Fig. 4. Right profile. The upper lip and the soft part of the nose are deformed upwards as a result of slight ice pressures. In addition one can see the depression in the right ear.

(diastema) between the two central, maxillary incisors. Tremata of various forms are frequently found in prehistoric populations (5). Lastly, the nose was strongly pressed upward to the right. The ossa nasalia remained undamaged. All of these observations indicate the effects of relatively slight but nevertheless continuous ice pressure in one direction. The right os zygomaticum moved nearly 2 mm in the sutura frontozygomatica toward the occipit; the right orbit was slightly displaced (Fig. 1).

One remarkable peculiarity was found on the right earlobe. It is a pit-like, sharp-edged rectangular depression covered by skin that cannot have developed post-mortem (Fig. 4). The edges are remarkably straight. Inflammatory processes, whatever their etiology might have been, would have left other forms of scars. This find may have resulted from body ornamentation. In graves dating from the Bronze Age, rings have been found that could be considered as earrings. This was shown by an archeological analysis of contents of graves (*10*). The form of the pit-like depression on the right earlobe could therefore be taken as indicating that the man wore an ornamental stone that was fitted into the earlobe a long time before his death. The CT images revealed that the distal humerus shaft of the left arm was fractured slightly above the trochlea. The possibility that the fracture happened during an initial recovery attempt cannot yet be excluded.

A word of warning is necessary in line with the importance of these data. From a scientific standpoint all efforts to describe the morphology and dimensions of the soft tissues and skeletal parts of the mummy must be viewed under the aspect of the singularity of the "man in ice." We have no knowledge about the variability of the population from which he descended. Especially the examination of small, sometimes locally closely neighboring Late Neolithic populations shows that there are remarkable differences of types (*4*). Very probably such differences depend on a strong endogamy, although additional barriers due to sociocultural reasons could have enhanced them. Although media coverage resulted in worldwide notoriety, it is important to relegate the individuality of this find into the form of a valuable piece of information about the development of human culture and history.

REFERENCES AND NOTES

1. In eyewitness reports the corpse was dressed with "leather wrapped" trousers and shoes before the official recovery. After the official recovery the corpse was undressed with the exception of the right shoe [G. Zissernig, *Bericht Über das Erste Internationale Symposium "Der Mann im Eis—Ein Fund aus der Steinzeit Tirols,"* Innsbruck, Austria, 3 to 5 June 1992, K. Spindler, Ed. (Veröffentlichungen der Universität Innsbruck, vol. 187, 1992)]. During the earlier recovery attempts the corpse was lifted out of the glacier ice in such a way that the trousers were torn. The corpse lacked the outer genitals, penis, and testes. The scrotum was in a good enough condition to determine the sex in context with the form of the angulus subpubicus. Currently the most probable hypothesis for this finding is that the prominent genitals, which were frozen to the clothing, were detached during the earlier manipulations.
2. G. Bonani, *Bericht über das Erste Internationale Symposium "Der Mann im Eis—Ein Fund aus der Steinzeit Tirols,"* Innsbruck, Austria, 3 to 5 June 1992, K. Spindler, Ed. (Veröffentlichungen der Universität Innsbruck, vol. 187, 1992).
3. D. zur Nedden, *ibid.*; *2nd European Scientific User Conference Somatom Plus*, Berlin, March 1992.
4. M. Teschler-Nicola, *Ann. Naturhist. Mus. Wien* **86**, 431 (1984).
5. _____, unpublished data.
6. G. Olivier, C. Aaron, G. Fully, G. J. Tissier, *Hum. Evol.* **7**, 513 (1978).
7. M. Traindl-Prohazka and H. Seidler, *Ann. Naturhist. Mus. Wien* **92**, 143 (1991).
8. V. Formicola, *Riv. Anthropol. Roma* **LXVII**, 307 (1989).
9. T. Sjøvold, *Hum. Evol.* **5**, 431 (1990).
10. C. Neugebauer-Maresch and J. W. Neugebauer, *Mitt. Anthropol. Ges. Wien* **118/119**, 101 (1988–1989).

28 May 1992; accepted 25 August 1992

Slowing of Mortality Rates at Older Ages in Large Medfly Cohorts

James R. Carey,* Pablo Liedo, Dina Orozco, James W. Vaupel

It is generally assumed for most species that mortality rates increase monotonically at advanced ages. Mortality rates were found to level off and decrease at older ages in a population of 1.2 million medflies maintained in cages of 7,200 and in a group of approximately 48,000 adults maintained in solitary confinement. Thus, life expectancy in older individuals increased rather than decreased with age. These results cast doubt on several central concepts in gerontology and the biology of aging: (i) that senescence can be characterized by an increase in age-specific mortality, (ii) that the basic pattern of mortality in nearly all species follows the same unitary pattern at older ages, and (iii) that species have absolute life-span limits.

