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Authors: Smith, Abigail L., Singleton, Grant R., Hansen, George M., and Shellam, Geoffrey

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A SEROLOGIC SURVEY FOR VIRUSES AND *MYCOPLASMA PULMONIS* AMONG WILD HOUSE MICE (*MUS DOMESTICUS*) IN SOUTHEASTERN AUSTRALIA

Abigail L. Smith,[1,2] Grant R. Singleton,[3] George M. Hansen,[1] and Geoffrey Shellam[4]

[1] Section of Comparative Medicine and [2] Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut 06510, USA

[3] Division of Wildlife and Ecology, Commonwealth Scientific and Industrial Research Organization, Canberra, Australian Capital Territory 2602, Australia

[4] Department of Microbiology, The University of Western Australia, Nedlands, Perth 6009, Australia

ABSTRACT: Plasma samples from 267 wild house mice (*Mus domesticus*) trapped at 14 sites in southeastern Australia were screened for antibody to 14 viruses normally associated with laboratory-reared rodents and to *Mycoplasma pulmonis*. Serologic prevalence was high for murine cytomegalovirus (99%, $n = 94$), murine coronavirus (95%), and murine rotavirus (74%). Samples from mice collected at all sites contained antibody to these viruses. The serologic prevalence was lower for mouse adenovirus, strain K87 (37%), parvovirus (33%), and reovirus type 3 (28%), with substantial site-to-site variation. Plasma from mice collected at 12 sites contained mouse adenovirus or reovirus antibody, and samples from mice at eight sites contained parvovirus antibody. Parvovirus-antibody positive mice were typically from high density populations or from low density populations that had recently declined from high density. Antibody to lymphocytic choriomeningitis virus (LCMV) and Sendai virus occurred at only three sites, and the serologic prevalence was very low (9.6% and 1.8%, respectively). All of the LCMV-positive mice were from northeastern New South Wales. The presence of this zoonotic virus in a mouse plague-prone region raises questions about human health risks resulting from cohabitation with large numbers of mice. It appeared that mouse populations at high density or declining from high density had higher prevalence of viral antibody than populations that had been at low or moderate density for some time. Thus, viral epizootics may occur among high-density populations and may be responsible for or precipitate declines in mouse density. These data raise the possibility of rodent viruses having potential as biological control agents.

Key words: Murine viruses, house mice, *Mus domesticus*, serologic survey, population survey, mouse plagues, zoonoses, *Mycoplasma pulmonis*.

INTRODUCTION

Very few surveys have been conducted among wild rodent populations to determine the serologic prevalence of viruses normally associated with laboratory rodents, and none have been done since the advent of serologic techniques with enhanced sensitivity over the traditional hemagglutination inhibition (HAI) and complement fixation (CF) tests. Kaplan et al. (1980) tested three genera of small British rodents (*Microtus, Apodemus, Clethrionomys*) for antibody to nine viruses, including seven that naturally infect laboratory rodents. Using HAI and CF tests, serologic evidence of past infection with ectromelia virus, pneumonia virus of mice (PVM), Sendai virus, lymphocytic choriomeningitis virus (LCMV) and Theiler's mouse encephalomyelitis virus (TMEV) was found in a substantial proportion of animals. Fewer than 5% of tested sera contained antibody reactive with mouse adenovirus (MAdV) or reovirus type 3 (reo 3) antigens. Descoteaux and Mihok (1986) subsequently reported results of a survey in which 486 samples from meadow voles (*Microtus pennsylvanicus*) in Manitoba, Canada, were tested for antibody to 11 common murine viruses. Using HAI tests, there were antibodies to TMEV and reo 3 in 5% and 7% of the samples, respectively. Three viruses, MAdV, LCMV and mouse hepatitis virus (MHV), lack hemagglutinins and, therefore, were assayed by CF test. Thirty-two to 40% of the samples tested by CF were anti-complementary (fixed complement in the absence of antigen) and had to be excluded from the analysis. Inspection of the serologic data

stratified on the basis of population density of meadow voles at the time of blood collection suggested that an epizootic of TMEV may have been responsible for an episode of high mortality in the population.

