The Ministry of Public Health will continue to strive to find the best preventive measure to stop the spread of HIV. It is the Ministry's responsibility to further reduce the yearly HIV infection rate in Thailand, which is currently 25,000.

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How Much at Risk Are Cone Snails?

IN THEIR LETTER, "THE THREAT TO CONE snails" (17 Oct., p. 391), E. Chivian *et al.* estimate that "hundreds of thousands" of cone snails are sacrificed annually for research purposes. We recognize that habitat loss and possible overexploitation of cone snails may indeed threaten the survival of *Conus* taxa, but we question Chivian *et al.*'s estimate. This number is huge and shocking in light of the low numbers of individual snails that we as members of the *Conus* and conotoxin research community typically utilize yearly. The techniques we apply require only small amounts of venom, tissue, or mRNA to identify and characterize conotoxin peptides and their gene sequences, and conotoxins are commonly synthesized for analyses of function. For example, Duda and Palumbi (*1*, *2*) sacrificed six specimens to identify 13 unique conotoxins from three *Conus* species, Sandall *et al.* (*3*) used less than 20 specimens to describe a conotoxin from *Conus victoriae* that shows tremendous promise in alleviating pain, and Raybaudi Massilia and colleagues (*4*, *5*) used less than 15 specimens to identify and characterize an unique bioactive conopeptide from *Conus ventricosus*. Moreover, we commonly milk venom from cone snails without sacrificing them (*6*).

Examination of the past 5 years of publications on *Conus* and conotoxins reveals that, at most, 20 research groups or individual researchers actively acquire cone snails from the field for conotoxin or other analyses. Each group would have to process 10,000 animals every year to be responsible for 200,000 *Conus* sacrificed yearly for research purposes, as estimated by Chivian *et al.* (under the assumption that "hundreds of thousands" represents at least 200,000). Based on experience in collecting *Conus* and studies of their maximum densities (*7*, *8*), sample sizes this large would require intensive search effort over large areas and considerable time in the field or teams of collectors. From actual numbers of animals we use and estimates for other research groups, we calculate that on average no more than 5000 animals per year, a number nearly two orders of magnitude less than that of Chivian *et al.*, are likely sacrificed collectively by *Conus* researchers.

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IN THEIR LETTER, "THE THREAT TO CONE snails" (17 Oct., p. 391), one of E. Chivian *et al.*'s recommendations for conserving cone snails is that companies "finance development of culturing techniques…", although they do not state if they are advocating culturing of *Conus* snails or of venom ducts. If the former, they would be well advised to read the pioneering studies of Frank Perron (*1*, *2*), who to date has been the only individual brave enough to try to culture Conidae under laboratory conditions. The multiyear life-span and the complex development of these organisms render this a major challenge for any marine mollusc, and the costs involved have been economically justified only for bivalve species cultured on mass scale for mariculture. Tissue or cell culture from *Conus* venom ducts is likely to be an equally difficult challenge, given the fact that to date, there is only one single molluscan cell line listed in the ATCC catalog, and that is from a freshwater species. The most effective method of conserving the 50,000 or so naturally occurring *Conus* toxins for future generations would be to set up a cDNA and protein extracts bank from 20 or so specimens per species. This is sufficient biological material to identify all toxins in a given venom by EST sequencing (*3*), and this could be followed up by identifying the posttranslational modifications on these toxins by high-resolution mass spectrometry (*4*). The principal threat to wild *Conus* populations, as well as other marine fauna, is most likely habitat loss and destruction. Unfortunately, a CITES listing is woefully inadequate to counteract such a threat.

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Response

WE ARE RELIEVED TO HEAR FROM DUDA *ET AL.* that they believe the extent of cone snail harvesting for research to be far less than we estimated, and we welcome Fainzilber's suggestions for reducing demand for wild-caught animals. Our figure was based on communication with a prominent cone snail researcher at a major university in the United States who had direct knowledge of at least one lab having acquired 1 kg of snail venom ducts, which we calculated would require the sacrifice of some 10,000 snails. We extrapolated from this figure to arrive at our estimated annual harvesting rate for research purposes. Although we acknowledge the anecdotal nature of this estimate, the availability of such a large number of ducts suggests that a well-organized harvesting apparatus is in place, given the difficulties of collecting so many snails, as Duda *et al.* rightly point out. Furthermore, this makes us suspect that this lab is not alone in making use of such services.

It seems clear that no one accurately knows the extent of cone snail harvesting, either for biomedical research or the ornamental shell trade. The latter undoubtedly is many times greater than the research take. There are thousands of known outlets for cone snail shells worldwide, and we estimate, conservatively, that millions of shells are traded annually. Increases in human population and in people's disposable income, combined with a greater globalization of trade, suggest that such exploitation may intensify over time, unless controls, like a CITES listing for cone snails, are enacted. We recognize the present limitations of CITES, which is why we recommend expanding its purview to all wild-caught species, thus moving it from a reactive to a more proactive management mechanism. Listing cone snails would require countries involved in their trade to develop management plans for their sustainable exploitation.

Finally, we agree that protecting the coral reef habitats of these remarkable creatures, in decline partly due to global warming (*1*), is an urgent priority.

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TECHNICAL COMMENT ABSTRACTS

COMMENT ON "Parasite Selection for Immunogenetic Optimality"

Philip W. Hedrick

Wegner *et al.* (Brevia, 5 Sep. 2003, p. 1343) reported that for an MHC gene, three-spined sticklebacks with an intermediate number of alleles appear to have the lowest parasite load. Using a population genetics model, I show that intermediate optimum selection does not generate the observed variation in gene numbers unless an unrealistically high mutation rate is assumed.

Full text at www.sciencemag.org/cgi/content/full/303/5660/957a

RESPONSE TO COMMENT ON "Parasite Selection for Immunogenetic Optimality"

K. Mathias Wegner, Martin Kalbe, Joachim Kurtz, Thorsten B.H. Reusch, Manfred Milinski

Hedrick's model contains some unrealistic implicit assumptions. We argue that variance around the optimal number of MHC alleles is a consequence of the allelic polymorphism of MHC genes. When balancing selection exerted by co-evolving parasites maintains this polymorphism, processes other than mutation—such as linkage and recombination—will inevitably generate the observed variance in allele numbers.

Full text at www.sciencemag.org/cgi/content/full/303/5660/957b