coagulants; whereas at higher temperatures (27°C. or higher) another enzyme from the plague organism and the same enzyme from the stomach of the flea will act to lyse the coagulum. In a country such as Vietnam, certain regions have median temperatures above 27°C. most of the time while other areas have lower temperatures at least part of the year. Occurrence of plague in humans appears to be associated geographically with cooler temperatures, and it is hypothesized that the blocking rate in fleas is lower when the fleas are above ground in the warmer areas, spontaneously reducing transmission to humans. Thus, in northern areas of Vietnam, plague may be more closely associated with the cool, wet season rather than the warm, dry season, although the dry season has always been associated with large numbers of fleas. Experimental evidence of comparable mechanisms in fleas other than X. cheopis is not available.

### D. Ectoparasite Control Studies

Current investigations supported by Walter Reed Army Institute of Research, and conducted by the New Mexico State Department of Health and Social Services on plague ecology and control were presented at the Fort Collins plague seminar (see IV below) by Mr. Bryan Miller. Systemic insecticides are being tested for the control of ectoparasites and preliminary data are encouraging. Further work must be done to determine the maximum effective dosage that will not result in avian or mammalian mortality or serious toxicity.

One problem in rodent-ectoparasite control is avoidance of bait containing sufficient levels of this chemical to kill fleas. Current New Mexico studies involve screening for chemicals that will reduce flea or rodent populations for a prolonged period while leaving minimal or transient residual pollutants. Another technique of promise, being investigated in collaboration with the U.S. Department of Agriculture, Gainesville, Florida, is the use of a volatile insecticide in a bait which the host will store in its nest, resulting in fumigation of the nest or burrow.

#### E. Retrospective Detection of Misdiagnosed Human Plague

California, Colorado, and Wyoming State health departments responded to a request for samples of human sera submitted to them for serologic diagnosis of suspect tularemia. The states sent 44, 3, and 24 human serum samples, respectively, 48 of which were from 1970. Antibody against fraction 1 of Y. pestis was evidenced in two persons, resulting in the detection of cases 4 and 10 in Table 1. One patient (case 4) was sent to a Denver hospital because of a lingering, undiagnosed illness. This patient's secondary illness was diagnosed as histiocytosis X; a causal relationship between this disease and his earlier infection with Y. pestis could not be established. The patient had a passive HA titer of 1:4,000 to fraction 1 of Y. pestis and a bacterial agglutination titer of 1:80, indicating a recent plague infection (2). The other patient (case 10) was a 10-year-old girl from California with onset of symptoms accompanied by axillary lymphadenitis on August 10. Fortunately, paired sera had been submitted for tularemia studies, and plague was confirmed serologically. The finding of two previously unsuspected cases of plague among 48 persons being tested for tularemia in 1970 is an important development. Expansion of this program for testing undiagnosed suppurative lymphadenitis cases may lead to the discovery of additional cases of plague.

### F. Analysis of Geographic Variation in Y. pestis

The plague organism may be differentiated into various recognizable groups and subgroups which may be associated with geographic distribution<sup>(3)</sup>. In some cases they may also be associated with virulent and nonvirulent "strains" or "types" routinely maintained in some laboratories. Antigens, production of enzymes, and various protein components are being identified and studied in an effort to establish clearer classification of geographic or host variations in the plague organism. Seventyeight isolates of the plague bacillus from geographic areas as widely separated as North America and Asia have been studied for quantitative variation in the production of proteins. Significant differences between plague isolates from different geographic areas were detected by acrylamide gel electrophoresis. Notable differences exist between certain groups of Y. *pestis* isolates from Java, the Burmese/ Vietnamese complex, and North America. The ability to determine the geographic origin of strains of plague may provide knowledge, for example, on whether the appearance of plague in a port city is an exogenous introduction or of local or regional origin. An application of this technique provided support to the conclusion, based on epidemiologic study, that the recent plague-positive rat flea pools from Tacoma were not introduced from South Vietnam (see below).