Subsequently, relatively little attention has been paid to the possibility that naturally occurring infectious diseases may play a major role in regulation of wild rodent populations. A notable exception is research on wild house mice (*Mus domesticus*) in southeastern Australia which has focused on the possible role of helminths in the regulation of mouse populations (Spratt, 1990; Singleton and McCallum, 1990). Southeastern Australia presents an ideal location for study of infection and population regulation in rodents, because the region historically has suffered periodic "plagues" (widespread irruptions and subsequent coincident eruptions of mouse numbers, with densities generally greater than 1,000 mice per hectare) of wild house mice. The magnitude of the problem is such that affected areas experience serious problems, both financially, through loss of crops, and socially, through the stress imposed by living with the sheer numbers of rodents involved (Singleton and Redhead, 1989).

Our objective was to perform a broad-based serologic survey of wild mice trapped in several areas of southeastern Australia to determine the presence of antibody to 12 viruses that naturally infect laboratory-reared mice and to *Mycoplasma pulmonis*. Selected samples also were tested for reactivity with Hantaan virus (a Bunyavirus normally associated with wild and laboratory-reared rats and with other small wild rodents excluding members of the genus *Mus*) and with murine cytomegalovirus (MCMV).

MATERIALS AND METHODS

The distribution and prevalence of murine viruses and *Mycoplasma pulmonis* were investigated by live-trapping mice at 14 sites, six of which were sampled twice, in eastern and southern Australia (Fig. 1). The sites encompassed a variety of soil types, habitats and climatic conditions. At one extreme were the sites in South Australia and northwestern Victoria which have sandy loam soils, winter crops only, and a Mediterranean climate, with hot summers and predominantly winter rainfall; see Singleton (1989) and Mutze et al. (1990) for details. In contrast, the sites in northern New South Wales and southern Queensland have dark self-mulching clays, both winter and summer crops, and predominantly summer rainfall. Also included were two coastal sites, the Werribee location, a treatment area for industrial and human waste (Singleton et al., 1991b), and the Sydney site, a zoological garden surrounded by suburbs. The habitats, collection dates, and demographic and breeding status of mice sampled are summarized in Table 1.

Mice, assumed to be *Mus domesticus* (Singleton and Redhead, 1989), were collected from one farm or building at each site. A minimum of 80 Longworth (Longworth Scientific, Abingdon, United Kingdom) live-traps were set at each site per night, and traps generally were set for two consecutive nights. The population density of mice was estimated from the percentage of traps that captured mice. A population was defined as "low density" if trapping success was less than 10%, "moderate density" if trapping success was 10 to 50%, and "high density" if trapping success was greater than 50%. If the population density was moderate, then a population was described as declining from high density if, within the previous three months trapping data indicated high densities of mice, or reports from local farmers of high densities of mice could be verified by State government personnel from that region.

The breeding status of the population was determined from the breeding condition of adult (head–body length >71 mm) females at necropsy. The uterine size of these females was scored on a scale of 0 to 2 (0 = thread, 1 = string, 2 = cord) (Marshal, 1981), with a score of 2 indicating breeding condition. More importantly, the uteri were examined for the presence of embryos and embryonic scars. Also, females were examined for obvious signs of lactation. A further index of the recent breeding history of the population was the presence or absence of juvenile (head–body length <72 mm) and young adult (head–body length between 72 and 77 mm) mice in the population sample. Combining all this information permitted a determination of the breeding history of the population ≤3 mo previous to trapping. The breeding histories of the Trangie and Walpeup populations were well known because those populations were trapped monthly as part of long term (exceeding one year) population studies.

TABLE 1. Summary of the habitat, time of year, and demographic[a] and prior breeding status of the mouse populations surveyed.

