Plaque

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Plague always has been one of mankind's worst enemies. As a pestilential disease, it can be traced back uninterruptedly to the third century before the Christian era when Dionysius spoke of it as a fatal disease in Libya, Egypt, and Syria. Prior to that time, Homer described plague among the Greeks at the siege of Troy in 1184 B.C., ascribing it to the wrath of Apollo who was angered at an insult to his high priest Chryses, and also to the god's malevolence and disgust at the filth lying about the camp. Probably the earliest known reference to plague occurs in the First Book of Samuel, Chapters 5 and 6, where mention is made of the disease having broken out in Canaan during military operations against the Israelites centuries before the Christian era. It is stated that the inhabitants of several cities were attacked with emerods, and that the pestilence caused a deadly destruction. In Bethschemesch, over 50,000 persons died. It also is recorded that in order that the plague might be stayed, the Philistines made propitiatory offerings of golden images of their tumors and of the mice that marred the land to the God of Israel. This appears to be the earliest reference to an epizootic among mice in connection with the disease.

Rufus of Ephesus, about 100 A.D., probably gave the first description of plague which has been preserved. The first recorded plague epidemic in the world's history occurred in the reign of Marcus Aurelius 164-180 A.D., the second, in Egypt in 542. The Great Plague of Justinian in the sixth century is said to have carried off half the population of the Roman Empire.

In the fourteenth century, a new European epidemic began which became known as the Black Death. It is estimated that it killed one-fourth of the population of Europe, or about 25 million persons. In some countries, however, the total deaths approximated 70 percent of the inhabitants. Plague continued to hold sway in Europe during the fifteenth, sixteenth, seventeenth, and eighteenth centuries, but seems to have disappeared by the middle of the nineteenth century. The present pandemic, which began in the Orient in 1894, has had the most widespread distribution of any of the known epidemics. It has invaded every continent of the world, and has been reported from nearly every country. India has suffered the most with about 12 million deaths reported in the last 54 years. Although the mortality rate per world population does not approach that of the Black Death of the fourteenth century, the present pandemic ranks alongside the most important previous ones as far as the total number of cases is concerned; and far exceeds all others in regard to its widespread distribution (table 1).

The New World was invaded by plague at Asuncion, Paraguay, in April 1899. Since that time there have been about 60,000 cases reported in North and South America. About 98 percent of these have occurred in South America. Although nearly 900 cases have been reported in Mexico, these occurred in two sharp outbreaks in 1902-3 and 1920-22, and there is no reason to believe that any endemic foci exist in either domestic or wild rodents.

While the United States is second in North America from the point of view of total cases reported, it is first in importance from the over-all viewpoint because of the existence of a tremendous endemic reservoir of infection in its wild rodent populations (table 2).

Quarantine officials began to be concerned about the importation of human plague into this country about the time that the present pandemic started. Their fears appeared to be justified when cases of plague were found on three occasions in 1899 and 1900, on board ships arriving at San Francisco, Calif.; New York, N.Y.; and Port Townsend, Wash. Although maritime quarantine was apparently successful in preventing the importation of human plague, little then was known of the role which the rat and its flea played in transmission, and it was inevitable that rodent plague would be imported. There is no available evidence to show when this occurred; but at some time during the last years of the nineteenth cen-

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Year First Repo	orted Location	Year First Reported	Location
1893 1894	Yunnan, China Canton, China		Marseille, France Cardiff, Wales Cape Verde Islands
1896	Formosa Bombay, India Basra, Turkey	1901	Naples, Italy Montevideo, Uruguay Siam
1897 1898	Jiddah, Arabia Osaka, Japan Maritiya, Modegaccar	1902	Mazatlan, Mexico French Indo-China Nairobe, Kenya
	Samarkand, Russia Vienna, Austria London, England	1903	Pisco, Peru Iquique, Chile Algería
1899	Alexandria, Egypt Santos, Brazil French Lyory Coast	1905	Sumatra Panama
	Lorenzo Marquez, P.E. Africa Lisbon, Portugal Bushire, Persia	1906	Liberia Canary Islands Tenerife
	Reunion Island Straits Settlements Paraguay Kolobooka Astrokhan Bussia	1907	Tunisia Trinidad
	Rosario, Argentina Honolulu, Hawaii Cape Town, British South Africa Numea, New Caledonia	1908	Azores Venezuela Ecuador Virgin Islands
	Barcelona, Spain Bairut Suria	1910	Morocco, Casablanca
	Zanzibar	1911	Java
1900	Sydney, Australia Auckland, New Zealand Persian Kuidistan	1912	Cuba Puerto Rico Granada
	Manila, Philippines	1915	Greece
	Glasgow, Scotland San Francisco, U.S.A.	1921	Bolivia
-	Hamburg, Germany	1939	Canada

