one or two endogenous circadian pacemakers govern the evening rise and morning fall in melatonin levels is controversial [H. Illnerova and J. Vanecek, *J. Comp. Physiol.* **145**, 539 (1982)]. If the former is the case, the melatonin onset time reflects the phase of the melatonin circadian pacemaker; in the latter case, the onset would mainly be reflecting the phase of the evening circadian pacemaker for melatonin production.

16. Patients were recruited through a newspaper ad in the fall of 1984. They were admitted into the study if they met Research Diagnostic Criteria (RDC) [J. P. Feighner *et al.*, *Arch. Gen. Psychiatry* **26**, 57 (1972)] for a major depression that developed during the fall or winter and remitted the following spring or summer (for at least the last two consecutive years) and had not used psychotropic drugs for at least 2 weeks prior to admission into the study. Control subjects were also screened with the RDC. There was no significant age difference between the two groups. Approximately one-fourth of the subjects in each group was male. In addition, six individuals with winter depression were studied as inpatients on the Clinical Research Center under a related, but different, set of lighting schedules (they were exposed to an additional 15 minutes of light from 0800 to 0815 and from 1645 to 1700 for the entire protocol). Consequently, the results from this group could not be combined with those of the outpatients, even though they were similar.
17. Subjects were instructed to sit at a 45° angle 2.5 to 3 feet in front of a fixture containing eight 40-watt, 4-foot fluorescent lamps and to scan their eyes across the fixture every few minutes. Subjects were randomly assigned to either Vita-Lite (Duro-Test) or cool white (General Electric) lamps for the entire study. Light intensities were approximately 2500 lux for both types of lamps. There were no significantly different effects on any dependent variables; consequently, data from both types of lamps could be combined.
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19. The standard Hamilton scale [M. Hamilton, *J. Neurol. Neurosurg. Psychiatry* **26**, 56 (1960); *Psychiatr. Neurol. Neurochir.* **72**, 201 (1969)] actually underestimates the severity of depression in winter depressive patients, because it includes hyposomnia and weight loss in the ratings; winter depressive patients tend to have hypersomnia and to gain weight when symptomatic.
20. The timing of the melatonin onset was not a result of difference in amplitude, as assessed by overnight collections of urine analyzed for 6-hydroxymelatonin, the major metabolite of melatonin, by the GC-MS technique [M. Tetsuo, S. P. Markey, R. W. Colburn, I. J. Kopin, *Anal. Biochem.* **110**, 208 (1981)].
21. Exposure to bright light in the middle of the day has less of a phase-shifting effect in animals (*13, 14*), although the precise boundaries of this "dead zone" are not known for either normal controls or patients.
22. In one of these studies (*7*), depression ratings fell significantly more under bright evening light than under dim evening light compared to baseline. However, depression ratings under bright evening light were not significantly different from those under dim evening light. These and other light treatment studies are reviewed more comprehensively elsewhere [A. J. Lewy and R. L. Sack, *Proc. Soc. Exp. Biol. Med.* **183**, 11 (1986)].
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25. The previously proposed "phase advance hypothesis for affective disorders" [M. Papousek, *Fortschr. Neurol. Psychiatr. Ihrer Grenzgeb.* **43**, 381 (1975); D. F. Kripke, D. J. Mullaney, M. L. Atkinson, S. Wolf, *Biol. Psychiatry* **13**, 335 (1978); T. A. Wehr, A. Wirz-Justice, F. K. Goodwin, W. Duncan, J. C. Gillin, *Science* **206**, 710 (1979)] states that affective disorders result from an internal phase angle disturbance in which the sleep pacemaker is not as advanced as the temperature pacemaker [whether or not these overt circadian rhythms represent different endogenous pacemakers (*26*), advancing sleep appeared to be transiently effective in ameliorating depressive symptoms in some of these patients]. Just as in these patients sleep was presumably not as phase-shifted (advanced) as their other circadian rhythms, we (*11*) proposed that sleep is not as phase-shifted (delayed) as the other circadian rhythms in the winter depressive patients of the present study. Thus, we think affective symptoms may result from an internal phase angle disturbance of either type. Accordingly, we (*11, 12*) have proposed that patients (who are thought to have a chronobiologic component to their sleep or mood disorder) be "phase typed" on an individual basis: phase-advanced patients should preferentially respond to evening bright light exposure and phase-delayed patients should preferentially respond to morning bright light (holding sleep time constant after it normalizes).
26. With regard to the mathematical models of the human circadian system, our findings appear to be more supportive of the one-oscillator model proposed by S. Daan, D. G. M. Beersma, A. A. Borbely [*Am. J. Physiol.* **246**, R161 (1984)] and C. I. Eastman [in *Mathematical Models of the Circadian Sleep-Wake Cycle*, M. C. Moore-Ede and C. A. Czeisler, Eds. (Raven, New York, 1984), pp. 81–103] than the two-oscillator model proposed by R. A. Wever (*23*) as modified by R. E. Kronauer, C. A. Czeisler, S. F. Pilato, M. C. Moore-Ede, and E. D. Weitzman [*Am. J. Physiol.* **242**, R3 (1982)].
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Wind Speed and Mortality Rate of a Marine Fish, the Northern Anchovy (*Engraulis mordax*)

