A Cry for Help from Kansas

DEAR LADIES AND GENTLEMEN OF THE American Science Community: As I write this from my troubled home state of Kansas, the State Board of Education is debating once again whether to de-emphasize the theory of evolution. Those in the majority on the Board have stated that they are considering changing the very definition of science to allow for science classes to discuss the merits of intelligent design. Kansas Attorney General Phill Kline has said that he would defend the Board's actions.

Kansas may be a far-off, conservative state for most of you, largely unimportant in the affairs of your professional lives, but this is a strong indicator that the very foundation of science in the United States is at risk.

> "What a shame it would be if unqualified politicians succeed in undoing centuries of scientific progress in both the public's perception of science and its continuing advancement."
>
> –REYNOLDS

Other states have had this problem recently, including Georgia, Alabama, and Ohio, and this could happen to your state. What a shame it would be if unqualified politicians succeed in undoing centuries of scientific progress in both the public's perception of science and its continuing advancement. This is a wake-up call, ladies and gentlemen. Please don't let this happen in your state.

You may write to the Board by visiting their Web site at www.ksbe.state.ks.us/Welcome.html.

ERIC REYNOLDS

Overland Park, KS, USA.

What Causes Lesions in Sperm Whale Bones?

THE DESCRIPTION OF "EXTENSIVE PROLIFERATION and remodeling of cartilage and woven bone" in sperm whales in the intriguing Brevia by M. J. Moore and G. A. Early ("Cumulative sperm whale bone damage and the bends," 24 Dec. 2004, p. 2215) is not compatible with their diagnosis of avascular necrosis (osteonecrosis). Avascular necrosis, attributed to bends, has been clearly documented in extinct whales (*1*). Absence of reactive new bone formation around areas of dead bone is visualized as intraosseous clefts or as articular subsidence, producing a depressed zone (*2*–*5*). Moore and Early's description is compatible with another known cetacean disease, spondyloarthropathy (*5*, *6*). This disorder is especially common in the cetacean *Lagenorhynchus*, and zygapophyseal joint erosions of spondyloarthropathy have also been found in a blue whale (*7*).

The reported frequency of sperm whale "avascular necrosis" is compatible with the 100% reported in certain genera of extinct mosasaurs (*2*), but substantially greater than the frequency of spondyloarthropathy found in other mammals (*5*). While Moore and Early's diagnosis of avascular necrosis cannot be substantiated, the pathology frequency they suggest is also outside anticipated ranges (5 to 50%) for spondyloarthropathy in mammals (*5*, *8*). Examination of their fig. 1 clearly explains the apparent variation. The figure illustrates bone character underlying normal articular surfaces and the subchondral erosions of spondyloarthropathy (*5*, *9*). The undulating surface with visible pores (in most of the sections) is characteristic of normal subchondral bone. Also illustrated is erosive damage with reactive new bone formation, characteristic of spondyloarthropathy (*4*, *5*, *8*).

BRUCE M. ROTHSCHILD

Arthritis Center of Northeast Ohio, Northeastern Ohio Universities College of Medicine, 5500 Market Street, Youngstown, OH 44512, USA.

References

1. B. M. Rothschild, A. Saunders, *J. Vertebr. Paleontol.* **17**, 72A (1997).
2. B. M. Rothschild, L. D. Martin, *Science* **236**, 75 (1987).
3. B. M. Rothschild, G. Storrs, *J. Vertebr. Paleontol.* **23**, 324 (2003).
4. D. Resnick, *Diagnosis of Bone and Joint Disorders* (Saunders, Philadelphia, PA, 2002).
5. B. M. Rothschild, L. D. Martin, *Skeletal Impact of Disease* (New Mexico Museum of Natural History Press, Albuquerque, NM, 2005).
6. E. O. Kompanje, *Z. Saeugetierkd.* **58**, 316 (1993).
7. B. M. Rothschild, V. Naples, *Ann. Rheumat. Dis.*, in press.
8. B. M. Rothschild, C. Rothschild, *Paleontol. Soc. Publ.* **8**, 330 (1996).
9. A. Boyde, E. C. Firth, *J. Anat.* **205**, 491 (2004).

IN THEIR BREVIA "CUMULATIVE SPERM WHALE bone damage and the bends" (24 Dec. 2004, p. 2215), M. J. Moore and G. A. Early interpret ontogenetically progressive, chronic osteonecrosis in specimens collected over 111 years as being caused by nitrogen emboli—with variations from or exogenous disruptions (anthropogenic sonar) to diving patterns possibly causing acute embolic disease.

