Ribonucleases in Ruminants

Jaap J. Beintema;, *et al.*

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On Stephen Jay Gould

AN IMPORTANT ASPECT OF STEPHEN J. Gould's life that was only referred to in passing in R. A. Fortey's otherwise excellent obituary (Retrospective, 14 June, p. 1984) is Gould's radical politics. Although it is not well known in the United States, Gould was a lifelong Marxist, and his science as well as the rest of his life was informed by this intellectual background.

Gould grew up in a family environment that was politically to the left, and his father was a Marxist (*1*). He remained politically active throughout his life, organizing demonstrations against racial segregation, opposing the Vietnam war, and showing up on picket lines. He participated in Science for the People, a radical science organization that emerged from the anti-war movement.

Gould's scientific work and science writing showed the influence of his political background and thought. He battled with creationists who were trying to suppress scientific explanations of our origins. He engaged in intellectual struggles with other scientists and public figures who believed that human behavior is innate and genetically hardwired. In particular, he responded to the initial public enthusiasm associated with the emergence of sociobiology—which presented the position that traits such as aggression and xenophobia are genetically based—by emphasizing the enormous flexibility of human behavior. Although he recognized violence, sexism, and general nastiness as biological because they represent one subset of a possible range of behaviors, he emphasized that peacefulness, equality, and kindness are just as biological and pointed out that we may see their influence increase if we create social structures that enable them to flourish.

Gould has been described as one of the few American scientists who came forward as a major public ally of the Left and as a formidable example of a supportive presence at Left events and causes. We should not dismiss this aspect of his life, as it was central to his character and provided the context of his thinking as a scientist and as a human being.

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Reference
1. See www.edge.org/documents/ThirdCulture/i-Ch.2.html.

Correction

IN OUR REPORT "EVIDENCE FOR AN ANCIENT osmium isotopic reservoir in Earth" (19 April, p. 516), we presented isotopic data from Os-rich alloys from peridotite bodies in the Klamath Mountains, United States. To explain the data, we proposed that Os was transported in plumes from Earth's core to the upper mantle, where the alloy formed. Previously, Bird *et al.* (*1*) presented similar Os isotopic data from these rocks and proposed that these alloys formed in the core or core-mantle boundary region and were then transported upward by plumes. We should have referred to this paper and discussed its similar data and conclusions.

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Reference
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Political, Not Scientific, Birth Control Solutions

IN THE ARTICLE "RESEARCH ON CONTRACEPTION still in the doldrums" (C. Holden, Reproductive Biology Special Issue, News, 21 June, p. 2172), the title and lead paragraph assume that "there's a particularly pressing need for new forms of fertility control" to solve demographic problems. This grossly oversimplified cry for a technological fix has often been debunked (*1*). Holden ignores the well-documented fact (*2*, *3*) that 12 to 20 years is the minimal time for development of practical new contraceptive "hardware," during which time the Third World's population will increase by 1 to 2 billion. Hence, the focus must remain on improvements in birth control "software"—the crucial cultural, economic, public health, and women's rights issues that have been shown to work with existing methods.

The remarkable drop in birthrate in China (the world's most populous country) or Mexico (11th most populous) in the past two decades was accomplished solely through "software" implementation using existing "hardware." Even Japan's population, in spite of a limited birth control armamentarium (the Pill was only legalized in 1999), has been below replacement level for years. Thus, it is nonsense to think that the dismal demographic facts of, for instance, Pakistan or Nigeria will be solved by some new birth control method. It is shameless grantsmanship to suggest that more money for the truly exciting scientific advances outlined elsewhere in the Reproductive Biology Special Issue of *Science* will lead within the next two decades to any new practical contraception. The pharmaceutical industry focuses quite understandably on diseases (Alzheimer's disease, inflammation, cancer, and so forth) of the affluent, geriatric countries, rather than some new "cheap, safe, reliable, convenient, reversible, and culturally acceptable" contraceptive for the pediatric, Third World countries. It is the word "cheap" (indispensable for the Third World) and the long development times (*2*) that keep the pharmaceutical industry out of the birth control field. Calling skin patches, implants, or vaginal rings of old steroids "new" is a vain attempt to sugarcoat a bitter pill. Only industry can convert basic new science into practical birth control, and, as correctly stated in the article, that boat has sailed. Software improvements are the province of governments, not industry. The solution is political, not scientific, and it ill behooves *Science* to offer politicians an illusionary excuse.