Age-specific mortality rates (*1*) are used by gerontologists, demographers, and biologists in a number of interrelated ways including quantifying senescence in populations (*2*), comparing species (*3*), and inferring species-specific life-span limits (*4*). Surprisingly, the pattern of age-specific mortality is well known only for *Homo sapiens*, and even for humans data are sparse after age 85. For 48 species scattered across various phyla, Finch estimated the level of mortality at the age of sexual maturity and the increase in the mortality rate with age, but he warned that the estimates "should be considered first approximations within a twofold range" (*5*). The estimates depend on the untested assumption that mortality increases at the same rate from sexual maturity to advanced old age; as Finch noted, "there is no a priori reason why mortality rates should conform to functions" of this type (*6*). The number of observations of age at death for any nonhuman species is small. In a typical study of mortality, the life-spans of some 20 to 50 individuals are observed in laboratory or field settings (*7*); only rarely has mortality in several thousand individuals been monitored (*8*). When only a few hundred individuals are observed, the pattern of age-specific mortality at older ages,

J. R. Carey, Department of Entomology, University of California, Davis, CA 95616.
P. Liedo, Centro de Investigaciones Ecológicas del Sureste, Apdo. Postal 36, Tapachula, Chiapas, 30700 Mexico.
D. Orozco, Programa Moscamed, Metapa, Chiapas, 30820 Mexico.
J. W. Vaupel, Odense University, Odense, Denmark, and Center for Demographic Studies, Duke University, Durham, NC 27706.
*To whom correspondence should be addressed.

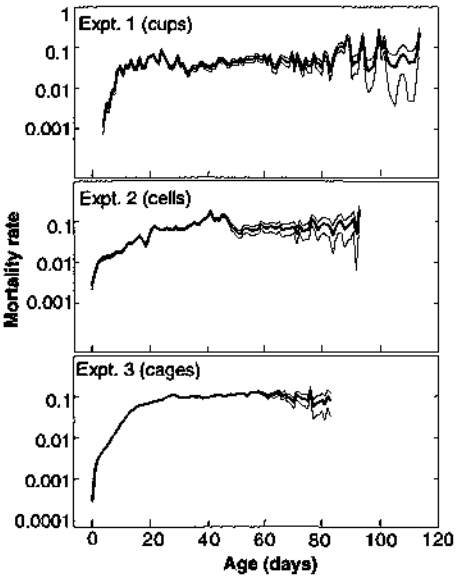

Fig. 1. Age-specific mortality rates for experiment 1 in which 21,204 medflies were maintained in individual cups (top); experiment 2 in which 27,181 medflies were held individually in tissue cells (middle), and experiment 3 in which 1,203,646 medflies were held in cages of approximately 7,200 each (bottom). Thin bounding lines are the 95% confidence limits.

when perhaps 90% of the population is dead, is beyond the scope of definitive study. It is unknown whether the pattern of mortality at advanced ages is typically one of high and increasing mortality, as among humans; moderate and constant mortality; or some other pattern.

We monitored age-specific mortality in more than 1 million Mediterranean fruit flies (*Ceratitis capitata*) over their lifetimes to determine the pattern of mortality at extreme ages. Cohorts that totaled 1 million flies were used to ensure that mortality rates at older ages would be based on large numbers. We used this information to determine whether mortality rates increased at advanced ages, whether the Gompertz mortality model (9) fit the mortality data at older ages, and whether patterns of age-specific mortality implied an upper life-span limit.

We studied medflies at a large rearing facility in Metapa, Mexico (*10*), where we were provided with essentially unlimited numbers of pupae of the same age. Three separate trials were conducted. In experiments 1 and 2, death rates were monitored in more than 20,000 medflies maintained in solitary confinement. In experiment 3, more than 1.2 million medflies were maintained in groups of approximately 7,200 (*11*).

Life expectancy at eclosion was highest for flies maintained in solitary confinement and lowest for flies maintained in groups (Table 1). Life expectancy decreased slightly in the interval between the age when 10% of the original cohort remained alive to the age when 1% of the original cohort remained alive. It then increased at the oldest ages. In all three experiments, the life expectancy for flies at the age when 90% of the original cohort was dead was similar to the life expectancy for individuals still alive at the age when 99.9% of the original cohort was dead. Life expectancy for medflies in each experiment either remained the same or increased with age at advanced ages (>45 days old).

