It is well established that wild pest and pathogen populations may evolve in response to anthropogenic forces of mortality (1), but is the same true of fisheries? Fishing mortality is highly selective. Exploited stocks typically display greatly truncated size and age distributions that lack larger and/or older individuals (2–4). This occurs not only because fishers may seek to exploit large individuals but also because regulatory measures often impose minimum size or gear regulations that ensure selective harvest of larger fish. Such harvesting practices could favor genotypes with slower growth, earlier maturation, or other changes that would lower population productivity. Despite mounting evidence of rapid life history evolution in wild fish populations (5–8), the unexpectedly slow recovery of populations overexploitation (9, 10), and warnings from theorists (3, 11), current models and management plans for sustainable yield ignore the Darwinian consequences of selective harvest.

Failure to consider evolutionary processes in fisheries management continues in part because proof that size-selective mortality causes genetic changes in population productivity is lacking. Here, we present results from experimentally harvested captive populations of a marine fish that demonstrate evolutionary effects of size-selective mortality on somatic growth, yield, and population biomass.

The Atlantic silverside, *Menidia menidia*, is a common marine fish along the North American east coast. Although landed commercially (mean annual landings in New York, from 1996 to 2000, were 20.5 metric tons), we chose this species as a model primarily for two other reasons. First, many of its life history characteristics are similar to those of other harvested marine species (e.g., high fecundity, small egg size (1 mm in diameter), external fertilization, spawning en masse, pelagic larvae, and schooling behavior), with one major exception. The short generation time of *M. menidia* (1 year) coupled with the ease with which large populations can be maintained in captivity enable experimental designs that would otherwise be impossible. Second, *M. menidia* from different latitudes display clinal adaptive genetic variation in somatic growth rate (12), a geographical pattern common to other harvested species (13–16). Hence, a key production trait (somatic growth rate) appears capable of evolving in the wild in these species.

We hypothesized that somatic growth rate and population levels of harvest would evolve in directions opposite to the size bias of harvest. To test this premise, we founded six captive populations of *M. menidia* by sampling randomly from a large, common gene pool of embryos produced by mass spawnings of adults collected from the middle portion of the species’ range. After the larval phase was completed, 1100 juveniles from each population were stocked in large tanks and reared to the adult stage. Allowing for 10% mortality during the juvenile phase, this resulted in about 1000 fish available for harvest per population. On day 190 postfertilization, 90% of each population was harvested (2, 11).

**Fig. 1.** Trends in average total weight harvested (A) and mean weight of harvested individuals (B) across multiple generations of size-selective exploitation. Closed circles represent small-harvested lines, open squares are the random-harvested lines, and closed triangles are the large-harvested lines. Each data point is the mean, and the vertical lines show the range of two replicate populations per treatment. Regression analyses showed that both total weight and mean weight harvested declined significantly in the large-harvested lines (slope = −0.82, SE = 0.20, *P* = 0.004; slope = −0.75, SE = 0.23, *P* = 0.01, respectively), increased significantly in small-harvested lines (slope = 0.07, SE = 0.26, *P* = 0.03; slope = 0.83, SE = 0.19, *P* = 0.002, respectively), and did not change in random-harvest lines (slope = 0.13, SE = 0.35, *P* = 0.70; slope = 0.21, SE = 0.34, *P* = 0.55, respectively).
In addition to growth, other life history traits changed that may also influence population dynamics in nature. Egg sizes were significantly smaller in the large- than in the small-harvested lines [generation 4: mean egg volumes were 0.61, 0.65, 0.72 mm³ in large-, random-, and small-harvested lines, respectively; nested analysis of variance, $F(2, 6) = 22.7, P = 0.002$], which may affect embryo quality and viability. Larval growth rates evolved in parallel—large-harvested populations evolved slower larval growth than did small-harvested lines (Fig. 4). In nature, slower growth would lengthen larval duration, perhaps leading to increased risk of predation or other sources of larval mortality (17, 18). Work in progress suggests that growth-rate differences result from changes in per capita rates of food consumption. Hence, selection on adult size caused the evolution of a suite of traits likely to influence population growth rate and productivity (19).

Our empirical model is obviously a simple one. Rates of evolution in captive populations of an annual species under controlled conditions may not be directly comparable to the likely rates of evolutionary change in nature where environmental variability, overlapping generations, and longer generation times of most stocks would reduce the efficiency of, and increase the time required for, response to selection on size. Several lines of evidence suggest that evolutionary responses like those described here are likely to occur in the wild. First, a heritability of 0.2 is typical of life history traits (19), and lab-based estimates compare favorably to those from the field in many organisms (20), including fishes (21). Given evidence of rapid life history evolution of fish in the wild (5–8), the potential for evolution in $M$. menidia is not exceptional. Second, the existence of adaptive genetic variation in growth among diverse taxa (12–16) proves that production traits like growth are capable of evolving in the wild. Third, although the selection differentials we imposed were severe, those imposed by fisheries are themselves substantial (22), with rates of fishing mortality often exceeding natural mortality by a factor of 2 to 3, and with stocks displaying greatly truncated size and age distributions, as compared with pre-exploitation conditions (2–4). Fourth, although the generation time of $M$. menidia is short, many longer-lived wild stocks have been harvested for tens or hundreds of generations, which is ample time for evolution.