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A Birth Control Alternative

"RESEARCH ON CONTRACEPTION STILL IN THE doldrums" (C. Holden, Reproductive Biology Special Issue, News, 21 June, p. 2172) is an excellent review of the birth control field, with one glaring exception. It omits "sterilization," specifically trancervical chemical sterilization using Quinacrine, which is the most important advance in birth control since the Pill. In an office procedure requiring only 5 min, 252 mg of Quinacrine in pellets is inserted into the uterus. The medication dissolves and flows into the oviducts (Fallopian tubes), where an inflammatory reaction leads to scar blockage. The procedure must be carried out twice, a month apart, and the scars can be seen on ultrasound.

Quinacrine sterilization (QS) is one-tenth the cost and has one-fiftieth the complication rate of surgical sterilization involved in laparoscopy. Kessel (*1*) reported 100,000 documented cases of QS with no mortality and no complications serious enough to require surgery. The evidence for the safety of this drug is overwhelming. It has been taken in large doses by more than 100 million people for over 70 years to treat and prevent malaria and is also used to treat giardia, tapeworm, lupus, and rheumatoid arthritis. Jaimie Zipper, who developed the method (*2*), has followed 1500 patients for over 20 years and reports no serious long-term effects, and there is no evidence of any increase in the incidence of cancer (*3*). It was not surprising that the U.S. Food and Drug Administration (FDA) granted approval for a phase I clinical trial of QS to be carried out at the Children's Hospital of Buffalo. This is nearly completed, and filing for FDA approval of phase II/III is being prepared.

Side effects of QS include itching, cramps, and headache, transient events that are easily managed. Although the pregnancy rate with Quinacrine is higher than with surgical sterilization (about 2% for QS versus about 1% for surgical sterilization), there are serious problems associated with surgery itself: The trocar may perforate the bowel, bladder, or the great blood vessels of the pelvis, or the cautery may burn viscera. None of this occurs with QS. Laparoscopic tubal ligation carries an admitted risk of three to 10 deaths per 100,000 (*4*, *5*). Surgical sterilization requires a general anesthetic with attendant risks, whereas QS needs no anesthesia.

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Ribonucleases in Ruminants

IN THE RECENT REVIEW BY S. A. BENNER *ET al.* ("Planetary biology—paleontological, geological, and molecular histories of life," 3 May, p. 864), Fig. 4 shows an evolutionary tree, which was previously published by the authors (*1*) and which was reproduced from a 1986 paper of ours (*2*), with two changes: (i) A clade of pronghorn antelope and giraffe is not connected with bovids, but with deer, and (ii) hippopotamus and pig are joined, contrary to our finding that they are separate divergences from an ancestral artiodactyl (*2*). The sepa-

rate divergence would seem to be more in agreement with Benner *et al*.'s review.

During the Oligocene cooling, rumination or ruminant-like digestion evolved with adative changes in the ribonuclease molecule three times: (i) in the hippopotamus, after its divergence from the ancestor of the cetaceans (whales and so forth), (ii) in an ancestral tylopod (after one ribonuclease duplication), and (iii) in an ancestral ruminant (after two ribonuclease duplications), leading in all three cases to pancreatic ribonucleases that were better adapted to dietary requirements (*3*, *4*). Recently, Zhang *et al*. (*5*) demonstrated very similar adaptations to ruminant-like digestion in ribonuclease structure and function after a duplication in the ancestor of leaf-eating monkeys.

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Response

IN THE "POSTGENOMIC ERA," STUDENTS RARELY learn that before DNA synthesis (and, therefore, DNA sequencing) became routine, the sequences of proteins were obtained directly from the proteins themselves. Much of this demanding work was directed toward understanding how proteins evolve. Beintema and his co-workers did much of the heavy lifting in this area. Indeed, many current papers in comparative genomics, proteome sequence analysis, and functional annotation are today simply rediscovering what has been known since the 1980s through research enabled (in part) by Beintema's efforts.