Constant or increasing life expectancies with age can only occur if the underlying age-specific mortality rates are also constant or are decreasing at older ages. This pattern of mortality rate decrease was observed for flies maintained in solitary confinement (experiments 1 and 2) and for flies maintained in groups (experiment 3) (Figs. 1 and 2 and Table 2). Rate of change in mortality slowed in each of the 167 cages of flies in experiment 3 at older ages (Fig. 3). There was little overlap in the distributions of rates of change in mortality with age between medfly cohorts 10 days old and cohorts 30 and 45 days old. In virtually all cohorts the rate of change in mortality at

Fig. 2. Smoothed age-specific mortality rates for the three medfly mortality experiments plotted on a linear scale (legend to Fig. 1). In all three experiments the upper 95% confidence limit when mortality rates were declining was lower than the lower 95% confidence limit at the mortality high point. Thus the observed declines were significantly different than a pattern of level mortality rates. The total number of individuals remaining alive at age 100 days for experiments 1 (cups), 2 (cells), and 3 (cages) was 307, 31, and 62, respectively.

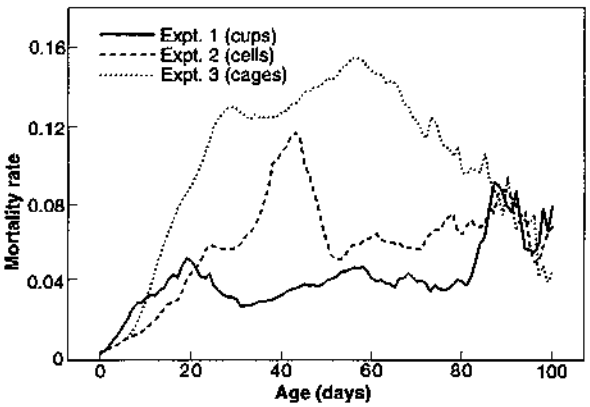

Table 1. Number alive, age (days), and remaining life expectancy (e_x) of medflies in each of three experiments. Survival rates at which these three parameters are reported differ by four to six orders of magnitude starting at 100% survival (proportion = 1.0) for flies in all three experiments to survival at one-millionth (proportion = 0.000001) of the original cohort in experiment 3. The greatest ages attained by flies in each of the experiments are as follows: experiment 1 = 216 days, experiment 2 = 241 days, and experiment 3 = 171 days.

Proportion remaining alive*	Experiment 1 (cups)			Experiment 2 (cells)			Experiment 3 (cages)		
	Number	Age	e_x	Number	Age	e_x	Number	Age	e_x
1.0	21,204	0	30.6	27,181	0	28.2	1,203,646	0	20.9
0.1	2,120	64	19.5	2,718	45	13.7	120,365	33	7.3
0.01	212	103	15.8	272	79	12.9	12,036	50	6.7
0.001	21	135	18.2	27	106	13.7	1,204	64	9.7
0.0001	2	170	34.5	3	117	86.8	120	86	24.8
0.00001							12	146	11.3
0.000001							1†	165	6.5

*Day on which the number living was ≤ the specified proportion. †The last two flies died on the same day. Thus, the age corresponding to this proportion remaining alive represents the age at which the initial cohort of 1.2 million flies were reduced to the last two flies.

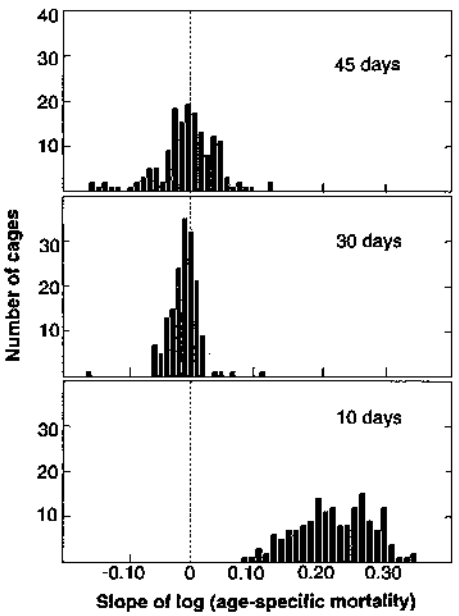

Fig. 3. Distribution of the estimated slopes of the logarithms of age-specific mortality at 10, 30, and 45 days in each of 167 medfly cages with an average initial density of 7200 adults (experiment 3). Slope estimates were made with a least-squares linear regression of the smoothed mortality curve for each cage centered on the specified age ±5 days.

older ages slowed down, leveled off, or decreased.

As flies aged, mortality rates decreased from a positive rate to a negative one in each experiment. For example, mortality rates decreased in the interval from 20 to 35 days in experiment 1, in the interval from 40 to 55 days in experiment 2, and in the interval from 60 to 100 days in experiment 3. Mortality rates in all cages increased at age 10 days but mortality rates decreased in over half of all cohorts after 30 and 45 days (Fig. 3). Mortality rates were not monotonic; rather they increased and decreased with age. Slowing of the change of mortality with age resulted in daily mortality rates that were uniformly low for the oldest flies in all three experiments. For example, average daily mortality for the last 1000 medflies was 4% in experiment 2 and 6% in experiments 1 and 3.

