Letters

Detecting Colon Cancer

The Research News article "Debate over colon cancer screening" by Gina Kolata (16 Aug., p. 636) focuses primarily on the usefulness of the Hemoccult test in detecting cancer of the colon. Julian Simon is quoted as stating that the major flaw of the test is the number of false positives that occur, such that only 5 to 10 percent of the positives are found to provide evidence of colon cancer.

I believe this underestimates the true predictive value of the test. Reports on results of screening populations with the Hemoccult test, including two randomized trials at Memorial Sloan-Kettering Cancer Center and the University of Minnesota, have shown that 15 to 40 percent of those whose tests were positive had adenomatous polyps of the colon. These polyps are well known as colon cancer precursors. Thus if one assesses the predictive value of a positive Hemoccult test overall for the detection of colorectal neoplasia, the result is generally in the 25 to 50 percent range.

Indeed, it is in the detection and removal of polyps that the test is likely to exhibit its greatest efficacy with regard to the prevention of colon cancer mortality. The finding of an invasive colon cancer, even in an early stage, as occurred with President Reagan, still leaves a substantial risk of cancer mortality, besides the morbidity associated with the necessary surgical procedures. The removal of an adenomatous polyp is generally an outpatient procedure with minimal morbidity and results in the prevention of an invasive cancer.

From the public policy point of view, this benefit is likely to be least observable. The observation of a reduction in mortality in a randomized controlled trial would require a follow-up period of 15 to 25 years in order to incorporate the benefits of polypectomy because of the long latency period involved. This is illustrated by Gilbertsen's uncontrolled evaluation of sigmoidoscopy for screening (*1*), which required a follow-up period of 25 years but showed a substantial reduction in rectal cancer mortality. Similarly, the benefits of Pap smears for cervical cancer screening probably result in large part from the detection of cervical dysplasia and carcinoma in situ rather than from the detection of early invasive cancer.

Thus, despite our laudable desire for "hard" scientific evidence of a reduction in mortality in a randomized trial, I believe we shall need to rely for the foreseeable future on our judgment and intuition in reaching conclusions in this area. The relative simplicity and positive predictive value of the Hemoccult test, as well as the low morbidity associated with colonoscopy would justify the current recommendations of the American Cancer Society until evidence to the contrary is available.

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References

1. V. A. Gilbertsen, *Cancer* **34**, 936 (1974).

Kolata's article on colon cancer screening describes some of the issues in a debate about a very important, complicated, and potentially confusing problem. However, I do not remember making two statements attributed to me at the end of the article. I happen to agree with one point I am quoted as attributing to critics ("The critics say the practice of medicine ought to be based on scientifically valid principles"), and I cannot even understand the other point ("The time should end when we do things because we think it would be good").

For the record, I believe in practicing medicine according to scientifically valid principles, and I believe in doing good. In fact, most participants in discussions about medical procedures agree on these goals. We also agree on the need to carefully estimate and balance the benefits, risks, and costs of a procedure before making recommendations or taking action. The real questions are how much and what type of evidence is needed to estimate benefits, risks, and costs.

When a medical procedure is evaluated, it is obviously desirable to have one or more randomized controlled trials (RCT's) that give unequivocal results. If that is the case, we are lucky. Unfortunately, very few medical procedures are backed by unequivocal RCT's, and to demand this kind of evidence would end a large part of medical practice. If we do not have unequivocal RCT's, there are several choices: (i) assume the procedure is not effective until "proved" otherwise (by an RCT), and reject the procedure; (ii) assume a procedure is effective until proved otherwise by RCT's, and use the procedure; (iii) look at one or two easily visible factors (for example, the sensitivity or false-positive rate of a screening procedure) and decide on the basis of those; or (iv) "scramble" harder to look at all the evidence and weigh it as best we can.

I propose the latter, with the provisos that great care be taken to incorporate all the important factors, to evaluate all the evidence about each factor fairly, and to combine the evidence according to scientific principles (for example, the axioms of logic, mathematics, and probability theory). The drawback of this approach is that for complicated problems, such as colon cancer screening, it is virtually impossible to do all these things in our heads. This explains the attractiveness of the first three choices; the gross oversimplifications, errors, and biases that commonly occur in the evaluation of medical procedures; and the frequency of disagreements. In such cases it can be helpful to write things down—to build a model. The role of a mathematical model is to help keep everything straight: you can include all the important factors, you are forced to state your assumptions explicitly, the model will perform all the calculations accurately, it can estimate the consequences of different options, you can explore the impact of uncertainty, and the entire analysis is open for review.

This is not a retreat from scientific principles; it is the use of scientific principles.

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I regret that Eddy's remarks were not clear in the context of my story. When Eddy told me, "The critics say the practice of medicine ought to be based on scientifically valid principles," he was speaking of investigators who believe that medical decision-making should hinge on results of randomized controlled clinical trials. Those are the "scientifically valid principles." When he

told me that critics say, "The time should end when we do things because we think it would be good," he interpreted it as implying that, according to the critics, we should stop making medical decisions on the basis of clinical impressions or less-than-ideal studies and should instead wait for the results of randomized controlled trials.