# G. Disseminated Intravascular Coagulation in in Severe Plague Cases

Lieutent Thomas Butler, M.D., Naval Medical Research Unit Number 2, Taipei, Taiwan, met with Zoonoses Section personnel to discuss clinical studies he is conducting on human plague. A series of sera from these cases was submitted to the Section to be examined for antibodies to Y. pestis. Dr. Butler's studies should make a significant contribution to the understanding of the pathogenesis of human plague. Of particular interest was his observation that severely ill plague cases showed evidence of disseminated intravascular coagulation (DIC)(4). This finding was based on lowered platelet counts, lowered serum fibrinogen, prolongation of prothrombin time or partial thromboplastin times, skin biopsy, and the ethanol gel test. Other patients, not as severely ill, also had some evidence of DIC. His findings are consistent with the clinical and pathological observations that severely ill or terminal plague patients have an intravascular coagulopathy suspected to result from Y. pestis endotoxin. Though unproven, it

is hypothesized that such an effect may be exaggerated in septicemic cases by excessive doses of bactericidal drugs such as streptomycin<sup>(5)</sup>. Dr. Butler saw no such effect from streptomycin therapy, but the doses of streptomycin used on his series of patients was in accordance with recommendations<sup>(6)</sup>

#### H. Eastern Fox Squirrel (Sciurus niqer) Population Studies

Followup ecological studies of eastern fox squirrel populations in eastern Colorado indicate they do not form an unbroken population chain along the river bottoms. Therefore, it is concluded that there is little possibility that these squirrels would transport plague into previously uninfected areas, including the eastern United States, as was initially considered and noted in *Plague Surveillance Report* Number 1 (July 1970). Limited plague epizootics among tree squirrels, such as occurred in Denver, Colorado, in 1968<sup>(7)</sup> should be expected and sought in urban or densely wooded areas where squirrel populations are high.

#### I. Rodent Plague in Tacoma, Washington, 1971

Two flea pools from Norway rats captured in south Tacoma in January 1971 were bacteriologically positive for plague. An intensive surveillance program involving the processing of several thousand fleas annually from Tacoma has been conducted since a major rat epizootic occurred there in 1942 through 1943(8). The last Y. pestis detected in this surveillance was a single isolate made in November 1954. The first plague-positive pool this year was obtained during the routine trapping program; the second positive was obtained during studies to determine the intensity and geographic extent of plague activity. The followup investigation revealed that the rat population appeared to be too scattered and discontinuous to support an extensive epizootic. No additional plague isolations have been made.

Epidemiologic and special plague strain typing techniques (see III-F above) supported the thesis that the source of infection was an extension from rural wild rodent plague indiginous to the United States rather than an exogenous introduction through international traffic. In fact, the isolates were made from fleas taken from Norway rats captured in south Tacoma, an area supporting a scattered, diffuse Norway rat population intermingled with wild rodents. A survey of the commercial and port areas of Tacoma revealed minimal rat populations. All specimens submitted from port and more densely urbanized areas of Tacoma were negative for plague.

The involved area of south Tacoma was mixed residential and commercial with small, older houses on large lots interspersed with undeveloped areas and vacant lots. Rodent harborage was abundant and consisted of blackberry thickets (*Rubus* sp.), unoccupied buildings, and trash piles. Norway rat burrows usually were associated with blackberry thickets and trash accumulations rather than occupied buildings. Rodent food sources were few. Commingling with Norway rats were deer mice (*Peromyscus maniculatus*), house mice (*Mus musculus*), meadow mice (*Microtus oregonus*), and an occasional black rat (*Rattus rattus*).

The second positive flea pool consisted of one northern rat flea (*Nosopsyllus fasciatus*), the predominant flea species taken in this investigation. Fleas from the first positive pool were not identified; however, spot checks over several years of surveillance have revealed the northern rat flea to be the predominant flea present in the area. No oriental rat fleas (*Xenopsylla cheopis*) have been taken in this area in recent decades.

Dr. M. Baltazard, a World Health Organization observing consultant on plague, was present during the early phase of the followup investigation. He participated in the evaluation of the findings and assisted in planning the followup investigation.

#### IV. PLAGUE SEMINAR, FORT COLLINS, COLORADO, OCTOBER 5-7, 1970

A 3-day seminar on plague was held to exchange information and discuss the future of plague

research in this country. In addition to the Center for Disease Control staff, participants in the seminar, listed in the appendix, included M. Bahmanyar, Institut Pasteur de L'Iran, Teheran, and representatives from five western states, the University of Maryland, Colorado State University, and the Walter Reed Army Institute of Research.

The critical ecologic factors potentially involved in the maintenance of plague were considered to be, at best, poorly understood. Among those needing investigation are (1) population densities of reservoirs and vectors in relation to disease transmission; (2) environmental stress among rodent reservoir species and its importance to disease occurrence, amplification, and transmission; (3) nutritional status of reservoir populations in relation to susceptibility or resistance to disease; and (4) the importance to plague epizootiology of such factors sociality, territoriality, home range, breeding cycles, population structure, and individual life span of involved species. It was acknowledged that while intensive ecologic studies have been or are being conducted on animal populations by various agencies, few have included consideration of the interaction of infectious agents.