Mortality rates were similar at the most advanced ages for flies maintained under different physical and biological conditions. Flies maintained in solitary confinement were subject to conditions that minimize mortality risk. Activity was restricted by the small cage size; there was no mating and little egg-laying. There was also minimal mechanical wear and no stress due to crowding. In contrast, flies held in groups of 7200 were subject to conditions that increase mortality risk—large cage size for flying, mating, some egg-laying, mechanical wear, and considerable stress due to crowding (*12*, *13*).

There are numerous reasons why mortality rates may slow, remain constant, or decline with age among older individuals in various species (*14*), including the possibility that repair mechanisms at older ages can compensate for damage at younger ages. Slowing of the rate of change in mortality with age may also be an artifact of compositional change in the cohort, resulting from heterogeneity in mortality patterns within the population of genotypes and phenotypes (*15*). As the population ages, it becomes more and more selected because individuals with higher death rates will die out in greater numbers than those with lower death rates, thereby transforming the population into one consisting mostly of individuals with low death rates. Therefore, the possibility exists that death rates fell at older ages, not because of a decrease in the risk of dying at the individual level, but because of heterogeneity at the cohort level.

Leveling off of mortality at older ages was reported in other insect studies on

Table 2. Survival of 1,203,646 medfly adults monitored in experiment 3. The N_x column gives the number remaining alive at age x in days and the q_x column gives the age-specific probability of dying in the interval x to $x + 1$ [$q_x = 1 - (N_{x+1}/N_x)$].

Age (x)	Number living (N_x)	Age-specific mortality (q_x)	Age (x)	Number living (N_x)	Age-specific mortality (q_x)	Age (x)	Number living (N_x)	Age-specific mortality (q_x)	Age (x)	Number living (N_x)	Age-specific mortality (q_x)
0	1,203,646	0.00000	44	26,214	0.14393	87	109	0.10092	130	21	0.00000
1	1,203,646	0.00144	45	22,441	0.13596	88	98	0.07143	131	21	0.00000
2	1,201,913	0.00401	46	19,390	0.13063	89	91	0.00000	132	21	0.04762
3	1,197,098	0.00508	47	16,857	0.13615	90	91	0.05495	133	20	0.00000
4	1,191,020	0.00638	48	14,562	0.14524	91	86	0.01163	134	20	0.00000
5	1,183,419	0.00753	49	12,447	0.13377	92	85	0.07059	135	20	0.00000
6	1,174,502	0.00977	50	10,782	0.15146	93	79	0.07595	136	20	0.05000
7	1,163,026	0.01232	51	9,149	0.13597	94	73	0.02740	137	19	0.00000
8	1,148,693	0.01642	52	7,905	0.14560	95	71	0.05634	138	19	0.00000
9	1,129,836	0.02184	53	6,754	0.15013	96	67	0.01493	139	19	0.00000
10	1,105,164	0.02982	54	5,740	0.13258	97	66	0.01515	140	19	0.00000
11	1,072,209	0.03786	55	4,979	0.16027	98	65	0.04615	141	19	0.10526
12	1,031,620	0.04521	56	4,181	0.16049	99	62	0.00000	142	17	0.05882
13	984,980	0.05885	57	3,510	0.15812	100	62	0.00000	143	16	0.12500
14	927,011	0.06344	58	2,955	0.16717	101	62	0.00000	144	14	0.00000
15	868,202	0.07223	59	2,461	0.16010	102	62	0.06452	145	14	0.14286
16	805,489	0.07569	60	2,067	0.13159	103	58	0.01724	146	12	0.08333
17	744,520	0.07925	61	1,795	0.13092	104	57	0.03509	147	11	0.09091
18	685,514	0.08264	62	1,560	0.12500	105	55	0.01818	148	10	0.10000
19	628,866	0.08499	63	1,365	0.13407	106	54	0.01852	149	9	0.00000
20	575,420	0.09228	64	1,182	0.14129	107	53	0.00000	150	9	0.11111
21	522,319	0.09680	65	1,015	0.16847	108	53	0.01887	151	8	0.00000
22	471,756	0.10024	66	844	0.12204	109	52	0.01923	152	8	0.00000
23	424,469	0.10585	67	741	0.13630	110	51	0.03922	153	8	0.12500
24	379,537	0.11022	68	640	0.10469	111	49	0.04082	154	7	0.14286
25	337,704	0.11581	69	573	0.12565	112	47	0.04255	155	6	0.16667
26	298,596	0.12989	70	501	0.07984	113	45	0.04444	156	5	0.00000
27	259,811	0.13360	71	461	0.11931	114	43	0.02326	157	5	0.00000
28	225,101	0.13610	72	406	0.12069	115	42	0.04762	158	5	0.20000
29	194,464	0.12802	73	357	0.10924	116	40	0.00000	159	4	0.00000
30	169,569	0.12129	74	318	0.10377	117	40	0.00000	160	4	0.00000
31	149,002	0.12141	75	285	0.09123	118	40	0.00000	161	4	0.00000
32	130,911	0.11682	76	259	0.12741	119	40	0.02500	162	4	0.00000
33	115,618	0.12409	77	226	0.06637	120	39	0.05128	163	4	0.00000
34	101,271	0.12500	78	211	0.08057	121	37	0.02703	164	4	0.50000
35	88,612	0.12664	79	194	0.06701	122	36	0.08333	165	2	0.00000
36	77,390	0.12235	80	181	0.06630	123	33	0.00000	166	2	0.00000
37	67,921	0.13385	81	169	0.07692	124	33	0.06061	167	2	0.00000
38	58,830	0.11537	82	156	0.08974	125	31	0.09677	168	2	0.00000
39	52,043	0.12488	83	142	0.08451	126	28	0.10714	169	2	0.00000
40	45,544	0.12125	84	130	0.06154	127	25	0.04000	170	2	0.00000
41	40,022	0.12793	85	122	0.05738	128	24	0.04167	171	2	1.00000
42	34,902	0.13014	86	115	0.05217	129	23	0.08696	172	0	
43	30,360	0.13656									