## Table 1 WORLD DISTRIBUTION OF PRESENT PLAGUE PANDEMIC

tury, infected rats must have left ships in San Francisco harbor and spread plague among the rats of that city. Recognized human cases did not appear until March 1900, although there is some reason to believe that unsuspected cases were occurring as early as 1898. The first San Francisco epidemic lasted for nearly 4 years and accounted for 127 cases, few of which recovered. This epidemic was notable for the fact that there was violent disagreement between the factions who claimed that it was and was not plague. Subsequent epidemics occurred in San Francisco in 1907; in Seattle in 1907; in New Orleans in 1914 and 1919; in Oakland in 1919; in Pensacola, Galveston, and Beaumont in 1920; and in Los Angeles in 1924 (figure 1, table 3). All of these, with the exception of the 1919 outbreak in Oakland which started when a squirrel hunter developed secondary pneumonic plague, took place at a time when domestic rats were involved in an active

### Table 2

- ARGOD UNDED AN ARE NEW HURL	P	LAGUE	CASES	IN	THE	NEW	WORL
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country	Cases	Percent of Total
Peru	21,664	36.5%
Ecuador	11,770	19.8%
Brazil	7,986	13.5%
Argentina	6,889	11.6%
Chile	5,125	8.6%
Bolivia	3,348	5.6%
Mexico	868	1.4%
Venezuela	565	0.9%
United States	503	0.8%
Paraguay	500	0.8%
Puerto Rico Cuba	88	
Trinidad	13	0.5%
Panama	21	
Granada	1	
Canada	IJ	
Total	59,391	100.0%

plague epizootic. The only time in our history when it was known that rats were involved in such epizootics and no human cases arose, was during the period from 1942-44 when the rats of Tacoma, Wash., were involved and over 100 were proved to be infected. At the present time, there is no city in the country where domestic rodents are known to be infected with plague, and active efforts constantly are being made to prevent this from happening.

At some time about the beginning of this century, plague spread from domestic rats in the San Francisco Bay area to the California ground squirrel. Again there is no evidence as to when this might have occurred. The first indication that it was a possibility was in 1903 when human cases were reported in rural Contra Costa County in an area where there were no rats. At that time, it was suspected that the source of the cases might have been from infected wild rodents, and a search was made but none were found. It was not until during the second San Francisco epidemic, in 1908, that infected ground squirrels were found on a ranch in Contra Costa County, where a human



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# Courtesy of the David J. Sencer CDC Museum

### Table 3

COUNT	IES	IN	THE	UNITED	STATE	S IN	WHICH
HUMAN	PLA	GUE	HAS	OCCURI	RED, 1	900-1	1950.

STATE AND County	CASES	DEATHS
California		
Alameda	41	28
Contra Costa	15	13
Fresno	1	1
Los Angeles	42	36
Modoc	1	1
Monterey	2	1
Placer	1	0
San Benito	4	3
San Bernardino	1	0
San Francisco	289	196
San Joaquin	1	0
San Luis Obispo	1	0
Santa Barbara	1	1
Santa Clara	1	0
Santa Cruz	2	0
Siskiyou	4	3
Sonoma	1	0
Stanislaus	2	0
Tulare	1	1
Florida	10	-
Escambla	10	- (
Idano		
Gem	1	1
Colores	51	19
Michigan	51	10
Washtanaw	1	0
Nevada	1	
Douglas		0
New Mexico	5.	Ű
Tage	1	0
Lincoln	1	1
Leo	i i	Ô
Sandoval	ī	0
Oregon		n sev
Lake	1	1
Texas		
Galveston	16	11
Harris	1	0
Jefferson	14	7
Utah		1
Beaver	1	0
Washington		
King	8	8
Total:		
11 States.		
34 Counties	520	338
or Goundaes	020	550