Plague infection in the flea, particularly changes in the agent after the flea imbibes a blood meal containing the plague organism or plague antibodies, was discussed. The effects of circadian rhythms and of micro-and macro-climate temperatures were concluded to be significant factors in the transmission potential of the flea. Dr. Bahmanyar summarized the conclusions of the meeting as follows:

The western United States has such diverse habitats, and so many species of rodents and fleas are involved with plague, that study is usually more difficult and complex than in most other countries where fewer hosts and habitats are involved. Many gaps remain in the knowledge and understanding of the occurrence of the infection in these circumstances.

The mechanisms of carryover or maintenance of plague (primary focus) in one area and of

introduction into another area still remain to be clarified. It has been observed that animals may die of plague after hibernation. In other areas where plague is present among non-hibernating rodents, other methods of maintenance must be investigated. Resistance and susceptibility are important factors to define as they relate to maintenance of plague or to epizootic plague.

It is suspected but not proved that the plague organism may persist in the soil for 10 to 20 years with no evidence of mammal or flea infection. Fleas also may play a role in shortterm maintenance, some living in the favorable climate of deep burrows for up to 2 years.

Dr. Bahmanyar concluded by saying it is imperative that the United States assume a leadership role in long-term plague studies, especially in cooperation with the World Health Organization.

#### V. INTERNATIONAL NOTES

#### A. World Plague

During 1970, provisional totals of 3,379 human cases and 73 human deaths due to plague were reported to the World Health Organization from countries in Africa, Asia, and the Americas. A summary of cases and deaths, by major political subdivision within each reporting continent, is presented in table 4.

The Republic of Vietnam was the principal location of reported plague in the world in 1970, accounting for 94 percent of plague cases and 74 percent of plague deaths reported. These provisional data for 1970 reflect a continuing pattern in the geographic distribution of reported plague which began in the middle 1960's (Table 5).

#### B. Surveillance of Retrograde Cargo from Vietnam

The Retrograde Cargo Preclearance Program, reported in *Plague Surveillance Report* Number 1, 1970, has proven effective in preventing the entry of potentially plague-infected rodents and ectoparasites from South Vietnam. The program, jointly operated by the Foreign Quarantine Program, CDC, the Plant Quarantine Division, U.S. Department of Agriculture, and the Department of Defense, is designed to inspect and pretreat ships, aircraft, and military cargoes for disease vectors and agricultural pests and diseases prior to their departure from South Vietnam. From January 1970 to January 1971, 497 ships and 6,795 aircraft with their cargoes were precleared under the program. Check inspections in the United States have resulted in the interception of 11 rodents during the same time period, eight of which were Rattus exulans. a species not presently established in the United States except in Hawaii (9).

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## APPENDIX

## PLAGUE SEMINAR PARTICIPANTS

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## TABLE 1 HUMAN PLAGUE CASES IN THE UNITED STATES - 1970

Case						
No.	Age	Sex	Onset	Adenopathy	History of Contacts and Probable Exposure	Place of Contact
1	39	М	16 May	Left inguinal	Hunted 10 May with no contact with wild mammals	Vicinity of Cochiti Pueblo area, Sandoval County, New Mexico
2	8	М	30 May	Left supra- clavicular, bi- lateral femoral	Camped amid an epizootic at Burney Falls, handled a dead <i>Spermophilus beecheyi</i> at Baum Lake; positive flea pool from latter site	Burney Falls State Park or Cassel Baum Lake, Shasta County, California
3	13	М	7 June	Right inguinal	Around house 5 days prior to onset; 3 household pets (2 dogs, 1 cat) found positive, suggesting nearby plague epizootic	Lyden, Rio Arriba County, New Mexico
4*	1/5	М	11 June	Post-auricular	Cat brought dead rodent into house prior to onset	Toadlena, San Juan County, New Mexico
5	16	М	26 June	Right inguinal	Worked for Forest Service cleaning camp sites	Canoncito, Bernalillo County, New Mexico
6	45	М	7 July	Right femoral	Positive chipmunk and seropositive dog from near home; visited Burney Falls only 20 minutes	Probably home at Big Springs, Lake Alamnor, Plumas County; possibly Burney Falls State Park, Shasta County, California
°7	7	F	12 July	Left inguinal	Two dead field mice seen, one fed to kitten, not touched by patient; fleas in living quarters (1 <i>Ctenocephalides felis</i> identified)	Stone Mountain Commune, 6 m. N., 3 m. E., Lindrith, Rio Arriba County, New Mexico
8	20	F	7 Aug	Left inguinal	Slept with dog which captures rodents, insect bites on body	Northern Santa Fe, Santa Fe County, New Mexico
9	9	F	19 Aug	Left anterior cervical	Dogs and cat frequently brought dead rodents and rabbits into house where they were handled by patient	Rio en Medio, 10 m. N. Santa Fe, Santa Fe County, New Mexico
10**	10	F	20 Aug	Left femoral	Hiked in Big Pine	Big Pine near Palisade, Glacier, Inyo County, California
11	15	М	15 Sept	Left axillary	Cleaned rental cabin 9-10 Sept, dead <i>Peromyscus</i> nest and hole in floor found; camped with Scout troop, insect bites on body	Tijeras, Bernalillo County, New Mexico
12	34	F	16 Sept	Right axillary	Cleaned rental cabin, insect bites on right upper arm	Tijeras, Bernalillo County, New Mexico
13	49	М	14 Nov; Expired 18 Nov	Right axillary	Cleaned, cooked, and ate cottontail rabbit along with 2 companions; patient eviscerated animal, one companion skinned animal	Near Imnaha, Wallowa County, Oregon