—GINA KOLATA

Predator and Prey Behavior

Charles W. Thayer (Reports, 28 June, p. 1527) makes a strong case that it is the "shell-protected" tissue of the brachiopod *Terebratalia* that predators find repellent, and my own observations do not refute this conclusion (*1*). But the cover photograph accompanying the paper shows that the brachiopod is covered by a variety of epibionts, notably sponge. Epizoitic sponges can influence the ecology, habit, and even morphology of their hosts (*2*) and, in the case of some pelecypod molluscs, may reduce the effectiveness of predators and so enhance survival.

Influences on predator and prey behavior in the wild are manifold, interactive, and subtle. Consequently, it is important to take into account as many factors as possible when speculating on their underlying mechanisms—especially when extrapolating from field and laboratory experiments to explain a major paleoecological phenomenon such as the "post-Paleozoic decline of articulates."

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References and Notes

1. *Terebratulina* from the Bay of Fundy bear a heavy growth of epizoitic sponge (A. Logan, personal communication). Unpublished observations by A. J. Forester showed that starfishes preferred mussels to brachiopods. Predation on the brachiopods was too low to determine whether the presence of epizoitic sponge conferred protection or not.
2. A. G. Beau, *Trans. R. Soc. N. Z.* **7**, 93 (1965); S. A. Bloom, *J. Exp. Mar. Biol. Ecol.* **17**, 311 (1975); M. L. Forbes, *Bull. Mar. Sci. Gulf Caribb.* **14**, 453 (1964); *ibid.* **16**, 273 (1966); A. J. Forester, *J. Exp. Mar. Biol. Ecol.* **36**, 1 (1979).

There is no doubt that sponges (and probably other epizoa) influence predation on benthos, including brachiopods. I was aware of Bloom's results when beginning my experiments. Epibionts were removed prior to laboratory tests and field transplants. Contrary to Forester's impression, the cover photograph was not part of any experiment. It does, however, show mature brachiopods (approximately 10 years old) that have obviously not been eaten.

The in situ caging experiment used as much of the undisturbed "real world" as possible to assess the kinds of effects Forester mentions, and epizoa (including a sponge usually associated with *Terebratulina,* the most abundant brachiopod) were not removed. The relatively high mortality of brachiopods in this experiment indicates that alternative prey (mussels) are more effective than epibionts in reducing predation.

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Modern Paleontology

I strongly sympathize with the feelings expressed by Farish A. Jenkins, Jr., *et al.* (Letters, 26 July, p. 330). However, I am not certain that the basic issue, as exemplified by the action of the Princeton Geology Department's getting rid of its fossil collections and getting out of the business of teaching paleontology, is that simple. Over the past 20 years it has begun to become clear that more than one of our leading departments of earth science have given up the serious pursuit of paleontology as a discipline involving full-time faculty and graduate student research. What we are apparently seeing is a slow, steady shift of paleontology (or "paleobiology," as it is now sometimes called) from departments of geology into departments of biology. Possibly departments of geology are just too overextended, what with the need for in-depth training in geochemistry and geophysics at the undergraduate level, to be able to cope with paleobiology-paleontology on a modern basis.

Perhaps what we should be doing is vigorously encouraging departments of biology to incorporate a modern approach to paleontology (the study of the life of the past and the history of life) as an integral part of the training necessary for first-rate scientists. Think how invigorating it can be to consider physiologic, biochemical, embryologic, immunological, and parasitic problems—to name a few—on an evolutionary basis buttressed by a sound background in the fossil record, rather than in the all-too-common "cookbook" manner. Possibly we should consider that the geology department's loss is the biology department's gain. I wonder whether the modern biology department could not do a much more effective job with paleontology than does the modern geology department. Perhaps biology departments have been deprived of their "roots" for too long. Certainly 19th-century biology felt comfortable with fossils and profited greatly from the association. It is entirely possible that many of the 20th century's biological problems would also benefit from a more historical viewpoint.

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Evaluations

Daniel E. Koshland, Jr.'s, editorial on "The undesirability principle" (5 July, p. 9) is of considerable interest to a member of Section X, who may or may not soon find herself transmuted into a maker of Social Policy; and especially to one who has just returned from a New England resort where the question of "How many tourists overwhelm the pleasures they have come to enjoy?" is already pressing.

May I, however, challenge Koshland's recommendations for dealing with the problem: "[C]hemical companies advocating less regulation would be required to detail the dangers to water supplies of minimal regulation. Environmentalists advocating stringent precautions would be required to state the cost to the consumer."

I daresay these interested parties should be heard from, but why should the consumer trust their evaluations? "Quis custodet ipsos custodes?" Or is the AAAS about to be invited to evaluate the evaluations?

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Who evaluates the evaluators is an excellent question. My answer would be, whoever is making the decision, Congress, public opinion, or judges, for example. Proponents of a particular position who have competently considered all aspects of other proposals would necessarily have higher credibility than others who reveal a cavalier disregard of the costs, dangers, et cetera of their courses of action.

—DANIEL E. KOSHLAND, JR.