However, their sample is from the post-1860s mechanized whaling era, with exposure to effects of both luse-jag—stalking to surprise prey—and prøysser-jag—persistent direct chasing to run down prey. An alternative hypothesis is that all the observed effects are related to human impacts and are not

Socializing sperm whales

biologically normal. To test both hypotheses, samples from open boat whaling (1710s to 1860s) that exploited the diving cycle of large bulls (*1*), historic pre-exploitation strandings, and prehistoric fossils must be studied. Anthropogenic impacts also might be causal in nonlethal implosions of mysticete auditory bullae due to dysbaric conditions (*2*).

EDWARD D. MITCHELL

Natural History Museum of Los Angeles County, 900 Exposition Boulevard, Los Angeles, CA 90007, USA. E-mail: edmnhm@ix.netcom.com

References

1. E. Mitchell, *Rep. Int. Whal. Comm. Spec. Iss.* **5**, 63 (1983).
2. F. C. Fraser, P. E. Purves, *Scott. Nat.* **65**, 154 (1953).

Response

IN RESPONSE TO ROTHSCHILD'S SUGGESTION that the sperm whale bone lesions we described as osteonecrotic are pathognomonic for spondyloarthropathy, we offer the following observations: The extensive proliferation and remodeling of cartilage and woven bone that we described in sperm whales is a central aspect of experimentally induced dysbaric osteonecrosis in sheep (*1*). However, in recent correspondence with Rothschild, he kindly shared with us two pertinent papers in press (*2*, *3*) that describe erosive subchondral lesions diagnosed as spondyloarthropathy somewhat comparable to some of the lesions we described in sperm whale bones. Our diagnosis of osteonecrosis can, of course, be questioned; however, the selective benefits of such a high frequency of spondyloarthopathy are obscure. In con-

Published by AAAS

trast, any dysbaric cost could well be outweighed by the trophic advantage of access to deep-sea squid and fish.

We remain puzzled by the large subspherical bubble-like cavities, in rib and chevron bones, illustrated in our paper. These lesions do not appear to be comparable to published descriptions of spondyloarthropathy, nor do the bizarre nasal bone changes also illustrated.

We therefore suggest that the diagnosis of osteonecrosis needs to be confirmed with further histological and radiographical study of nonautolyzed material from future sperm whale mortalities.

Mitchell suggests that the progressive osteonecrotic lesions observed in sperm whales over 111 years are best interpreted as resulting from lesions induced by whaler harassment and are thus human impacts. We agree that further studies of earlier whaling, stranding, and fossil cases are warranted to test the alternative hypothesis. We are aware of two pre-1860s stranded specimens: one described by Melville (*4*) stranded in Tunstall, Yorkshire, UK, in 1825, and another that was beached and killed in 1661 at Easington, County Durham, UK (*5*). In the former case, weathering precludes diagnosis of bone condition. Photographs of the latter show no obvious lesions. Nevertheless, we will continue to pursue Mitchell's concerns and report further as warranted.

MICHAEL J. MOORE AND GREG A. EARLY
Woods Hole Oceanographic Institution, Woods Hole, MA 02543, USA.

References
1. T. F. Lin *et al.*, *Undersea Hyperbaric Med.* **23**, 39 (1996).
2. B. Rothschild, F. Ruhli, *Am. J. Primatol.*, in press.
3. B. Rothschild, F. Ruhli, *Am. J. Primatol.*, in press.
4. H. Melville, *Moby Dick* (Harper & Brothers, New York, 1851), chap. 102.
5. J. Drury, *Durham County Local Hist. Soc. Bull.* **39** (15 Dec. 1980).

Ethics of Tobacco Company Funding

AS ONE OF THE RESEARCHERS INTERVIEWED BY David Grimm for his article on tobacco company funding of research ("Is tobacco research turning over a new leaf?", News Focus, 7 Jan., p. 36), I felt that it was an informative and well-written piece. I took some exception, however, to the last sentence, which construed not accepting funding from tobacco companies as taking "the moral high road." Those of us who accept tobacco company funding with the aim of saving lives through our research are just as much on the "moral high road" as those who oppose tobacco funding. Our research, using tobacco company funding, is dedicated to the development of improved smoking cessation treatments, which will help save lives (*1*–*3*).