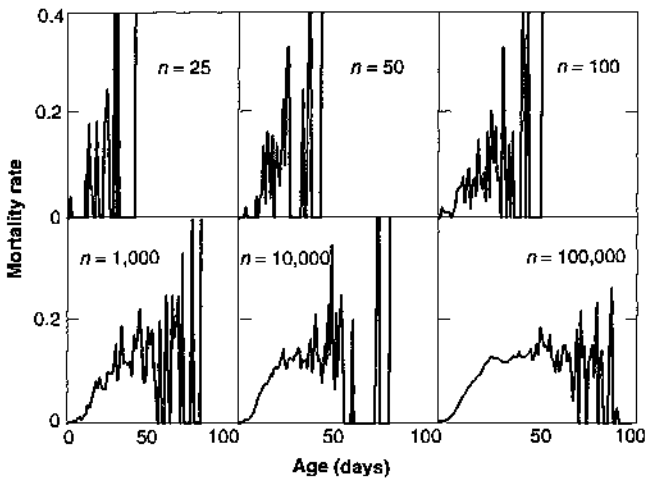

Fig. 4. Age-specific mortality rates computed for cohorts of six different sizes from $n = 25$ to $n = 100,000$. Cohorts were created by randomly subsampling the 1.2 million medfly deaths observed in experiment 3. The results reveal the inadequacy of small cohort size for determining age-specific mortality rates even at young ages and show that large cohorts are needed to determine mortality patterns at advanced ages. Larger n values provide new information on mortality rates at progressively older ages.

Drosophila (*16*), houseflies (*17*), medflies (*18*), and bruchiid beetles (*19*). Also, several studies have suggested a slowing of the rate of increase of mortality with age for humans after age 85 years (*20–24*).

The medfly mortality pattern casts doubt on three central concepts in gerontology and the biology of aging and mortality. One concept is that senescence can be operationally defined and measured by the increase in mortality rates with age. Because mortality rates fluctuate up and down around a rough average over most of the life-spans of medflies, medflies' lives, according to this definition, are characterized by alternating periods of positive and negative senescence. It is questionable whether it is helpful to define the word "senescence" in this way.

Another concept that is not consistent with our data is that the basic pattern of mortality at adult ages in nearly all species follows the same unitary pattern described by the Gompertz model (exponential increase). The finding that medfly age-specific mortality is not described by this model at old ages provides direct empirical evidence that Gompertz's law does not hold in all populations (*25*).

Finally, our data are inconsistent with the concept that species can be characterized by their species-specific life-spans as measured by: (i) the oldest age attained, even in a relatively small populations of 100 or fewer individual; or (ii) a pattern of age-specific mortality tending toward unity at the maximal age. Different maximum life-spans were observed in our experiments, and none of the trajectories of age-specific mortality tended toward unity as would have been expected if a species-specific life-span limit existed. Furthermore, if small samples were taken, different maximum life-spans would be observed. It is possible to estimate life expectancy but medflies appear not to have a characteristic life-span.