Location	Habitat	Date (mo/yr)	Demographic status	Breeding status
Cereal regions				
Walpeup	Wheatlands	10/87	Decline from high density[a]	Non-breeding
		11/89	Low density for 18 months	Breeding for 2 mo
Trangie	Oilseed crops	05/89	Moderate density	Breeding for >4 mo
Trangie (Haig Farm)		02/90	Moderate density, increasing	Breeding for >2 mo
Warren	Oilseed and wheat crops	03/90	Moderate density	Breeding for >3 mo
Moree[b] (Pearce Farm)	Oilseed and cotton	05/89	Declining from high density	Breeding for >3 mo
		08/91	Low density for 2 yr	Non-breeding
Moree[c] (Kirkby Farm)	Oilseed and sorghum	05/89	High density, end of plague	Breeding for >3 mo
		08/91	Low density for 2 yr	Non-breeding
Narrabri	Farm buildings	07/89	Low density after plague	Non-breeding
		08/91	Low density for 2 yr	Non-breeding
Darling Downs (Site #1)	Sorghum, buildings	06/89	High density, plague	Non-breeding
	Wheat, buildings	10/89	Low density after plague	Breeding just begun
Darling Downs (Site #2)	Wheat, roadside	06/89	High density, plague	Non-breeding
		10/89	Low density after plague	Breeding just begun
Cowell	Wheat	09/90	Declining from high density	Non-breeding
Penong	Wheat	09/90	Declining from high density	Non-breeding
Urban sites				
Sydney	Zoological garden	02/88	Commensal, medium density	Breeding
Gungahlin	Buildings, fields	04/90	Commensal, medium density	Breeding for >3 mo
Werribee	Grassland, sewage farm	12/89	Commensal, medium density	Breeding for >2 mo

[a] Density was determined from percent trapping success: low density, <10%; moderate density, 10–50%; high density, >50%.
[b] 20 km east of Moree.
[c] 25 km northwest of Moree.

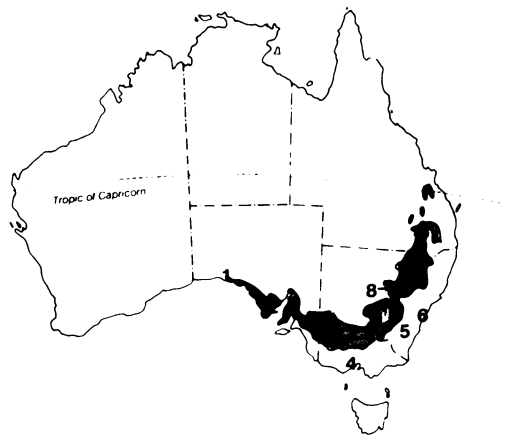

FIGURE 1. Locations within the cereal-growing region of southeastern Australia where wild house mice were trapped. There were two sites at Trangie, Moree and the Darling Downs. (1) Penong, 31°56'S, 133°01'E; (2) Cowell, 33°41'S, 136°55'E; (3) Walpeup, 35°08'S, 142°02'E; (4) Werribee, 37°55'S, 144°40'E; (5) Gungahlin, 35°13'S, 149°08'E; (6) Sydney, 33°53'S, 151°13'E; (7) Trangie, 32°02'S, 147°59'E; (8) Warren, 31°42'S, 147°50'E; (9) Narrabri, 30°20'S, 149°47'E; (10) Moree, 29°28'S, 149°51'E; (11) Darling Downs, 27°46'S, 151°27'E.

Only mice >75 mm in length (most were >80 mm) were screened serologically. These mice were estimated to be ≥8 wk old and most were ≥12 wk old. Sex ratios were approximately equal.

Up to 1.25 ml of whole blood from the retro-orbital venus plexus of mice that were not anesthetized was collected in heparinized hematocrit tubes. After centrifugation for 8 min at 1,500 rpm, plasma samples were stored at −20 C in the field and during transport to the laboratory, and at −70 C in the laboratory. Plasma samples shipped to Yale University (New Haven, Connecticut, USA) were lyophilized with a SpeedVac concentrator and refrigerated concentration trap (Savant Instruments, Inc., Farmingdale, New York, USA) prior to shipment. Plasma screened for antibody to murine cytomegalovirus (MCMV) was shipped on dry ice to The University of Western Australia (Perth, Australia).