Federal sources of funding for research on tobacco dependence are all too scarce. Even those who vehemently oppose taking money directly from tobacco companies take money indirectly from tobacco companies, such as that from the Master Settlement Agreement. However, sadly, far too little of the funding from the Master Settlement Agreement is going into the intended uses of supporting research and treatment of tobacco addiction. Awarding grants directly from tobacco companies to university-based research groups provides better assurance that the money will be used to combat tobacco addiction and related problems. Understandably, safeguards must be set in place to prevent tobacco companies from controlling the direction of the research or censoring the publication of results. We have instituted such safeguards in our research program.

> **"Awarding grants directly from tobacco companies to university-based research groups provides better assurance that the money will be used to combat tobacco addiction and related problems."**
>
> –ROSE

Current long-term success rates with smoking cessation treatments in real-world settings are dismally low, often less than 20% (*4*). Tobacco company funding can be instrumental in the development, evaluation, and dissemination of more effective treatments.

JED E. ROSE
Director, Center for Nicotine and Smoking Cessation Research, Duke University Medical Center, 2200 West Main Street, Suite B-150, Durham, NC 27705, USA. E-mail: rose0003@mc.duke.edu

References
1. J. E. Rose, E. D. Levin, F. M. Behm, C. Adivi, *Clin. Pharmacol. Ther.* **30**, 323 (1990).
2. J. E. Rose, F. M. Behm, E. C. Westman, *Exp. Clin. Psychopharmacol.* **6**, 1 (1998).
3. E. C. Westman, F. M. Behm, J. E. Rose, *Chest* **107**, 1358 (1995).
4. S.-H. Zhu, T. Melcer, J. Sun, B. Rosbrook, J. P. Pierce, *Am. J. Prev. Med.* **18**, 305 (2000).

Merits of a New Drug Trial for ALS?

AS NEUROSCIENTISTS WORKING ON AMYotrophic lateral sclerosis (ALS), we read with interest the Perspective "Treating neurodegenerative diseases with antibiotics" by T. M. Miller and D. W. Cleveland (21 Jan., p. 361) and the article on which it comments, by J. D. Rothstein *et al.* on the use of β-lactam antibiotics to treat ALS (*1*). We are impressed by the screening of 1040 U.S. Food and Drug Administration–approved compounds for increased glutamate transport, which began in the spring 2002 and led to initiation of a clinical trial in ALS with ceftriaxone in spring 2005. We are concerned that the previous results of clinical research on ceftriaxone have been overlooked. In fact, a Medline search identified eight negative trials with ceftriaxone in ALS patients, published between 1992 and 1996 (*2*–*9*).

The fact that ceftriaxone increased glutamate uptake in rat spinal cord sinaptosomes has already been published (*2*), and this prompted us to verify the efficacy of the drug in 108 ALS patients, with disappointing results (*2*).

Thus, it seems that, although for basic science the new molecular biology approaches have provided elegant and specific contributions to explain the mechanism by which ceftriaxone increases glutamate uptake, from a clinical perspective, scientific research into ALS has actually not improved over the last 10 years. The emphasis on this drug as a possible solution to "one of the big challenges of this century" is not appropriate, considering the previous negative results.

ETTORE BEGHI,* CATERINA BENDOTTI, TIZIANA MENNINI
Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea, 62, 20157 Milan, Italy.
*To whom correspondence should be addressed. E-mail: beghi@marionegri.it

References
1. J. D. Rothstein *et al.*, *Nature* **433**, 73 (2005).
2. The Italian ALS Study Group, *Eur. J. Neurol.* **3**, 295 (1996).
3. F. H. Norris, *Arch. Neurol.* **51**, 447 (1994).
4. J. R. Gil Llano, I. Casado Naranjo, *Neurologia* **9**, 205 (1994).
5. P. Couratier, J. M. Vallat, L. Merle, P. M. Preux, J. Hugon, *Therapie* **49**, 146 (1994).
6. V. Carelli, R. Liguori, C. Cordivari, G. Bianchedi, P. Montagna, *Ital. J. Neurol. Sci.* **15**, 66 (1994).
7. F. J. Carod Artal, I. Perez Lopez-Fraile, M. Gracia Naya, J. A. Giron Mombiela, *Neurologia* **9**, 29 (1994).
8. W. Robberecht, *Lancet* **340**, 1096 (1992).
9. L. G. Smith, *Lancet* **340**, 379 (1992).