Our results have two methodological implications. One is that it may not be possible to determine the mortality pattern of a species from data on 100 or even fewer individuals (Fig. 4). Only with 20,000 or 30,000 (experiments 1 and 2) and more than a million individuals (experiment 3) was it possible to determine the pattern of medfly mortality through advanced ages. The second implication is that survival curves are poorly suited for summarizing mortality patterns. Survival curves are useful in studying survival. That is, what proportion of the initial cohort is alive at a certain age. It is, however, difficult to discern the pattern of mortality rates by looking at a survival curve; mortality curves are superior for this purpose. Survival curves are often plotted not because they are the best curve for studying mortality patterns but because they are fairly smooth and regular, even for small populations. In contrast, mortality curves tend to fluctuate erratically when population sizes are small. This problem can be alleviated with the use of larger populations or various techniques of smoothing.

REFERENCES AND NOTES

1. Denoted q_x in the life table, age-specific mortality is defined as the fraction of those alive at age x dying in the interval x to $x + 1$. C. L. Chiang, *The Life Table and Its Applications* (Krieger, Malabar, FL, 1984), p. 116.
2. C. Finch, *Longevity, Senescence, and the Genome* (Univ. of Chicago Press, Chicago, 1990), p. 12.
3. ———, *ibid.*, p. 14.
4. J. F. Fries, *N. Engl. J. Med.* **303**, 130 (1980); L. A. Gavrilov and N. S. Gavrilova, *The Biology of Life Span: A Quantatitive Approach* (Harwood Academic, Chur, Switzerland, 1991), p. 128.
5. C. Finch, *Longevity, Senescence, and the Genome* (Univ. of Chicago Press, Chicago, 1990), pp. 46 and 123.
6. ———, *ibid.*, p. 246.
7. R. Pearl and J. R. Miner, *Q. Rev. Biol.* **10**, 60 (1935); P. H. Leslie and R. M. Ransom, *J. Anim. Ecol.* **9**, 27 (1940); E. S. Deevey, Jr. *Q. Rev. Biol.* **22**, 283 (1947); L. C. Birch, *J. Anim. Ecol.* **17**, 15 (1948); A. Comfort, *The Biology of Senescence* (Churchill Livingstone, Edinburgh, ed. 3, 1979); D. E. L. Promislow, *Evolution* **45**, 1869 (1991); D. G. Hazzard, H. R. Warner, C. E. Finch, *Exp. Gerontol.* **26**, 411 (1991).
8. R. Pearl and S. L. Parker, *Am. Nat.* **58**, 71 (1924); M. Rockstein and H. M. Lieberman, *Gerontologia* **3**, 23 (1959); D. B. Mertz, *Physiol. Zool.* **48**, 1 (1975); K. G. Collatz and R. S. Sohal, Eds., *Insect Aging Strategies and Mechanisms* (Springer-Verlag, Berlin, 1986).
9. B. Gompertz (1825), *Mathematical Demography: Selected Papers*, D. Smith and N. Keyfitz, Eds. (Springer-Verlag, Berlin, 1977), pp. 279–282. The Gompertz formula is given as $\mu_x = ae^{bx}$ where μ_x denotes mortality at age x, a denotes the initial rate of mortality, and b is the exponential mortality rate coefficient.
10. Moscamed, the Mexico and U.S. medfly mass rearing facility where the studies were conducted, is located in Metapa. The medfly strain currently reared at the facility was started from several hundred field-collected individuals in 1983 in Antigua, Guatemala, is maintained at 2 to 3 million breeding adults, and has a weekly pupal production rate averaging 500 million. Technical details on the production process, larval and adult diets, seeding densities, and environmental conditions are given in A. Schwartz *et al.*, *Fla. Entomol.* **68**, 467 (1985) and R. I. Vargas, in *Fruit Flies: Their Biology, Natural Enemies and Control*, A. S. Robinson and G. Hooper, Eds. (Elsevier, Amsterdam, 1989), vol. 3B, pp. 141–151.
11. Adult flies in the three experiments were maintained under the following environmental conditions. Experiment 1: continuous light, 25.2°C (±2°), 67% relative humidity (RH) (±8%); experiment 2: 12:12 light-dark (LD) cycle, 25.6°C (±2°), 67% RH (±8%); experiment 3: 12:12 LD cycle, 24.0°C (±2°), and 65% RH (±9%). In experiment 1, a single pupa and adult food (3:1 sugar to protein dry mixture) were placed in 1-ounce cups. The cups were then attached by the upper rim to the underside of a 60 cm by 90 cm screened tray which, in turn, was placed in a vertical holding rack. Water was supplied to each fly with a moist dental wick. Flies in experiment 2 were also confined alone. Conditions in this experiment differed from those in experiment 1 in three respects—3.5-ml tissue culture cells (Falcon 24-cell units) were used rather than the 1-ounce cups; sugar alone was the food source, and flies obtained water from a layer of saturated cotton placed on top of the cells. In experiment 3 approximately 7200 medflies emerging from one-of-five pupal size classes were maintained in each of 167 mesh-covered, 15 cm by 60 cm by 90 cm aluminum cages. Adults were given a diet of sugar and water, ad libitum, and each day dead flies were removed and counted and their sex was determined. Sex- and size-specific mortality patterns were similar to the broad patterns reported here and the demographic details will be published elsewhere (J. R. Carey *et al.*, in preparation). Complete life tables by sex for the 1.2 million medflies monitored in experiment 3 are contained in J. R. Carey, *Applied Demography for Biologists* (Oxford Univ. Press, New York, 1992).
12. Initial cage densities ranged from 2600 to 9700 flies per cage with a mean of 7260 flies per cage. The correlation coefficient of life expectancy at eclosion versus density for the 167 cages was $r = 0.41$.
13. J. Maynard Smith, *J. Exp. Biol.* **35**, 832 (1958); T. Aigaki and S. Ohba, *Exp. Gerontol.* **19**, 267 (1984); J. R. Carey, D. Krainacker, R. Vargas, *Entomol. Exp. Appl.* **42**, 159 (1986); L. S. Luckinbill *et al.*, *Evol. Ecol.* **2**, 85 (1988); L. Partridge and K. Fowler, *J. Insect Physiol.* **36**, 419 (1990); R. Pearl and S. L. Parker, *Am. Nat.* **61**, 289 (1927); S. S. Ragland and R. S. Sohal, *Exp. Gerontol.* **8**, 135 (1973); R. S. Sohal and P. B. Buchan, *ibid.* **16**, 157 (1981).
14. C. Finch, *Longevity, Senescence, and the Genome* (Univ. of Chicago Press, Chicago, 1990), pp. 248–297.
15. J. W. Vaupel, K. G. Manton, E. Stallard, *Demog-*

