

JOINT LETTER PROTESTING CONFLICTS OF INTEREST AND IMBALANCE
AT THE FEB. 20 NIAID CONFERENCE ON NEONATAL HERPES

January 18, 2007

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Dear Drs. Zerhouni, Fauci, Dempsey, and Deal,

On February 20, 2007, the National Institute of Allergy and Infectious Diseases will hold a national Conference on Neonatal Herpes. The goals of this conference are to formulate and publish recommendations for the assessment of pregnancies at risk for neonatal herpes infection, and to come up with guidelines for the management of newborns exposed to or infected by herpes simplex.

Though a relatively rare condition, neonatal herpes transmission appears to be a highly contentious field. A review of recent articles and letters that have appeared in leading journals in the OB/GYN field shows sharp differences in opinion regarding the medical and economic rationale for universal herpes testing as a tool for preventing transmission.¹
² Moreover, a recent front page story in the *Wall Street Journal* documented the private sector's financial role in the debate. Specifically, the story documented how

GlaxoSmithKline has bankrolled the physicians and continuing medical education sessions that are promoting universal herpes screening for pregnant women. The story also pointed out that universal testing could lead to an upsurge in prescriptions for Glaxo's Valtrex to prevent neonatal transmission of herpes simplex virus (HSV).³

Given the controversy surrounding this subject, we were surprised to see the lineup of speakers for the 2/20 meeting, which was included in the invitation that went out to physicians in November. The lineup did not reflect the diversity of views on this subject, nor did the invitation reveal the conflicts of interest of virtually every invited presenter.

Specifically, there were five presenters listed. Of those five:

- Dr. Anna Wald of the University of Washington, who will cover the epidemiology and detection of HSV, has received grants and research support for her work on herpes from Glaxo and Roche, and received honoraria from Novartis, all of whom make antiviral drugs for herpes;
- Dr. Zane Brown of the University of Washington, who will cover screening and treatment, gives “two to three lectures a week advocating universal herpes testing for pregnant women, earning \$1,000 to \$2,500 per talk.” Most of those sessions were financed by Glaxo grants to the CME providers, according to the *Journal* article;
- Dr. Laura Riley of Harvard Medical School, who will lead the first session on guideline writing, is secretary/treasurer of the American Herpes Foundation, a “patient advocacy” non-profit run by a for-profit medical marketing firm; its board contains no patients and its \$183,000 budget in 2004 was almost entirely funded by Glaxo and Roche; and
- Dr. Richard Whitley of the University of Alabama at Birmingham, who will lead the final session of the day on guideline writing, serves on the speakers bureaus for Glaxo and Novartis and serves on the board, and receives stock options and compensation from the start-up firm Fermavir, which is developing next-generation drugs aimed at the herpes family of viruses. Moreover, Dr. Whitley carried out these private sector activities while running NIAID's “Collaborative Antiviral Study Group,” which received over \$16 million in government grants in FY2004-05 to run clinical trials on this subject.

This is not an isolated case. Many consumer groups, professional societies, individual physicians, and medical journals have long been concerned about the role of commercial entities in influencing medical practice, from prescribing drugs to continuing medical education. In recent months, new concerns have arisen with regard to the writing of clinical practice guidelines. Specifically, there have been commentaries in leading journals questioning the guidelines that involve Amgen, Epogen and dialysis patients and Eli Lilly, Xigris and sepsis patients. According to the commentaries, the guidelines, whose writing by expert panels had been unduly influenced by the drug manufacturers, wound up harming patients.^{4 5}

We, the undersigned physicians, consumer organizations, scientists, and health professionals believe the National Institutes of Health, the crown jewel in the nation's medical research establishment, should have a higher standard. NIH must serve as an honest broker in the development of medical evidence that will inform clinical practice. When holding conferences aimed at writing guidelines, it should seek balanced presentations. When appointing guideline writing committees, it must strive to ensure that all members are free from conflicts of interest.

Unfortunately, several centers and institutes at NIH routinely ignore these common sense standards. A quick search for clinical practice guidelines authored by NIH entities in the national clearinghouse (<http://www.guidelines.gov/>) turned up the following examples:

- The 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, a product of the National Heart Lung and Blood Institute, was written by a committee where 9 of 11 physicians had financial ties to manufacturers of blood pressure control medications;⁶
- The 2004 update of the 3rd Report of the National Cholesterol Education Program Expert Panel on Detecting, Evaluating and Treatment of High Blood Cholesterol in Adults, also from NHLBI, was written by a committee where 8 of 9 physicians had financial ties to manufacturers of statin drugs;⁷ and
- The Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, sponsored by NIAID, included 11 of 23 physicians with ties to firms that made drugs for treating HIV/AIDS.⁸

The upcoming meeting on neonatal herpes transmission as presently structured will only add to this sad record. First, with four of five listed speakers having close ties to drug manufacturers with an interest in this field, the meeting is completely unbalanced with regard to its presentations.

Second, given the leadership of the workshops devoted to guideline writing, it is likely the writing panels will contain numerous if not a preponderance of members with conflicts of interest. It is our belief that when it comes to guideline writing, NIH must adopt the standard long in place at the Office of Medical Applications of Research inside the Office of the NIH Director. According to its guidelines, OMAR prohibits physician-scientists with conflicts of interest from serving on its consensus panels.⁹

In recent years, there have been many suggestions for improving the quality of medicine in the U.S. There is a movement among insurers and others to enact pay-for-performance standards for physicians, hospitals and other medical providers. Such efforts assume quality can be improved by encouraging physicians to adopt evidence-based standards reflected in widely-accepted clinical practice guidelines.

But what evidence will be considered when writing those guidelines? And who will write the guidelines? Why should either practicing physicians or patients have faith in

guidelines written by researcher-physicians with ties to providers whose financial well-being is driven by the content of those recommendations?

We believe the time has come for NIH to adopt a simple set of agency-wide rules: Any Institute or Center that writes or funds a group to write a clinical practice guideline should require that the writing committee exclusively be composed of members without conflicts of interest. And those committees should seek out the full range of evidence on a subject before sitting down to write.

Sincerely,

(See attached list)

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¹ Urato AC, Caughey AB. Universal prenatal herpes screening is a bad idea in pregnancy. *Lancet*. 2006 Sep 9;368(9539):898-9.

² Thung SF, Grobman WA. The cost-effectiveness of routine antenatal screening for maternal herpes simplex virus-1 and -2 antibodies. *Am J Obstet Gynecol*. 2005 Feb;192(2):483-8.

³ Armstrong, David. Drug Firm's Cash Sways Debate Over Test for Pregnant Women. *Wall Street Journal*, Dec. 13, 2006; p. A1.

⁴ Steinbrook, Robert. Hemoglobin concentrations in chronic kidney disease. *The Lancet*. 2006; 368:2191-2193.

⁵ Eichacker PO, Natanson C, Danner RL. Surviving sepsis—practice guidelines, marketing campaigns, and Eli Lilly. *N Engl J Med*. 2006 Oct 19;355(16):1640-2.

⁶ Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003 Dec;42(6):1206-52.

⁷ Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, Pasternak RC, Smith SC Jr, Stone NJ. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004 Jul 13;110(2):227-39.

⁸ Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Bethesda (MD): U.S. Department of Health and Human Services; 2006 Oct 26. 120 p.

⁹ See <http://consensus.nih.gov/ABOUTCDPPDF.pdf>, accessed Jan. 16, 2007.

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