Response

OUR PERSPECTIVE HIGHLIGHTED THE REmarkable discovery that a well-known penicillin derivative, ceftriaxone, was not only effective in fighting infection within the nervous system, but also induced (at the transcriptional level) the synthesis of the major glutamate transporter within the spinal cord (*1*). This transporter, which serves to quickly dampen chemical signaling from one neuron to another and thereby to limit repetitive, excitotoxic neuronal firing, is known to be lost in ALS, a disease that

Published by AAAS

causes severe paralysis from a progressive loss of motor neurons over a typical 2- to 5-year course. Beghi *et al.* correctly note that previous efforts (*2*–*8*) using short-term administration of ceftriaxone (between 1 and 8 weeks) in a small number of patients were conducted in the early 1990s after a case report claiming a remarkable benefit in a single patient (*9*). None of these short-term efforts were double-blinded, nor were placebo controls used, important trial design features that would be necessary for a persuasive outcome. In the most comprehensive of these (conducted by Beghi, Mennini, and others), one-third of the 21 patients treated with ceftriaxone for the longest period (5 to 8 weeks) were claimed to have shown improvement (*8*). These prior efforts do not dampen enthusiasm for the discovery of induction of glutamate transport by a drug already known to be safe and to penetrate the blood-brain barrier. A long-term, double-blinded, and placebo-controlled trial in ALS is just what the evidence warrants.

TIM MILLER AND DON CLEVELAND
Ludwig Institute for Cancer Research and the Department of Medicine and Neurosciences, University of California, San Diego, La Jolla, CA 92093, USA.

References

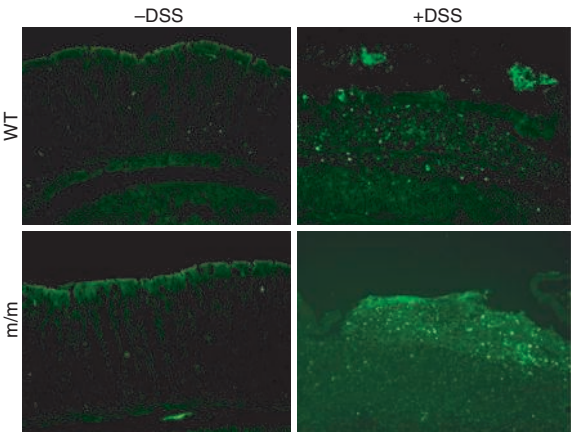
1. J. D. Rothstein *et al.*, *Nature* **433**, 73 (2005).
2. F. H. Norris, *Arch. Neurol.* **51**, 447 (1994).
3. J. R. Gil Llano, I. Casado Naranjo, *Neurologia* **9**, 205 (1994).
4. P. Couratier, J. M. Vallat, L. Merle, P. M. Preux, J. Hugon, *Therapie* **49**, 146 (1994).
5. V. Carelli, R. Liguori, C. Cordivari, G. Bianchedi, P. Montagna, *Ital. J. Neurol. Sci.* **15**, 66 (1994).
6. F. J. Carod Artal, I. Perez Lopez-Fraile, M. Gracia Naya, J. A. Giron Mombiela, *Neurologia* **9**, 29 (1994).
7. W. Robberecht, *Lancet* **340**, 1096 (1992).
8. The Italian ALS Study Group, *Eur. J. Neurol.* **3**, 295 (1996).
9. L. G. Smith, *Lancet* **339**, 1417 (1992).

CORRECTIONS AND CLARIFICATIONS

News Focus: "Mounting evidence indicts fine-particle pollution" by J. Kaiser (25 Mar., p. 1858). The article should not have described the lungs of asthmatics in a clinical study as "damaged." Lung function of these mildly asthmatic subjects was not affected by exposure to ultrafine particles. Asthmatics had 6 times more particles in their lungs than healthy subjects only when exercising asthmatics were compared to resting healthy subjects. Finally, many, but not all, short-term epidemiologic studies have linked sulfates and health effects. A study cited in the sidebar "How dirty air hurts the heart" appeared in the April/May issue of *Inhalation Toxicology*.

News of the Week: "Play and exercise protect mouse brain from amyloid buildup" by J. Marx (11 Mar., p. 1547). In the story, Gary Arendash was mistakenly identified as David Arendash. Also, Orly Lazarov's name was misspelled in the story and the image credit.