Individual samples diluted 1:10 in normal saline and heat-treated for 20 min at 60 C were tested for reactivity with MHV, rotavirus (epizootic diarrhea of infant mice [EDIM] virus), LCMV, ectromelia virus, mouse adenovirus (MAdV) strains FL and K87, parvovirus, reovirus type 3, Sendai virus, TMEV, polyoma virus, PVM and *M. pulmonis*. Selected samples were tested with Hantaan virus antigen. Two strains of MAdV were used because MAdV-FL, used as antigen by most rodent diagnostic serology laboratories, no longer circulates in laboratory mice tested in the U.S. and does not detect MAdV-K87 antibody (Smith et al., 1986). The viruses, detecting antigens and original sources, as well as cell lines used for antigen preparation, are given in Table 2. *Mycoplasma* antigen consisted of L929 cells (American Type Culture Collection, Rockville, Maryland, USA) incubated for 3 days with one colony-forming unit per cell of stock *M. pulmonis*, originally obtained from Dr. Gail Cassell (Department of Microbiology, The University of Alabama, Birmingham, Alabama, USA). The *M. pulmonis* test used in these studies does not detect antibody to *M. arthritidis* (Smith, unpubl.), the second most common *Mycoplasma* species infecting laboratory rodents. The method used for all serologic testing except tests for murine cytomegalovirus (MCMV) antibody was indirect immunofluorescence (IFA) (Smith, 1986), and samples were scored as either positive or negative. All samples that were reactive with Sendai, LCMV or *M. pulmonis* antigens were retested on antigen-positive and on uninfected control cells. Antibody to MCMV was detected by enzyme-linked immunosorbent assay (ELISA) as described by Lawson et al. (1988) using horseradish peroxidase-conjugated goat anti-mouse IgG and IgM antibody (Tago, Inc., Burlingame, California, USA) to detect MCMV-specific antibody. A test sample was considered positive if the optical density was equal to or greater than the mean value plus three standard deviations for normal mouse serum controls. Additional samples from mice trapped in 1989 at one site in Moree were tested for antibody to LCMV in an attempt to verify and expand the initial screening results. The Narrabri site and two Moree sites were sampled approximately 2 yr after the initial collections for the same reason.

Proportions of mice seropositive to a single virus at two different times or at two different, but nearby, sites were compared using contingency Chi-square analysis (Sokal and Rohlf, 1969). Probability values of <0.05 were considered significant.

RESULTS

We collected blood from 267 rodents at 14 sites. None of the tested plasma reacted with antigens of ectromelia virus, TMEV, polyoma virus, PVM or Hantaan virus. High proportions of mice trapped at the eight sites that were sampled once had antibody to MHV and rotavirus (Table 3). In fact, 100% of mice at seven of the eight sites were MHV-seropositive, and 100% of

TABLE 2. Virus strains and cell lines used to prepare antigens for immunofluorescence serology.

Virus[a]	Detecting antigen[a]	Strain	Original source[a]	Cell line	Source[a]
MHV	MHV	S, JHM	ATCC	NCTC 1469g	ATCC
Rotavirus (EDIM)	NCDV	Lincoln	ATCC	MA104	MA Bioproducts[b]
LCMV	LCMV	771422	Yale (field isolate)	BHK21	ATCC
Ectromelia	Vaccinia	IHD-T	MA Bioproducts[b]	BSC-1	ATCC
MAdV-FL	MAdV-FL	FL	G. Lussier[c]	L929	ATCC
MAdV-K87	MAdV-K87	K87	K. Hashimoto[d]	CMT-93	ATCC
Parvovirus	MVM	i	P. Tattersall[e]	C6	ATCC
Reo 3	Reo 3	Dearing	W. Joklik[f]	BHK21	ATCC
Sendai	Sendai	771076	Yale (field isolate)	BHK21	ATCC
TMEV	TMEV	GDVII	H. Lipton[g]	BHK21	ATCC
Polyoma	Polyoma	—	P. Tattersall[e]	NIH 3T3	P. Tattersall[e]
PVM	PVM	—	MA Bioproducts[b]	BHK21	ATCC
Hantaan	Hantaan	ROK 76-118	ATCC	Vero E6	G. French[h]

[a] MHV, mouse hepatitis virus (coronavirus); EDIM, epizootic diarrhea of infant mice; LCMV, lymphocytic choriomeningitis virus (arenavirus); MAdV, mouse adenovirus; Reo 3, reovirus serotype 3; TMEV, Theiler's mouse encephalomyelitis virus (enterovirus); PVM, pneumonia virus of mice (pneumovirus); NCDV, Nebraska calf diarrhea virus (rotavirus); MVM, minute virus of mice; ATCC, American Type Culture Collection (Rockville, Maryland).
[b] Bethesda, Maryland.
[c] Institut Armand-Frappier, Laval, Quebec, Canada.
[d] Tokai University School of Medicine, Isehara, Japan.
[e] Departments of Laboratory Medicine and Genetics, Yale University, New Haven, Connecticut.
[f] Department of Microbiology and Immunology, Duke University, Durham, North Carolina.
[g] Department of Neurology, Mt. Sinai School of Medicine, New York, New York.
[h] Salk Institute, Swiftwater, Pennsylvania.