In wild exploited populations, increased growth resulting from lower fish density may at first obscure the genetic response to selection, unlike in our experiments where density was standardized. Nonetheless, there are well-documented cases where size at age has declined over time in response to fishing (8, 23–25), and over-harvested stocks frequently rebound slowly when fishing ceases (9, 10). Reduced size at age and failure to rebound are consistent with the evolutionary response demonstrated here.

Our study illustrates how well-intentioned management plans that appear to maximize yield on ecological time scales may have the opposite effect after accounting for evolutionary dynamics. Management plans that ignore the evolutionary consequences of fish-
ing may repeat the lessons learned in attempts to control pests and pathogens (J), albeit over a somewhat longer time scale. Moreover, the genetic changes caused by selective harvest may be irreversible; cessation of harvest does not guarantee reverse selection back to the original state (22). Ignoring evolutionary consequences of selective harvest contradicts the precautionary approach to resource conservation.

What forms of management might help to reduce or incorporate evolutionary changes due to selective fishing? First, the establishment of no-take reserves or marine protected areas may, if properly designed, provide for the maintenance of natural genetic variation by allowing a portion of the stock to express an unconstrained range of sizes and growth rates (26, 27). Second, reliance on minimum size restriction (all fish below a given size are protected) as a basis for management needs rethinking. Where feasible, maximum size limits (all fish above a given size are protected) may offer some important advantages: (i) fast-growing fish types that pass more quickly through the period of vulnerability would be favored by selection; (ii) the age structure would broaden, thereby increasing spawning stock biomass; and (iii) the ecosystem services provided by large animals would be restored (2). Harvest regimes that account for the Darwinian effects of fishing need serious consideration if yields are to be truly sustainable.

References and Notes

R E P O R T S
30. We thank J. Travis, E. Schultz, T. Hurst, T. Essington, and three anonymous reviewers for critical comments on the manuscript; and T. Lankford, E. Hillebrand, C. Knakal, and numerous members of the Conover Lab for technical assistance. Supported primarily by the National Sea Grant College Program of NOAA under award number NA86RG0056 to the Research Foundation of the State University of New York for New York Sea Grant, and by a grant from the NSF (OCE-0081916). The views expressed herein do not necessarily reflect the views of those organizations.

Supporting Online Material
www.sciencemag.org/cgi/content/full/297/5578/94/DC1
Materials and Methods
17 May 2002; accepted 5 June 2002

An Essential Role of N-Terminal Arginylation in Cardiovascular Development
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The enzymatic conjugation of arginine to the N-termini of proteins is a part of the ubiquitin-dependent N-end rule pathway of protein degradation. In mammals, three N-terminal residues—aspartate, glutamate, and cysteine—are substrates for arginylation. The mouse ATE1 gene encodes a family of Arg-tRNA protein transferases (R-transferases) that mediate N-terminal arginylation. We constructed ATE1-lacking mouse strains and found that ATE1−/− embryos die with defects in heart development and in angiogenic remodeling of the early vascular plexus. Through biochemical analyses, we show that N-terminal cysteine, in contrast to N-terminal aspartate and glutamate, is oxidized before its arginylation by R-transferase, suggesting that the arginylation branch of the N-end rule pathway functions as an oxygen sensor.

Substrates of the ubiquitin (Ub)–dependent N-end rule pathway include proteins with destabilizing N-terminal residues (1–4). A set of amino acids that are destabilizing in a given cell yields a rule, called the N-end rule, that relates the in vivo half-life of a protein to the identity of its N-terminal residue (1–3, 5–8). The N-end rule has a hierarchical structure. Specifically, N-terminal Asn and Gln are tertiary destabilizing residues in that they function through their deamidation, by N-terminal amidohydrolases (7), to yield the secondary destabilizing residues Asp and Glu, whose activity requires their conjugation, by ATE1-encoded Arg-tRNA protein transferases (R-transferases) (5), to Arg, one of the primary destabilizing residues. The latter are recognized by the Ub ligases (E3 enzymes) of the N-end rule pathway (Fig. 1A) (3, 4, 9).

In mammals, the set of destabilizing residues that function through their arginylation includes not only Asp and Glu but also Cys, which is a stabilizing (nonarginylated) residue in the yeast Saccharomyces cerevisiae (5, 10, 11). ATE1-1 and ATE1-2, the isoforms of mammalian R-transferase, are produced through alternative splicing of ATE1 pre-mRNA and have the same specificity as the yeast R-transferase: They arginylate N-terminal Asp or Glu but not Cys (5). This raises the question of how N-terminal Cys is arginylated in mammalian cells. To address this issue and the physiological functions of arginylation, we constructed ATE1−/− mouse strains (12).

Whereas ATE1+/− mice were apparently normal, the ATE1−/− genotype conferred embryonic lethality (12). The ATE1 allele was marked with NLS-β-galactosidase (βgal) (12). During embryonic day (E) 9.5 to 12.5, the expression of βgal was high in the neural tube and other specific (often sharply delineated) regions of developing embryo (12). ATE1−/− embryos were pale and had thinner blood vessels and frequent edemas of the skin (Fig. 1, B and C; Fig. 2, A and B) (12). Hemorrhages were a consistent feature of ATE1−/− embryos and were the likely proximal cause of their death (Fig. 1, D and E). Of 22 ATE1−/− hearts (E13.5 to E15.5) examined, 85% had a ventricular septal defect (VSD) (Fig. 1, C and J). The atria of ATE1−/− hearts were thin walled, with sparse trabeculae and a large atrial septal defect (ASD) (Fig. 8 refferred to the text).