Reports: "*Nod2* mutation in Crohn's disease potentiates NF-κB activity and IL-1β processing" by S. Maeda *et al.* (4 Feb., p. 734). It was brought to the authors' attention that the two control panels in Fig. 4A look alike. After examining the issue, it was realized that during preparation of the figure, one of the control panels was mistakenly inserted twice, and the other control was omitted. The correct figure is shown here. The authors apologize for any possible confusion and inconvenience that may have been created. The results and conclusions remain as before, i.e., increased macrophage apoptosis in the lamina propria of *Nod2*^{2939ic} (m/m) mice after DSS treatment.



Policy Forum: "Do the largest protected areas conserve whales or whalers?" by L. R. Gerber *et al.* (28 Jan., p. 525). On page 525, in the second column, last paragraph, the heading should read, "Lack of an adaptive design." In the third column, second paragraph, the first sentence should read, "Current debate has polarized IWC members into those who advocate widespread sanctuary use and those who believe that they are redundant under the RMP/RMS [see supporting online material (SOM)]." In the same paragraph, the fourth sentence should read, "We assumed typical life history parameters for baleen whales (i.e., we used demographic parameters for the gray whale *Eschrichtius robustus*) (*13, 14*)." On page 526, first column, first full paragraph, the first sentence should read, "Although this result was robust to small (±0.02) changes in parameter values, our model includes dispersal as diffusion, rather than as explicit migration, and does not consider density dependence, demographic stochasticity, or environmental noise." The second sentence in that paragraph should begin "However, given the uncertainties..." The third sentence should read, "Our results are consistent with results from previous work..." In the fourth to last line of this column, the citation should be (*16*) instead of (*14*). In the second column, first paragraph, the fifth sentence should read, "A starting point would be the establishment of IWC sanctuaries conforming to more ecologically based designation." In the second paragraph, lines 5 through 7 should read, "populations of whales during certain time periods (e.g., in breeding grounds and/or feeding areas)..." In the third column, the first line should read "(SOM)" rather than "(*22*)." The second sentence in the third column should read, "Nevertheless, the adherence to a quota system would enhance whale conservation by restricting the times and areas of whale harvesting, and by limiting the total catch." In the References and Notes, in (*2*), the first line should read, "In accordance with the IWC, 'whaling' refers to the...," and the citation in the last line should be (*22*). In (*9*), the third author's initials appear twice (K.D.). Note (*22*) is now omitted, as the SOM is mentioned in the text, and (*23*) and (*24*) should become (*22*) and (*23*). The new note (*23*) [formerly (*24*)] should read, "We thank D. P. DeMaster and two anonymous reviewers for helpful comments, and the chair (A. Zerbini)..."

Perspectives: "The maser at 50" by R. L. Walsworth (8 Oct. 2004, p. 236). The figure legend is incorrect. The photo shows the second maser, not the first.

Perspectives: "NAD to the rescue" by A. Bedalov and J. A. Simon (13 Aug. 2004, p. 954). In reference 7, the first author's name was mispelled. It should be A. Sajadi.

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 through the Web (www.submit2science.org) or by 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.

TECHNICAL COMMENT ABSTRACTS

COMMENT ON "Ecosystem Properties and Forest Decline in Contrasting Long-Term Chronosequences"

Kanehiro Kitayama

Wardle *et al.* (Reports, 23 July 2004, p. 509) demonstrated that forest decline following a transient peak biomass is a common forest ecosystem dynamic caused by increased soil-phosphorus limitation over time. However, the decline they observed is attributable to the lack of phosphorus use–efficient species, and is confined to regions of low tree species diversity.
Full text at
www.sciencemag.org/cgi/content/full/308/5722/633b

RESPONSE TO COMMENT ON "Ecosystem Properties and Forest Decline in Contrasting Long-Term Chronosequences"

D. A. Wardle, L. R. Walker, R. D. Bardgett

Kitayama correctly recognizes that our study did not include hyperdiverse tropical forests. However, the data set he uses to test our ideas for tropical forests is not relevant to the spatial scale that we considered, and the mechanism that he proposes for these forests is not supported by current ecological theory.
Full text at
www.sciencemag.org/cgi/content/full/308/5722/633c

Ethics of Tobacco Company Funding

Jed E. Rose

Science **308** (5722), 632.
DOI: 10.1126/science.308.5722.632a