As Beintema points out, the great Oligocene cooling had repercussions throughout the biosphere and in many orders of mammals. This included the emergence of ruminant-like digestion in several mammalian lineages, including nonhuman primates.

The human genome also contains a record of adaptation in the Oligocene. Much of the change appears to be focused on the nervous system. This suggests that whereas the ancestor of the ox may have learned to eat grass to survive this global cataclysm, the ancestor of humans became more intelligent. This perhaps prepared humankind to adopt the "generalist" adaptive strategy that became so important during the climatic fluctuations of the Ice Ages, leading to the ascendency of humans as the dominant large animals on the planet today.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

A Soldier's View of the USAMRIID

IN MARTIN ENSERINK'S ARTICLE "ON biowarfare's frontline," (News Focus, 14 June, p. 1954), the detractors of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), as well as Enserink, neglect to mention its most crucial and fundamental function, which is the basis for all the actions that seem so inexplicable to civilians. USAMRIID is an organ of the U.S. Army. Its ultimate focus and purpose are to save the lives of soldiers. It is funded by U.S. taxpayers, and it has to answer to the Congress for how it spends that money.

The idea that the managing officers of USAMRIID are obsessed with being promoted is unfair and unreasonable. There is nothing wrong with working for a promotion; civilians do it all the time. If an officer or an enlisted person isn't promoted, they're put out of the Army.

Frequent transfers aren't contrived to annoy civilian co-workers—they're a vital tool to developing a soldier's career. An Army doctor who has spent his entire career working with civilian researchers in Ft. Detrick, Maryland, isn't going to be able to function in a combat environment. He's expected to be able to perform more than his specialty, and the only way to achieve a multifaceted experience is to be transferred to different environments. Combat zones aren't characterized by state-of-the-art hospitals or research labs. Usually, it's a tent or a small building, with only as much light as a diesel generator can muster. Soldiers die in combat zones, and if your only neurologist dies, your podiatrist is going to have to do the neurologist's job. Ultimately, an Army doctor is more than just a doctor—he's also a soldier.

The "ticket punches" that C. J. Peters complains about aren't merely catered tea parties in the general's flower garden—they're advanced courses in combat and warfare. An Army doctor is expected to provide medical care to wounded soldiers, but he's also expected to be able to administer a hospital in a combat zone. That means ensuring that there are enough medical supplies and organizing water, food, fuel, shelter, clothing, ammunition, medical and support personnel, air and ground vehicle support, patient care, and defense of the hospital itself. He also must be capable of moving that hospital at a moment's notice.

When the civilian ax-grinders understand that the USAMRIID is an Army facility, perhaps then they will understand why it operates the way it does.

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Image not available for online use.

USAMRIID researchers at work in a high-containment laboratory.

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CORRECTIONS AND CLARIFICATIONS

REPORTS: "A new skull of early *Homo* from Dmanisi, Georgia" by A. Vekua *et al.* (5 July, p. 85). Captions for two of the panels in Fig. 2 were transposed. Fig. 2D should have been identified as the inferior view, and Fig. 2E should have been identified as the posterior view.

RANDOM SAMPLES: "Biotech boomtowns" (5 July, p. 47). On the map that illustrated the distribution of urban areas in the United States having a major biotechnology industry presence, the marker for the cities of Raleigh and Durham, North Carolina, was erroneously placed within the boundaries of the Commonwealth of Virginia.

REPORTS: "Bmf: a proapoptotic BH3-only protein regulated by interaction with the myosin V actin motor complex, activated by anoikis" by H. Puthalakath *et al.* (7 Sept., 2001, p. 1829). In Fig. 1A, the sequence lables are switched: The sequence for mouse Bmf represents human Bmf, and the sequence for human Bmf represents that for mouse Bmf. The sequences submitted to GenBank are attributed to the correct species. Also, in the supplementary material, there is a single letter error in one of the PCR primers mentioned. The correct sequence for the reverse PCR primer for bmf is 5′CAGAGCTGACAAAGGCAcAG3′.