case had died. At about the same time, a boy in Los Angeles was bitten by a squirrel and developed plague. A search for infected squirrels revealed one in the same general area of the city. Because of these findings, a general survey of California ground squirrels was started in April 1909. The disease was found so widespread in the squirrels of Contra Costa and Alameda that the survey was extended to other California counties, and by the middle of 1910 plague foci had been found in 10 of the 25 counties which represented all but the extreme northeastern and eastern range of the California ground squirrel.

In 1911, infected squirrels had been found in so many counties that fears began to be expressed that plague might already have spread to other States, and reconnaissance surveys were made in the counties of Oregon, Nevada, and Arizona which bordered on California. No infected squirrels were found outside of California at that time.

It then appeared that (1) in order to prevent the reinfection of domestic rodents from wild rodent sources and (2) in order to prevent the establishment of endemic foci of plague which would be a menace not only to California cities but to the rest of the country, it was desirable to eradicate plague in the California ground squirrel. The eradication proposal was divided into two major parts: first, a squirrel-free zone would be created around the cities of the San Francisco Bay area in order to prevent the reintroduction of plague into the domestic rodent populations of those cities; and second, rural plague was to be eradicated by the use of every tool known to be effective.

The program was launched as a fairly long-range proposition which might take several years to accomplish. Federal, State, and county funds were provided to carry on these activities. Literally millions of ground squirrels were killed during the years that millions of dollars were poured into this activity. The Public Health Service maintained an active interest in the eradication of plague in ground squirrels until 1936 when it turned over its share of the work to the California State Department of Health. The State of California has continued some type of plague control ever since, although it long since has given up the idea of being able to eradicate plague in the ground squirrel, which never was accomplished.

A second phase in the history of plague among wild rodents began in 1934 when a sheepherder came down with the disease in Lake County, Oreg.

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The following year, a search was made for infected rodents in the same area and plague-infected squirrels were found. This was the first evidence that the wild rodents of any State outside of California were involved. These findings led the Service to concentrate its efforts on determining just how widespread plague actually was in the West.

During the past 14 years, from 4 to 14 mobile survey units have been sent out into the field during the spring, summer, and fall months. These units are field laboratory trucks equipped for hunting and trapping. A two-man crew traps and shoots wild rodents, performs autopsies, and removes ectoparasites from the animals obtained. If the animal's organs appear infected, samples are expressed to the San Francisco laboratory in iced thermos jugs. Here the tissue is macerated and injected into or inoculated onto the skin of a guinea pig. If plague is present, the guinea pig generally dies in about 5 days and a presumptive diagnosis can be made at autopsy. This diagnosis then is confirmed by bacteriological procedures and serological tests. All ectoparasites removed from wild rodents are placed in 2 percent saline in glass vials and shipped to the laboratory in mailing tubes. The ectoparasites are counted, identified as to species, macerated in mortars, emulsified in normal saline, and injected into or inoculated onto the skin of guinea pigs.

Beyond the earlier, historical findings of plague which followed introduction in Texas, Louisiana, and Florida, surveys now have been made in 17 of the westernmost States, and nearly every county west of the 100th meridian has been surveyed one or more times. Over 11/2 million wild rodents and their ectoparasites have been examined, and nearly 4,000 found to be plague-infected. Plague foci have been found in 131 counties of 15 of these Western States. In addition to California and Oregon, plague first was found in the following States in the years given: Montana, 1935; Idaho, Nevada, Utah, and Wyoming, 1936; Arizona, New Mexico, and Washington, 1938; Colorado and North Dakota, 1941; Oklahoma, 1944; Kansas, 1945; and Texas, 1946 (figure 2). Human cases resulting from contact with infected wild rodents have occurred in California, Nevada, Oregon, Idaho, Utah, and New Mexico (figure 1). (The single case in Washtenaw County, Mich., is a laboratory infection.)