mice at three of the sites were rotavirus-seropositive. About 40% of the mice had antibody to MAdV-K87, with substantial site-to-site variability in prevalence. At only one site, Penong, were all mice antibody-positive to MAdV-K87. Plasma from one mouse at this site also reacted with MAdV-FL. Parvovirus antibody prevalence was

TABLE 3. Prevalence of murine virus antibodies in sera from wild house mice at sites that were trapped during only one season.[a]

Site	MHV[b]	Rotavirus	MAdV-K87[b]	Parvovirus	Reovirus	Sendai	MCMV[b,c]
Cowell	10/10[d]	10/10	8/10	8/10	4/10	0/10	7/7
Penong	10/10	4/10	10/10	8/10	6/10	0/10	3/3
Warren	10/10	6/10	2/10	0/10	2/9	1/10	
Trangie (Haig Farm)	10/10	6/10	0/10	0/10	1/10	0/10	
Trangie	15/15	15/15	10/15	0/15	2/15	1/14	
Sydney (Taronga Zoo)	2/2	3/3	0/3	1/3	1/3	0/3	
Gungahlin	10/10	5/8	1/10	1/10	5/10	0/10	4/4
Werribee	6/10	9/10	1/10	3/10	0/10	0/10	8/8
Total:	73/77 (95)	58/76 (76)	32/78 (41)	21/78 (27)	21/77 (27)	2/77 (3)	22/22 (100)

[a] All mice were seronegative for lymphocytic choriomeningitis virus, ectromelia virus, Theiler's mouse encephalomyelitis virus, polyoma virus, pneumonia virus of mice, and Hantaan virus, and *Mycoplasma pulmonis*.
[b] MHV, mouse hepatitis virus; MAdV-K87, mouse adenovirus strain K87; MCMV, murine cytomegalovirus.
[c] An enzyme-linked immunosorbent assay was used for MCMV, and the indirect immunofluorescence test was used for all other antigens.
[d] Number of reactive sera/number of sera tested; ( ) = percent of tested sera that were reactive.

TABLE 4. Prevalence of murine virus antibodies in sera from wild house mice trapped in 1989 and 1991 in northeast New South Wales.[a]

Site	Date (mo/yr)	MHV[b]	Rotavirus	MAdV-K87[b]	Parvovirus	Reovirus	Sendai	LCMV[b]	MCMV[b,c]
Narrabri	10/89	6/6[d]	5/6	1/6	0/6	0/6	0/6	1/6	
	08/91	10/10	3/10	0/10	0/10	0/10	0/10	6/19	
Moree	05/89	7/7	8/8	5/8	0/7	1/8	2/8	6/8	
(Pearce Farm)	08/91							2/11	
Moree	05/89	10/10	10/10	8/10	0/10	4/10	1/20	10/19	16/17
(Kirkby Farm)	08/91							6/17	
Totals	1989	23/23	23/24	14/24	0/23	5/24	3/34	17/33	16/17
		(100)	(96)	(58)		(21)	(9)	(52)	(94)
	1991	10/10	3/10	0/10	0/10	0/10	0/10	14/47	
		(100)	(30)					(30)	

[a] All mice were seronegative for ectromelia virus, the FL strain of adenovirus, parvovirus, Theiler's mouse encephalomyelitis virus, polyoma virus, pneumonia virus of mice and Hantaan virus, as well as *Mycoplasma pulmonis*.

[b] MHV, mouse hepatitis virus; MAdV-K87, mouse adenovirus strain K87; LCMV, lymphocytic choriomeningitis virus; MCMV, murine cytomegalovirus.

[c] An enzyme-linked immunosorbent assay was used for MCMV, and the indirect immunofluorescence test was used for all other antigens.

[d] Number of reactive sera/number of sera tested; ( ) = percent of tested sera that were reactive.

also variable with mice from three of eight sites being seronegative. The overall prevalence of reovirus antibody was identical to that of parvovirus antibody; mice from one site were reovirus-seronegative. Of 77 samples tested for antibody to Sendai virus, two were reactive. All mice tested from four sites were MCMV-seropositive (Table 3).