raphy **16**, 3 (1979); K. G. Manton, *Milbank Mem. Fund Q.* **60**, 183 (1982); J. W. Vaupel and A. Yashin, *Am. Stat.* **39**, 176 (1985); _____, K. G. Manton, *Math. Popul. Stud.* **1**, 21 (1988); A. Rogers, *Demography* **29**, 31 (1992).
16. R. S. Pearl, L. Parker, B. M. Gonzalez, *Am. Nat.* **57**, 153 (1923); J. Miquel, P. R. Lundgren, K. G. Bensch, H. Atlan, *Mech. Ageing Dev.* **5**, 347 (1976); J. W. Curtsinger, H. H. Fukui, D. R. Townsend, J. W. Vaupil, *Science* **258**, 461 (1992).
17. M. Rockstein and H. M. Lieberman, *Gerontologia* **3**, 23 (1959).
18. Pooled data on 1999 medfly adults reared from different fruit hosts and held in cages of 30 to 80 individuals. D. A. Krainacker, thesis, University of California, Davis (1986); _____, J. R. Carey, R. Vargas, *Oecologia* **73**, 583 (1987).
19. M. Tatar, in preparation.
20. R. E. Beard, in *Biological Aspects of Demography*, W. Brass, Ed. (Taylor and Francis, London, 1971), pp. 75–68.
21. V. Kannisto, *Popul. Stud.* **42**, 389 (1988).
22. A. R. Thatcher, *J. Inst. Actuaries* **109**, 346 (1982).
23. L. A. Gavrilov and N. S. Gavrilova, *The Biology of Life Span: A Quantitative Approach* (Harwood Academic, Chur, Switzerland, 1991), p. 129.
24. A. C. Economos, *Age* **2**, 74 (1979); *Arch. Gerontol. Geriatr.* **1**, 3 (1982).
25. J. F. Fries, *Milbank Mem. Fund Q.* **61**, 397 (1983); *Gerontol. Perspecta.* **1**, 5 (1987).
26. We thank J. Reyes, director of the Moscamed Program in Mexico, directors J. L. Zavala, A. Villaseñor, and W. Enkerlin for use of the facilities in Metapa; H. Celedonio, A. Oropeza, R. Rincon, M. Reyes, H. Esquinca, and C. Fredersdorff for technical assistance; L. X. Li for assistance with data analysis; and A. Clark, M. Tatar, and T. Prout for critical review of the report. Research supported by the National Institute on Aging (grant AG08761-01).