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Large variability in recruitment of marine fishes creates challenging management problems. In northern anchovy (*Engraulis mordax*), there is a significant linear relation between larval mortality rate and the frequency of calm, low wind speed periods during the spawning season, possibly because calm winds permit maintenance of concentrated patches of larval food. Neither cannibalism on larvae nor offshore transport contributed significantly to interannual variation in early larval mortality. These results are consistent with the hypothesis that wind-driven turbulent mixing affects variability in survival of young fish larvae. However, abundance of recruits does not necessarily reflect abundance of larvae surviving through this early stage.

INTERANNUAL VARIABILITY IN ABUNdance of a new cohort of young fish (recruitment) is usually large in marine fish species (the coefficient of variation is typically 80%) (*1*). In some species, this variability appears to be heavily influenced by large-scale physical processes, and there are correlations in annual recruitment among diverse marine fishes throughout large areas (*2*). Evidence that wind is a cause of variability in recruitment and in larval fish mortality has been found on three time scales: evolutionary, interannual, and daily. First, many marine fish species with pelagic eggs and larvae spawn in seasons and in locations that on average have favorable wind conditions for survival of offspring (*3*). Second, some species show low recruitment indices in years when there is extensive wind-driven transport of water away from larval nursery areas (*4*). Third, days of high winds associated with storms dissipate concentrated patches of food that are vital to survival of larval fish (*5*).

We tested the mechanism of Lasker's "stable ocean" hypothesis (*5*), which states that "the upper mixed layer of the ocean must be in a stable (nonturbulent) state" to generate sufficient concentration of food to ensure good survival of first-feeding larval fish. We used a wind speed index as a measure of turbulent mixing of the upper ocean and tested whether low wind speeds tend to be associated with low mortality. In addition, we tested the relative importance of offshore transport and cannibalism on larval mortality.

To examine these hypotheses, we used data on the central population of the northern anchovy, *Engraulis mordax*, off the coast of southern California. This is one of the most intensively studied marine fish species; detailed data exist since 1954 on adults, eggs, larvae, and relevant oceanographic variables (*6, 7*). Most spawning occurs from January through April (*8*) and the buoyant eggs hatch into yolk-sac larvae after 3 or 4 days (*9*). The yolk sac is absorbed 1 to 3

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days later depending on temperature, and the larvae must find sufficient food within 1.5 to 4.5 days after yolk absorption or their mortality rate increases greatly (*9*). Eighty-five percent of larvae are found within 50 m of the sea surface (*10*); this depth range is rich in food and predators, but is also most subject to disturbance by winds.

We used Lo's (*7*) mortality rates of northern anchovy larvae (about age 5 to 19 days and 4 to 10 mm in length, that is, after yolk-sac absorption). These mortality rates were estimated from ichthyoplankton survey data for 23 years between 1954 and 1984 (*11*). Larval mortalities were high; an average of 95% of each annual cohort died during each sampled 15-day larval period.

Average daily wind speed was derived from synopses of real-time observations (*12*). These daily data covered January through April at 33°N latitude, 119°W longitude, which is in the major spawning area (*13*). From the wind speed data we developed an index that was relevant to survival of fish, as follows. Oceanographic models with parameters empirically estimated for latitudes including southern California waters show that wind speeds of more than 10 m/sec cause turbulent mixing of the upper water column (*14*), which can potentially dissipate patches of concentrated larval food (*5*). At such wind speeds, wind-driven mixing dominates the stabilizing effect of solar radiation on upper ocean structure (*14*). Data suggest that about four consecutive days of calm winds are necessary to maintain the high concentration of food required for good survival of anchovy larvae (*15*). Therefore, we calculated for each year the number of periods per month that had four consecutive days with winds of less than 10 m/sec (*16*). Timing of spawning varies each year and therefore, to account for the effect of winds on larvae, we weighted each month's number of calm periods by the proportion of each year's spawning that occurred in that month, as estimated from the observed monthly egg abundance (*17*). We limited our analysis to the 13 years that had egg abundance estimates for all four main spawning months. The weighted annual wind speed index therefore represented the weighted average number of 4-day periods per month with wind speed below 10 m/sec.

