## Genetic Variation in Marine Bivalvia (Mollusca)

Levinton (*1*) has reported that the absolute and effective number of alleles at the phosphohexose isomerase (PHI) (E.C. 5.3.1.9) and leucine aminopeptidase (LAP) (E.C. 3.4.1.1) loci in six species of bivalve mollusks from the Long Island Sound region decreased with depth of burial within the sediment intertidally and with depth of water subtidally. It was concluded that environmental variability regulates genetic variability at these loci.

However reasonable the postulate that environmental variability may alter significantly levels of genetic variability within populations or species, the data presented by Levinton can not be regarded as strong evidence in its favor. The specific hypothesis tested was "that species which burrow more deeply have less genetic variability at these two loci" (*1*). Of the six species analyzed for PHI variability, five can be said to be burrowing forms. *Mytilus edulis*, as rightly stated, is not a burrowing species, and may not be typical of epifaunal mollusks in PHI variability. [In the nonburrowing species *Ostrea edulis*, for example, only two PHI alleles have been detected in a study of more than 300 individuals (*2*)]. The data on one other species (*Mya arenaria*) are, as stated by Levinton, subject to question. Of the remaining species, the least variable—*Nucula annulata*—is a shallow, not a deep, burrower. Indeed this latter species is included more as an example of a subtidal mollusk than as a burrowing species. What significance, within the terms of the hypothesis, is to be placed on the observed differences between the three remaining species is not clear. At the LAP locus, for instance, there is no difference whatever in the actual number of alleles observed in these three species.

As to the other hypothesis tested, at least implicitly—that genetic variability decreases with depth of water subtidally—it appears unwarranted to generalize from a comparison of one subtidal species with five intertidal.

The real value of Levinton's report lies in its exposition of multiple alleles at the PHI locus in a number of bivalve mollusks. We have observed (*3*) similarly high numbers of alleles at this locus in other burrowing and epifaunal species of mollusks on the west coast of Ireland. The significance of these observations certainly warrants thorough investigation at both molecular and ecological levels.

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### References

1. J. Levinton, *Science* **180**, 75 (1973).
2. N. P. Wilkins and N. F. Mathers, *Anim. Blood Groups Biochem. Genet.* **4**, 41 (1973).
3. ———, in preparation.

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If Wilkins limited his point to lack of strong diminution of the absolute number of alleles (*A*) with burrowing depth at the LAP locus, then I would agree. However, the data for *A* at the PHI locus and the data for the effective number of alleles at both loci clearly show the trend that I describe. Further, I disagree with the proposition that *Mytilus edulis* cannot be considered comparatively with burrowing species. After all, *Modiolus demissus* is only semi-infaunal, while *Mercenaria mercenaria* is a very shallow burrower. My selection of species was for the purpose of having a gradational series of epifaunal (zero burrowing depth) to deep infaunal species. I mention the difficulty of producing objective field measures of environmental variability. It is all too easy to look at your data and invoke an ad hoc combination of variables to explain them. This was my reason for choosing burrowing depth, a parameter that can be measured. I do not imply that there are no other factors, stochastic included, that contribute to the variation within my data. This must certainly be true. Although some other authors have come to conclusions similar to my own concerning genetic variability and environmental variability within restricted geographic regions (*1*), Wilkins' and other data (*2*) show that it is not possible to make easily interpretable comparisons of different realms of geography or geologic history at present. Some popular models of genetic evolution are certainly too simplistic. I look forward to further research and spirited discussion of this problem in the future.

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### References

1. J. L. Hamrick and R. W. Allard, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 2100 (197→ M. S. Johnson, *Heredity* **27**, 205 (1971); R. K. Koehn, F. J. Turano, J. B. Mitton, *Evolution* **27**, 100 (1973); J. R. Powell, *Science* **174**, 1035 (1971); G. Wium-Anderson, *Ophelia* **8**, 267 (1970).
2. J. L. Gooch and T. J. M. Schopf, *Evolution* **26**, 545 (197→ F. J. Ayala, D. Hedgecock, G. Zumwalt, J. W. Valentine, *ibid.* **27**, 177 (1973).