\*Pestis minor; this infant recovered without specific antibiotic therapy. \*\*Retrospective serologic and epidemiologic diagnosis.

## TABLE 2

## SPECIMENS EXAMINED FOR PRESENCE OF <u>Yersin a pestis</u> BY THE ZOONOSES SECTION, 1970

Submitting State		Mammals		Ectoparasites				
or Agency	Examined Positive		% Positive	Examined	Positive	% Positive		
Indian Reservations								
(Arizona and New Mexico)	96	1	1	9,575	104	1		
Other 25 Projects	15	0	0	3,985	1	0.03		
California	142	14	10	8,643	0	0		
Colorado	94	1	1	934	2	0.2		
New Mexico	154	0	0	137	0	0		
Oregon	2	0	0	251	0	0		
Texas	5	0	0	243	5	2		
Washington	1	0	0	16,894	0	0		
U.S. Air Force, Navy, and								
Quarantine Service*	16	0	0	134	0	0		
Totals	525	16	3	40,796	112	0.3		

\*Rodents from ships and airplanes returning from overseas.

## TABLE 3

## SEROLOGICAL TESTS FOR EVIDENCE OF Yersinia pestis INFECTION

## PERFORMED BY THE ZOONOSES SECTION, 1970

Submitting Agency		Sorex			Human		Rodent		Carnivore			Lagomorph			Other			
		No. Pos.	% Pos.	No. Test	No. Pos.	% Pos.												
New Mexico State Health Dept.				61	16	26	500	10	2	34	9	26	2	0	0			
California State Health Dept.				55	6	11	328	23	7	6	1	17						
Other State Health Depts.				38	1	3										1	0	0
USPHS Hospitals, Foreign Quarantine, Aerospace Medical Group, and others				21	9	43	4	0	0	7	7	57				46	0	0
Naval Medical Research Unit No. 2				• 93	22	24												
Zoonoses Section Activities:																		
Fort Collins Laboratories				163	4	2	723	3	0.4	64	12	19	4	0	0	9	0	0
San Francisco Field Station	14	0	0				719	30	4				1	0	0	1	0	0
Window Rock Field Station				1	0	0	37	0	0	32	9	28	1	0	0			
Totals	14	0	0	432	58	13	2311	66	3	143	35	24	8	0	0	57	0	0

5800 1432 1480 13 184

## TABLE 4

## HUMAN PLAGUE BY GEOGRAPHIC AREA AS REPORTED TO THE WORLD HEALTH ORGANIZATION, 1970

	Cases	Deaths
AFRICA		
Congo	12	_
. Malagasy Republic	10	3
AFRICA TOTAL	22	3
ASIA		
Burma	42	3
Indonesia (Java)	14	3
Vietnam	3162	54
ASIA TOTAL	3218	60
AMERICAS		
Brazil	55	
Equador	26	1
Peru	45	8
United States	13	1
AMERICAS TOTAL	139	10
WORLD TOTAL	3379	73
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#### TABLE 5

## HUMAN PLAGUE CASES AND DEATHS REPORTED TO THE

## WORLD HEALTH ORGANIZATION 1965-1970

	١	/ietnam	Wor	ld Total
Year	Cases	Deaths	Cases	Deaths
1965	374	40	1324	61
1966	353	26	1318	47
1967	5574	246	5930	271
1968	779	37	1472	146
1969	616	27	1165	63
1970*	3162	54	3379	73

\*Provisional total

## FIGURE 1

HUMAN PLAGUE CASES IN THE UNITED STATES BY YEAR – 1925 TO 1970



13

YEAR

### FIGURE 2