The instantaneous daily mortality rate of northern anchovy larvae was linearly related to this wind speed index (slope and standard error, -0.011 ± 0.002; $r^2 = 0.65$, $n = 13$, $P < 0.001$) (Fig. 1). The standard deviation for residuals from this regression line was 0.040. Years with numerous periods of low wind speeds during the spawning season generally exhibited low mortality. When we used, for those same 13 years, the average

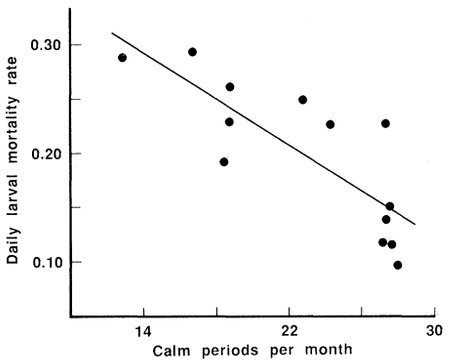

Fig. 1. Average instantaneous mortality rate (M) of northern anchovy larvae in relation to weighted average number of calm 4-day periods per month (x) during the main spawning season, for 13 years. The line represents the linear regression of mortality rate on wind speed index alone [$M = 0.442 \quad (\pm 0.055) - 0.011 \quad (\pm 0.002)x$; $r^2 = 0.65$]. The standard deviation of residuals was 0.040.

number of calm periods per month without weighting by monthly egg abundances, the relation weakened ($P = 0.02$, and the standard deviation of residuals from the line increased to 0.056) showing the importance of the relative timing of spawning and periods of high wind speed.

We tested two other sources of larval mortality: cannibalism and offshore transport of larvae. Cannibalism by adult northern anchovy can account for 20 to 28% of the mortality of their eggs (*18*), and Hunter and Kimbrell (*18*) proposed that young northern anchovy larvae may also be significantly cannibalized by adults. In addition, when larvae of some nearshore marine fishes are found offshore, they appear to suffer high mortality (*4, 19*). To estimate the significance of cannibalism and offshore transport, we fitted a multiple linear regression, $M = b_0 + b_1x_1 + b_2x_2 + b_3x_3$, where M is larval mortality rate, x_1 is the wind speed index, x_2 is annual total biomass (in 10^3 metric tons) of adult anchovy (ages ≥ 1) (*20*) as an index of cannibalism, and x_3 is Bakun's mean monthly estimate of the offshore component of Ekman transport (in cubic meters per second per 100 meters of coastline) (*21*). The resulting coefficient for the cannibalism variable was $3.89 \times 10^{-5} \pm 5.07 \times 10^{-5}$ ($P = 0.46$) and for offshore transport $-2.37 \times 10^{-6} \pm 3.54 \times 10^{-4}$ ($P = 0.99$). Only the wind speed index coefficient was statistically significant ($-8.90 \times 10^{-3} \pm 3.36 \times 10^{-3}$; $P = 0.027$). The standard deviation of residuals from the multiple regression was 0.039, which is virtually the same as that resulting from use of the wind speed index alone in Fig. 1. The wind speed coefficient from the multiple regression was also similar in sign and magnitude to the slope on wind speed estimated from the simple linear regression above.

Adult anchovy biomass and offshore transport contributed little to interannual variation in larval mortality rate compared with wind speed. The range of mortality rates predicted by the model at the mean wind speed and at the extreme observed values of the other two variables is only 13% to −6% of the mean mortality, whereas when the extreme observed values of wind speed are also included, mortality ranges from 58% to −29% of its mean. Therefore, wind speed has a greater effect on interannual variability in mortality during the first 15 days of larval life than does cannibalism or offshore transport (*22*). Offshore transport may be a significant source of variability in recruitment of 1-year-old fish if it affects mortality after the 15-day larval period covered by our mortality data (*23*), but few data on this later stage exist for this stock.

These results support the predicted effects of short-term wind-driven turbulent mixing (*5, 24*), and these effects are strong enough to influence interannual variation in larval fish mortality. Spawning seasons with many high wind speed events were associated with high mortality rate among young larvae of northern anchovy. While wind-driven upwelling of nutrient-rich water could lead to the opposite effect by increasing productivity of larval food, our data show that this process did not offset the detrimental effect of winds. By focusing on a short, well-documented larval period instead of the lengthy egg-to-recruitment period, we increased our statistical power compared with many previous studies. In contrast with findings on other species that emphasize transport mechanisms (*4*), our results are most consistent with Hjort's food hypothesis (*25*) and Lasker's modification of it (*5*).