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## Vasectomy: Long-Term Effects

Despite the lapse of more than 50 years since vasectomy was first performed for surgical reasons, the long-term effects of this procedure have not yet been completely determined. Nevertheless, Sackler *et al.*'s indictment of vasectomy contained in their opening statement, "Valid social ends do not justify invalid, unscientific means" (*1*), seems premature and unscientific.

The report has several important flaws. Although findings in one species cannot be directly correlated with those in others, these authors extrapolate from their findings in rats to draw conclusions about human vasectomy. The laboratory rat is unique in many ways; certainly with regard to vasectomy, it responds differently from the guinea pig, rabbit, rhesus monkey, and man. After vasectomy, the epithelial cells of the rat epididymis assimilate the dammed spermatozoa (*2*) whereas in the rhesus monkey and apparently in man the blocked spermatozoa are ingested and digested by macrophages (*3*).

Sackler *et al.*'s study was done on immature rats. To base one's conclusions about how vasectomy affects sexually mature human beings on studies performed on immature rats is surely to stretch the limits of valid extrapolation. Moreover, the 17-ketosteroid assay that was used to check the androgen secretion of the testes does not give an unequivocal indication of androgen activity. Dehydroepiandrosterone and some of the corticosteroids contribute more to the urinary excretion of 17-ketosteroids than testosterone and androstenedione (*4*). Perhaps even more importantly, no other studies have shown that vasectomy has effected a change in androgen secretion in man (*5*) or the

rhesus monkey (*6*). Whether or not such changes occur in the rat is irrelevant; the results in the rat should not be interpreted as evidence that the surgical technique affects the androgen output in man in the same way.

While such descriptions as "yellowish cysts" and "purplish coloration" are picturesque, they are no substitute for an adequate histological description. The authors imply that these masses were spermatozoa that had formed cysts in the body; but there is no evidence that they do. A vasectomy without vasoligation is, in effect, a draining fistula that extravasates spermatozoa. The antibodies formed against these spermatozoa probably account for the reduction in the size noted in the testes of the vasectomized group. Histological examination would have resolved this question.

Whether vasectomy is always a safe procedure for permanent contraception remains to be seen. However, to extrapolate from a study on rats to a condemnation of vasectomies for men is hardly warranted.

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#### References

1. A. M. Sackler, A. S. Weltman, V. Pandhi, R. Schwartz, *Science* **179**, 293 (1973).
2. C. J. Flickinger, *Anat. Rec.* **173**, 277 (1972); N. J. Alexander, *Z. Zellforsch. Mikrosk. Anat.* **136**, 177 (1973).
3. N. J. Alexander, *J. Reprod. Fertil.* **31**, 399 (1972); A. M. Phadke, *ibid.* **7**, 1 (1964).
4. H. J. van der Molen, in *The Androgens of the Testis*, K. B. Eik-Nes, Ed. (Dekker, New York, 1970), p. 145.
5. R. G. Bunge, *Invest. Urol.* **10**, 9 (1972); R. G. Wieland, M. C. Hallberg, E. M. Zorn, D. E. Klein, S. S. Luria, *Fertil. Steril.* **23**, 279 (1972).
6. J. A. Resko and C. H. Phoenix, *Endocrinology* **91**, 499 (1972)

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To characterize our comment that "valid social ends do not justify invalid, unscientific means" as seemingly "premature and unscientific" is remarkable. It is not made less so by terming our report an "indictment of vasectomy." Perhaps our comment may be viewed against Alexander's (*1*) first sentence: "Despite the lapse of more than 50 years since vasectomy was first performed for surgical reasons, the long-term effects of this procedure have not yet been completely determined." The qualification "completely" is noteworthy. It was precisely the paucity of both short-term and long-term experimental and controlled clinical studies that led to our animal investigation.