The treatment of human plague has been improved greatly in recent years. Formerly, bubonic

#### HANDLING OF ECTOPARASITES



Removing ectoparasites from wild rodents.



Counting and identifying ectoparasites.



Injecting ectoparasites into skin of guinea pig.



plague killed about two-thirds while pneumonic plague was almost invariably fatal. While many types of therapy have been tried, there were but two which were at all effective: serum with which to treat cases, and vaccines to prevent the disease. Serum was fairly effective if given early in large doses. Vaccines have been used on a large scale in various parts of the world, but are not 100 percent effective, and the period of protection is limited to several months. In the late thirties, sulfa drugs were found to be of value in the treatment as well as in the prophylaxis of plague, and sulfadiazine is probably the most efficacious. Streptomycin is an even better drug. A combination of streptomycin and sulfadiazine, if given early enough and in adequate doses, is capable of curing even pneumonic plague (figure 3).

The development of almost specific methods of treating plague has taken away some of the fears which were so justly warranted when this disease struck a community. However, there are still ample reasons why vigilance cannot be relaxed against plague at this time, merely because good methods of treatment now are possessed. Plague still demands respect because of the fact that in 15 of our Western States there is perhaps the largest focus of wild-rodent plague in the world and many species of wild rodents and ectoparasites are known to be involved in the broad spectrum of this disease. The vastness of the area involved makes it impractical even to think about the eradication of plague in these rodents even if one could forget the illuminating story connected with attempts to eradicate plague in the California ground squirrel.

While it appears biologically and economically impractical to eradicate wild-rodent plague, there is no reason why good preventive measures should be neglected. Experience with plague in this country has demonstrated that epidemics usually begin after domestic rodents have become infected and wild-rodent plague becomes important then for two reasons: first, it is a constant potential source for the infection of domestic rodents in urban communities which are located in the vicinity of plague foci; second, it will continue to cause isolated, single, widely scattered cases of human plague. The infection of domestic rodents can lead quickly to human epidemics. The



occurrence of human cases infected by wild rodents does not lead necessarily to epidemics unless the patient develops a secondary plague pneumonia and starts a pneumonic epidemic.

The single cases of human plague of wildrodent origin are handled best by educating physicians to recognize the disease when it occurs and start treatment early. This enhances the possibility of recovery and prevents the development of pneumonic signs.

The prevention of the transmission of wildrodent plague to domestic rodents can be accomplished best, not by efforts directed against wild rodent foci, but by programs of domestic-rodent control. By combating domestic rodents with every possible means, their numbers can be kept down to a point at which they will not be capable of supporting an epizootic of plague. There are effective means of eliminating such epizootics that may occur in domestic rodents: DDT, compound 1080, ratproofing, garbagedisposal methods, and good community housekeeping methods should be able to wipe out a plague epizootic in short order should one chance to gain a foothold. However, an opportunity will be missed if efforts are not made to eliminate the possibility of such epizootics by establishing permanent domesticrodent control programs in all Western cities which are anywhere near known plague foci.

The future program of the Western Communicable Disease Center Laboratory follows these general principles: (1) Surveillance over the eastward spread of plague; (2) Promotion of domestic rodent control programs; (3) Education of the medical profession in early recognition, early diagnosis, and early treatment methods; (4) Continuation of plague research.

At the present time, surveillance over the eastward spread of plague is being limited to the eastern boundary of the known infected territory; that is, to those States which lie between North Dakota and Texas inclusive. Domestic-rodent control is being promoted actively in Washington, Oregon, Idaho, Montana, Colorado, Utah, New Mexico, and Wyoming. It is hoped that the scope of this activity will be extended in the future until there is effective coverage in all States with known plague foci. The education of the public and of the medical profession is being promoted extensively so that knowledge of the epidemiology, diagnosis, and treatment of plague will become common knowledge. Studies on all phases of plague prevention and control will be continued in the hope that more effective methods will result.

Plague may have been one of mankind's worst enemies, but the knowledge and the tools now possessed should make it a far less formidable opponent in the future than it has been in the past.

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