Although our results support Lasker's proposed mechanism of variability in larval mortality, it does not necessarily follow that abundance of 1-year-old recruits is related to abundance of surviving 19-day-old larvae. Variable mortality after 19 days may tend to destroy such a relation (*23*); more data are needed before a link with recruitment can be established. Nevertheless, our findings add to the understanding of processes that affect mortality of northern anchovy and perhaps other marine fishes.

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$$M = \left[\int_{t_1}^{t_2} (\beta/t)\, P_t\, dt\right] \Big/ \left(\int_{t_1}^{t_2} P_t\, dt\right)$$

12. A. Bakun (Pacific Fisheries Environmental Group, National Marine Fisheries Service, Monterey, CA) provided us with daily wind speed data for 1954 through 1984 (for standard reference height of 10 m). These data were derived from marine observations (archived in National Climatic Center, Tape Data Family 11, Asheville, NC) by use of synoptic wind-pressure analyses.
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15. Histological field data show 35 to 46% mortality per day due to starvation among first-feeding northern anchovy larvae (*19*). Insufficient food in the first 1.5 to 4.5 days of feeding by these larvae can reduce survival substantially (*9*). Because high wind speeds can dissipate food patches, we assumed that calm periods of 4 days are required for good survival through this critical first-feeding period.
16. For example, eight continuous days of low wind speed, followed by one of high wind, were tallied as five overlapping 4-day calm periods, one starting on each of days 1 through 5. This method reflects the uncertain exact date of spawning. If a calm period began in one month but ended in the next month, it was tallied in the month when the calm period began. Although we report only results for analyses based on overlapping calm periods, we did the same analyses based on nonoverlapping periods (the 8-day example above counted as two calm 4-day periods). Because high speed winds were relatively infrequent and clustered in time, these analyses led to identical conclusions in all cases, although significance levels were slightly different. In addition, conclusions did not change when wind speed indices were calculated using two, three, or five consecutive days of low wind speeds as the criterion for a calm period, instead of four.
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22. Although transport is influenced by wind, our wind speed index and the transport variable were not related ($P = 0.94$) because (i) wind direction determines whether transport is offshore or onshore and (ii) our wind speed index is not a summation of daily wind speeds but a tally of days below the 10 m/sec threshold, regardless of wind direction.
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Technical Comments

In Vivo Activation of CD4$^+$ Cells in AIDS

T-CELL ACTIVATION PLAYS A PIVOTAL role in the expression of human immunodeficiency virus (HIV) cultured in CD4$^+$ cells (*1*). Since immunologic activation of HIV-infected CD4$^+$ cells leads to interleukin-2 (IL-2) and interferon-gamma (IFN-γ) production and then to HIV expression and cell death, these processes appear to be closely linked in vitro. Studies of neopterin excretion in risk groups for AIDS suggest the situation is similar in vivo (*2*). Neopterin is a sensitive indicator of T-cell activation, since it is produced from macrophages specifically in response to IFN-γ (*3*), which is secreted from activated T lymphocytes.

However, other studies demonstrate a reduced ability of lymphocytes from patients with AIDS and AIDS-related syndrome (ARC) to react to antigens or to produce IFN-γ in vitro (*4*). It has even been suggested that this failure contributes to the development of opportunistic infections.

While we do not question the validity of the data obtained in vitro, we propose an alternative explanation on the basis of data from studies of patients with systemic lupus erythematosus (*5*). There is an inverse correlation between the concentration of serum IFN and the production of IFN by lymphocytes in culture. The decreased production of IFN-γ in patients with AIDS and ARC appears to be restricted to studies in vitro and thus does not indicate defective IFN-γ production in vivo. Other data also support this view. It has been shown that CD4$^+$ cells from AIDS patients proliferate spontaneously at a higher rate than CD4$^+$ cells from controls (*6*); the blood of AIDS patients contains high levels of thymosin α-1 (*7*), acid-labile IFN-α (*8*), and activated lymphocytes as well as cells expressing the receptor for IL-2 (*9*). These data support the view that the activation of T cells is important as a cofactor for HIV expression not only in vitro (*1*) but also in vivo, and that the decreased production of IFN-γ from cells from AIDS and ARC patients in vitro results from the continuous endogenous exposure to IFN in vivo.

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