Our conclusion pointed to "the need for caution and extensive investigations in man before recommending vasectomy as a simple, innocuous, 'physiologic' means to ensure conceptual control" (*2*). The extrapolation from rats to man is Alexander's. Our report clearly stated that we were studying immature rats; that it "remains to be determined whether a comparable reduction in weight of testes or of the urinary 17-ketosteroids (or both) would be reproducible in mature rats," let alone mature man. The 17-ketosteroid assay is not and was not claimed to be an "unequivocal indication of androgen activity." We, likewise, doubt that the cited findings of no change in androgen secretion in ten vasectomized monkeys studied (*3*) over an 18-month period to be an "unequivocal indication of androgen activity," long-term in vasectomized man. Neither do we believe that the pre- and postvasectomy findings of plasma testosterone on 50 consecutive healthy males, 4 weeks after vasectomy, as having "completely determined" all the short-range effects of vasectomy on testosterone secretion (*4*). Alexander's observation, "Whether or not such changes [in androgen secretion] occur in the rat is irrelevant," may truly be, or may not be irrelevant. What is not "irrelevant" are the findings of cysts in the cauda epididymis and vas deferens regions in our vasectomized and vasoligated rats because spermatic granulomas in the vas deferens and/or epididymis have been reported in man as a complication of vasectomy (*5*). No reference is made to our findings of significant increases in white blood cell counts even though she refers to the findings of antibodies against spermatozoa [which has been reported by Shulman (*6*) in man]. Alexander assumes that a "vasectomy without vasoligation is, in effect, a draining fistula that extravasates spermatozoa." This assumption may be invalid in the rat. It is inconsistent with our observation postmortem (28th week) that occlusion of the severed proximal end usually, if not always, occurred.

Because of space limitation we could not include a full pathologic report on the testes, epididymis, vas deferens and cysts rather than simple "picturesque" comment on gross pathology (*7*).

We are sensitive as to the uniqueness of the laboratory rat, and perhaps also the rabbit, in respect to vasectomy, but we are likewise sensitive to the uniqueness of man. Some comments on our report seem distinguished more by zeal or emotional content than by a desire to examine the physiological innocuousness of a surgical procedure that has become so routine that it has been performed upon millions of males throughout the world. Does not one "stretch the limits of valid extrapolation" when one simply assumes from uncontrolled, clinical assumptions and a limited world literature the innocuousness of a surgical procedure which is then practiced routinely on man by the millions? We have not extrapolated a condemnation of vasectomy in man from a single study, but rather have suggested "that pending extensive study of the endocrine and somatic effects of vasectomy in man greater caution be observed in the use of vasectomies as a routine contraceptive procedure." Suitable conception control techniques can only be safely and physiologically defined by the most rigid adherence to scientific criteria in the study of long- as well as short-term effects in man.

Since the writer of the critical letter states, "Whether vasectomy is always a safe procedure for permanent contraception remains to be seen," then surely she must be in agreement with the central thrust of our thesis. The burden of proof as to the safety of vasectomy rests upon those who would promote and practice it, while the demonstration of its innocuousness "remains to be seen."

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#### References

1. N. J. Alexander, *Science* **182**, 946 (1973).
2. A. M. Sackler, A. S. Weltman, V. Pandhi, R. Schwartz, *ibid.* **179**, 293 (1973).
3. J. A. Resko and C. H. Phoenix, *Endocrinology* **91**, 499 (1972).
4. R. G. Bunge, *Invest. Urol.* **10**, 9 (1972).
5. N. B. Friedman and G. L. Garske, *J. Urol.* **62**, 363 (1949); F. J. Glassy and F. K. Mostofi, *Am. J. Clin. Pathol.* **26**, 1303 (1956); S. S. Schmidt, *Fertil. Steril.* **17**, 467 (1966).
6. S. Shulman, E. Zappi, U. Ahmed, J. E. Davis, *Contraception* **5**, 269 (1972).
7. A. M. Sackler, A. S. Weltman, V. Pandhi, L. Johnson, *Fed. Proc.* **32**, 310 (1973).

27 September 1973