21 May 1992; accepted 18 August 1992

Demography of Genotypes: Failure of the Limited Life-Span Paradigm in *Drosophila melanogaster*

James W. Curtsinger,* Hidenori H. Fukui, David R. Townsend, James W. Vaupel

Experimental systems that are amenable to genetic manipulation can be used to address fundamental questions about genetic and nongenetic determinants of longevity. Analysis of large cohorts of ten genotypes of *Drosophila melanogaster* raised under conditions that favored extended survival has revealed variation between genotypes in both the slope and location of age-specific mortality curves. More detailed examination of a single genotype showed that the mortality trajectory was best fit by a two-stage Gompertz model, with no age-specific increase in mortality rates beyond 30 days after emergence. These results are contrary to the limited life-span paradigm, which postulates well-defined, genotype-specific limits on life-span and brief periods of intense and rapidly accelerating mortality rates at the oldest ages.

A limited life-span paradigm underlies much gerontological thinking (*1*). Individuals are assumed to be born with a maximum life-span potential that is "genetically fixed" (*2*, p. 5). If an individual survives the various hazards that might result in premature death, life will be "terminated by a sharp decline mandated by senescence" (*2*), ending in "natural death" (*2*). Environmental improvement—including better health care and more salubrious behavior in the case of humans—can reduce premature death but cannot delay senescent death (*2*). Fries (*3*) provides the most specific hypothesis for humans: Each individual is genetically endowed with a maximum life-span potential that is approximately normally distributed among individuals with a mean of 85 years and a standard deviation of 7 years.

The limited life-span paradigm as well as Fries's specific hypothesis have come under increasing scrutiny (*4*). We have now performed experiments that directly test the predictions of the limited life-span paradigm in a model system. Our findings are based on a new approach that might be called the experimental demography of genotypes: We have applied methods of demographic analysis to survival data from large cohorts of genetically identical *Drosophila melanogaster* reared under controlled laboratory conditions. The combination of demography and genetics in an experimental setting creates a hybrid perspective that may provide insights beyond those attainable by either field in isolation (*5*).

If there were well-defined limits on life-span, they should produce rapid acceleration in mortality rates and corresponding sharp declines in survivorship at advanced ages in large, single-genotype cohorts raised under conditions that favor survival. The absence of brief periods of intense mortality at advanced ages would constitute evidence against the limited life-span paradigm. Previous experimental studies provide little information on this issue because, as noted by Finch (*6*, p. 16), "survivorship curves are often based on small samples, the curves may not be smooth, and the resulting mortality estimates are not very precise." It is customary in experimental gerontology to use 100 or fewer individuals per strain or treatment, yielding ten or fewer individuals in the oldest 10% of cohorts. Our experiments were designed to provide estimates based on hundreds of individuals in the tail of the survivorship curve.

We used genetically homogeneous lines because age-specific and genotype-specific mortality rates are estimable in cohorts but not in individuals. By studying highly inbred lines, we were able to estimate mortality rates for single genotypes—a feat that cannot be accomplished by studies of heterogeneous populations. We also studied crosses between inbred lines, which are genetically homogeneous in the F_1 generation but lacking in the depression of vigor and life span often associated with complete homozygosity (*7*).

Four highly inbred lines (*8*) of *D. melanogaster* were cultured under standard conditions (*9*) for three generations and then crossed within and between lines to produce ten genotypes: four inbred and six F_1. Genotype "$i \times j$" was produced by crossing females from line i with males from line j. Males of all ten genotypes were collected within 12 hours of emergence, lightly anesthetized with CO_2, and placed in groups of five in 4-dram shell vials with medium. Vials were assigned random locations in a single incubator and were examined daily; the numbers of both live and dead flies were recorded. Flies were transferred to fresh medium once (blocks I, II, and IV) or twice (block III) per week. Four experimental blocks were set up: three with all ten genotypes and one with a large sample of a single genotype.

Average life-spans (days after emergence) for ten genotypes studied in three nonoverlapping experiments are shown in Table 1. Sample sizes varied from block to block because of genotypic variations in fertility. There is statistically significant variation in mean life-span between blocks and between genotypes, as well as block × genotype interaction (*10*). The significant genotypic effect demonstrates genetic variation between lines that influences average life-span and is consistent with previous demonstrations of genetic variation for this character in *Drosophila* (*6*, *11*). The significant interaction, largely due to line 3 × 2 in block III where the estimated longevity was roughly 20 days lower than expected, indicates that genotypes responded differently to microenvironmental variations from block to block. Inbred lines tended to have lower longev-

J. W. Curtsinger, H. H. Fukui, D. R. Townsend, Department of Ecology, Evolution, and Behavior, University of Minnesota, Minneapolis, MN 55455.
J. W. Vaupel, Odense University Medical School, Odense, Denmark; and Center for Demographic Studies, Duke University, Durham, NC 27706.
*To whom correspondence should be addressed.