Among samples collected in 1989 from three sites in northeast New South Wales, all contained antibody to MHV, and most contained rotavirus antibody (Table 4). None contained parvovirus antibody, and prevalence for MAdV-K87 and Reo 3 were variable from site to site. Seventeen samples collected in 1989 from the three sites contained antibody to LCMV (Table 4). Initially, ten plasma samples from mice trapped at the Kirkby Farm in Moree were screened for antibody to Sendai virus and LCMV. None of those reacted with Sendai virus, and six were LCMV antibody-positive, with one additional reacting with uninfected control cells. Based on the LCMV reactivity, more samples from that site were screened, resulting in one Sendai virus reactor and four additional LCMV reactors. Reactivity with virus antigens was reproducible, and fluorescence of uninfected cells was not observed. Plasma was collected from mice trapped at the Narrabri site and the two farms in Moree about 2 yr after the initial sampling. Samples from mice at the Narrabri site were tested with the entire panel of antigens; all 10 were reactive with MHV, 3 of 10 with rotavirus, and 6 of 19 were reactive with LCMV (Table 4). The Kirkby and Pearce farms in Moree were sampled 27 mo after the initial collections; six of 17 samples from the former and two of 11 from the latter reacted with LCMV antigen.

Plasma was collected in June and October 1989 from mice at two sites on the Darling Downs. A mouse plague occurred in June. By October, population numbers were near their lowest post-plague levels and breeding had just commenced. This was the first time the mice had bred since the previous autumn. Thus, the October samples represented those animals that had survived the plague to form the nucleus of the next breeding population. Antibodies were detected to five of the 12 viruses tested and to *M. pulmonis* (Table 5). The prevalence of viral antibody was generally higher at Darling Downs–1, both in June

TABLE 5. Prevalences of antibodies to murine viruses and *Mycoplasma pulmonis* in sera from wild house mice trapped on Darling Downs and at Walpeup.[a]

Site	Date (mo/yr)	MHV[b]	Rotavirus	MAdV-K87[b]	Parvovirus	Reovirus	*M. pulmonis*	MCMV[b]
Darling Downs-1	06/89	30/30[d] (100)	17/30 (57)	9/30 (30)	11/30 (37)	9/30 (30)	0/30	
	10/89	17/20 (85)	16/20 (80)	5/20 (25)	3/20 (15)	3/20 (15)	0/20	
Darling Downs-2	06/89	19/20 (95)	9/20 (45)	2/20 (10)	1/20 (5)	2/20 (10)	1/20 (5)	
	10/89	8/11 (73)	9/11 (82)	2/11 (18)	1/11 (9)	1/11 (9)	0/11	
Totals		74/81 (91)	51/81 (63)	18/81 (22)	16/81 (20)	15/81 (19)	1/81 (1)	
Walpeup	10/87	55/55 (100)	44/55 (80)	32/55 (58)	51/54 (94)	27/54 (50)		55/55 (100)
	11/89	28/29 (97)	19/29 (66)	2/29 (7)	0/29 (0)	7/29 (24)		
Totals		83/84 (99)	63/84 (75)	34/84 (40)	51/83 (61)	34/83 (41)		55/55 (100)

[a] All mice were seronegative for lymphocytic choriomeningitis virus, ectromelia virus, the FL strain of adenovirus, Sendai virus, Theiler's mouse encephalomyelitis virus, polyoma virus, pneumonia virus of mice and Hantaan virus.

[b] MHV, mouse hepatitis virus; MAdV-K87, mouse adenovirus strain K87; MCMV, murine cytomegalovirus.

[c] An enzyme-linked immunosorbent assay was used for MCMV, and the indirect immunofluorescence test was used for all other antigens.

[d] Number of reactive sera/number of sera tested; ( ) = percent of tested sera that were reactive.

and October. Differences in the proportions of mice at the two sites having parvovirus antibody in June were significant ($\chi_1^2 = 6.6$, $P < 0.01$). Rotavirus was the only agent for which there was a significant increase in antibody prevalence between June and October (pooled data for two sites: $\chi_1^2 = 6.6$, $P < 0.01$), and this occurred at both sites. The post-plague prevalence of antibody to parvovirus and reovirus was lower than that of the June trapping, but the differences were not significant. A single sample from a mouse trapped in June 1989 at Darling Downs–2 ($n = 20$) reacted strongly with *Mycoplasma pulmonis*. This was the only seropositive mouse in the entire study ($n = 267$), and the sample did not react with uninfected cell antigens.

The influence of host density on serologic prevalence could be confounded by seasonal effects. The Walpeup mouse populations were sampled around the same time of year and when mouse density was low. The 1987 samples were collected immediately after a decline from high host density, whereas the 1989 samples followed 2 yr of low host density. Antibodies were detected to six of the 13 viruses tested in October 1987, and to four of 12 viruses in November 1989 (Table 5). Murine cytomegalovirus serology was not performed on the samples collected in 1989. Serologic prevalences were higher for all viruses in October of 1987. These differences were significant for MAdV-K87 ($\chi_1^2 = 20.5$, $P < 0.001$), parvovirus ($\chi_1^2 = 71.5$, $P < 0.001$), and reovirus ($\chi_1^2 = 6.7$, $P < 0.01$).

DISCUSSION

Despite marked habitat and climatic differences among sites, nearly all mice tested in the present study had sustained, at some earlier time, infection with MCMV and with the murine coronavirus, MHV, and the majority had been infected with mu-

rine rotavirus. The prevalence of prior infections with adenovirus, parvovirus and reovirus was relatively lower with substantial site-to-site variability. Antibody to MAdV-K87 and reovirus was found in samples collected from 12 of 14 sites. The serologic prevalence of parvovirus appeared to be positively associated with population outbreaks; highest prevalence was frequently recorded in populations with high mouse density and in those undergoing a post-outbreak decline (Table 1). Exceptions were Narrabri and the two Moree sites, where the serologic profile of mice collected was unique due to the occurrence of LCMV antibody. The results probably do not represent maternal antibody, because the mice trapped for these studies were all adults.

With the exception of ectromelia virus, none of the agents surveyed in this study commonly produce clinical signs during the course of natural infections in the adult, immunocompetent laboratory mouse. Some, such as MHV, can produce fatal infections in the newborn laboratory mouse (Barthold et al., 1982). Others, such as PVM, rarely produce disease but can induce a wasting syndrome in genetically immunocompromised hosts (Weir et al., 1988). The availability of defined inbred strains of mice has revealed a spectrum of genetically determined susceptibility and resistance for some of the better studied agents, such as MHV, Sendai virus, MCMV and parvovirus (Barthold and Smith, 1987; Brownstein et al., 1981; Allan and Shellam, 1984; Brownstein et al., 1991). The ability of these agents to produce disease in the wild house mouse is presently unknown. This is, in fact, the first large scale serologic survey of *M. domesticus* for viruses that usually are considered to be restricted to laboratory-reared mice.

The results of tests for Sendai virus antibody deserve special consideration. Sendai virus infection is thought to be restricted to laboratory-reared rodents. In a survey of 400 feral mice trapped in four U.S. states, Parker and Reynolds (1968) found no evidence of Sendai virus reactivity. In the current study of 267 plasma samples, five reacted with Sendai virus antigen. It should be noted, however, that all five of these samples stained a smaller proportion of infected cells than did the positive control serum (obtained by experimental Sendai virus infection of laboratory mice). Since uninfected cells were not stained by the five reactive Australian samples, it is assumed that the reactivity was specific for a parainfluenza type 1 virus. However, the possibility must be considered that these samples contained antibody to a parainfluenza virus related to, but antigenically distinct from, Sendai virus.

The implications of LCMV infection in wild rodents that undergo population outbreaks also are noteworthy. Lymphocytic choriomeningitis virus is a zoonotic agent that causes a spectrum of infections in man, ranging from subclinical to fatal. Most serious human LCMV infections have been linked to contact with infected hamsters or hamster tissues. However, during mouse plagues, humans are in contact with enormous numbers of mice that may be excreting additively very high concentrations of virus. An unknown at this time is whether the LCMV infection in the mouse population of New South Wales is acute and self-limiting or whether it is a chronic carrier infection (Lehmann-Grube, 1982). Attempts currently are being made to isolate virus from tissues of mice trapped at the Moree and Narrabri sites. The level of difficulty encountered during attempts to isolate the virus will suggest which epidemiologic form prevails.

A notable difference between our results and those reported by others (Kaplan et al., 1980; Descoteaux and Mihok, 1986) is our inability to detect any evidence of infection with TMEV. Workers in the prior studies had used the HAI test to assay for TMEV antibody, and that test has been noted to yield some positive reactions that are nonspecific (Smith, 1986). The earlier studies of small rodents also had concentrated on woodmice (*Apodemus* spp.) and

various species of voles (*Microtus* spp., *Clethrionomys* spp.), whereas we surveyed wild house mice. The possibility exists, therefore, that rodents other than species of *Mus* may be quite susceptible to infection with TMEV. Additional studies of experimentally infected rodents would be required to support this hypothesis.

Based on comparisons of the serologic prevalences among and between sites, we believe that mouse populations at high density or declining from high density had higher seropositive rates than populations that had been at low or moderate density for some time. The best evidence for this came from the Walpeup population (Table 5) sampled at low density around the same time of year but 2 yr apart. The 1987 samples were taken after a rapid decline in mouse numbers from a high population density (Singleton, 1993), whereas the 1989 samples were obtained after the population had remained at low density for 2 yr. Comparing the two sampling intervals, three of five murine viruses circulating in the Walpeup population were significantly more prevalent in 1987. Experimental studies in laboratory mice have shown that some murine viruses, such as MCMV and MHV, are immunosuppressive (Allan et al., 1982; Smith et al., 1987, 1991; de Souza et al., 1991). Functional suppression of the immune system either by virus infection, malnutrition (Pena-Cruz et al., 1989; Teo et al., 1991) or the stress induced by overcrowding may render wild house mice more susceptible to super-infection or to the deleterious effects of infections with other agents. Evidence for such an effect abounds in the infectious disease literature (Peterson et al., 1991). On the other hand, transmission rates of agents normally found at low prevalence are likely to be higher in high-density populations of mice.

The viruses found in urban sites where plagues do not occur (e.g., Sydney, Gungahlin and Werribee) were similar to those found in cereal-growing regions, where plagues do occur. We believe that the external environment and presence or absence of other rodents (*Rattus rattus* and *Rattus norvegicus* occur at the urban sites, but rarely or at low density at the other sites tested) have little influence on the persistence of viruses in mouse populations. The prevalences of infection may be influenced by these factors, but we currently have insufficient data to determine that.

An enigma to wildlife ecologists and small mammal biologists is why mouse plagues occur in agricultural areas only in Australia and in the northwest plateau region of China (Redhead, 1988). Many theories have been proposed to explain this limited occurrence (Redhead et al., 1991), and the favored hypothesis is lack of competitors. The wild house mouse is virtually the only small mammal granivore/omnivore found in the cereal belt of southern and eastern Australia (Singleton, unpubl.). It is commonly believed that none of the native small mammals could adapt to the intensive cultivation and resulting drastic changes in habitat that have occurred in the region. A possibility raised by our data is that introduction of *Mus domesticus* and its viruses into Australia's indigenous small mammal populations, that had probably been isolated from such viruses for many thousands of years, cleared the way for house mice to dominate the cereal growing regions. While no studies of infectious diseases in other small Australian mammals have been conducted, the hypothesis parallels the documented experiences of many isolated human populations that were decimated through introduction of infections such as measles or smallpox (Black, 1978; Benenson, 1978). There is probably no single answer that explains the occurrence of mouse plagues in restricted areas of the world; however, habitat destruction combined with the occurrence of infectious diseases present an attractive, but more complex, hypothesis to test.

The high prevalence and diversity of murine viruses in field populations of Australian mice were not expected. These results highlight how little is known about

the diseases of wild mice and their potential as agents to control mouse plagues. Biological control of mouse plagues using viruses is an appealing concept because it would replace the current ad hoc use of chemicals during plagues (Redhead, 1988; Singleton et al., 1991a) and could use agents that are strictly species-specific. Detailed investigations of the interactions between viruses and wild mouse populations, building on the work of Singleton et al. (1993), are required to determine the validity of such an approach. Without such studies, it would be difficult to predict the pathogenicity of a given virus, the likelihood that a particular virus would establish itself in a population or the likely rate of transmission through field populations of mice. Our current knowledge of the agents is derived almost entirely from laboratory studies of purpose-bred mice. Virtually nothing is known about the susceptibility of native Australian rodents to viruses of laboratory rodents. Epizootiologic studies of murine viruses in populations of *Mus domesticus* and other native rodents will dramatically expand our understanding of these agents and are urgently required if their potential use in biological control of population outbreaks of wild mice is to be pursued.

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