

Comment from Advocates for Informed Choice (AIC) for the Presidential Commission for the Study of Bioethical Issues

February 28, 2010

Public Commentary

The Presidential Commission for the Study of Bioethical Issues
1425 New York Ave. NW, Suite C-100
Washington, DC 20005

To The Commission:

On behalf of Advocates for Informed Choice (AIC), a non-profit organization that advocates for the legal and human rights of children born with disorders of sex development (DSD) and their families, we seek to draw the attention of the Commission to the ethical concerns raised by the practices described in this letter that affect these vulnerable children. We write to express AIC's grave concern over ethically questionable clinical research involving pregnant women that has been reportedly conducted under the auspices of Mount Sinai Medical Center and Weill-Cornell Medical College, Cornell University, under the direction of Dr. Maria New. Specifically, we are concerned about the off-label use of dexamethasone on pregnant women for the purpose of preventing genital virilization in fetuses who might be 46,XX fetuses affected by 21-hydroxylase deficiency, a form of Congenital Adrenal Hyperplasia (CAH).

This treatment raises significant ethical dilemmas that have gone unaddressed for over 20 years, involving a vulnerable population. Prenatal treatment with dexamethasone is an unapproved use of a strong steroid in pregnant women, intended to avoid a cosmetic issue associated with CAH, rather than to treat the medical issues that should be the primary concern of physicians.ⁱ Use of prenatal dexamethasone has been demonstrated to bear significant iatrogenic risk.ⁱⁱ Studies have demonstrated that prenatal dexamethasone treatment results in detrimental changes to the brains of children,ⁱⁱⁱ specifically, problems with working memory, verbal processing, and anxiety.^{iv} Severe and long-lasting adverse effects on treated pregnant women have also been reported.^v Pregnant women are considered a vulnerable population in the research context, and they are being exposed to risky and experimental treatment in order to potentially benefit the fetus. However, 90% of fetuses so treated will not benefit from this treatment. Only 1 in 8 fetuses started on this treatment are actually 46,XX CAH, which means that the 7 in 8 who are not are being treated unnecessarily. We are also particularly concerned that Dr. New's studies were intended, at least in part, to determine whether prenatal dexamethasone treatment would prevent lesbianism and tomboyish behavior.^{vi}

The Maria New Children's Hormone Foundation webpage claims that "with nearly 20 years' experience, the treatment has been found safe for mother and child,"^{vii} despite the fact that Dr. New has simultaneously been conducting follow-up studies to determine the unknown long-term effects of prenatal dexamethasone treatment. Although Dr. New appears to have consistently had IRB approval to do post-natal follow-up observational and survey studies of women and children exposed to prenatal dexamethasone, she seems to have conducted no proper clinical trials and thus obtained no IRB oversight for the actual prenatal treatment of the 600+ pregnant women and their fetuses involved. In public correspondence with Dr. New in 2001, a committee of the American Academy of Pediatrics urged that "prenatal glucocorticoid therapy for CAH should be confined to centers doing controlled prospective, long-term studies.," pointing out that "[t]he memory of the tragedies associated with prenatal use of ... thalidomide demands no less."^{viii}

We have alerted the federal Office of Human Research Protections (OHRP) and the Food and Drug Administration to the controversy surrounding Dr. New's studies, and, while they have investigated, they have taken no action. In fact, the National Institutes for Health has funded these studies for decades, without insisting on proper clinical trials. The federal government continued to fund this ethically troubling project even while suing Weill-Cornell for fraud over Dr. New's use of federal funds, and even after uncovering serious problems with Weill-Cornell's IRB process.^{ix}

In spite of considerable public outcry^x neither the OHRP nor Weill-Cornell will reveal what the pregnant women who were prescribed dexamethasone were told or why Cornell's IRB approved this research. The OHRP has not responded to Freedom of Information Act requests on these points.

In closing, it is important to note that this is not the only ethical issue affecting children with DSD with which AIC is concerned presently. There are numerous situations in which children with DSD become the subjects of questionable methods of medical inquiry and practice.

As another example, we also have grave ethical concerns about the follow-up tests used by Dr. Dix P. Poppas under the auspices of New York-Presbyterian Hospital and Weill-Cornell for assessing clitoral sensitivity in young girls after conducting clitoral reduction surgeries on them. Dr. Poppas's unorthodox follow-up tests consist of applying medical vibratory devices to the genitals of girls as young as age 5 to collect data on post-operative clitoral sensitivity.^{xi} Given the well-documented psychological harm that can come to girls with DSD simply as a result of excessive visual genital exams,^{xii} it seems likely that Poppas's far more invasive tests pose substantial risk of psychological harm to young girls. Dr. Poppas's follow-up tests may have been conducted without IRB scrutiny; it is difficult to see how an IRB could have approved such a study considering the controversy around genital surgery in general, let alone follow-up tests which seem to have no benefit for the patient. Again, in spite of considerable public outcry^{xiii}, neither Weill-Cornell nor the OHRP have taken action in this matter.

AIC seeks to alert the Commission to the ethical issues that concern us as advocates for the legal and human rights of children born with DSD and their families. Children with DSD and their families constitute a particularly vulnerable population that has long been considered subject to exceptions to the usual ethical rules for medical practice and research. These children and their families deserve the protections that all patients and human subjects of research are entitled to receive.

Thank you for your attention to these matters.

Sincerely,

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Executive Director

Johanna Michael
Legal Intern

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□ Miller WL. “Dexamethasone treatment of Congenital Adrenal Hyperplasia in utero: an experimental therapy of unproven safety.” J Urol 1999; 162:537-40.

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□ National Institutes of Health Consensus Development Panel, “Antenatal Corticosteroids Revisited: Repeat Courses. National Institutes of Health Consensus Development Conference Statement, August 17-18, 2000.” Obstet Gynecol 2001; 98:144-50.

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□ French NP, Hagen R, Evans SF, Mullan A, Newnham JP. “Repeated antenatal corticosteroids: effects on cerebral palsy and childhood behavior.” Am J Obstet Gynecol 2004; 190:588-95.

iv

□ See, for example: [a] Hirvikoski T, Nordenstrom A, Lindholm T, et al. “Cognitive functions in children at risk for congenital adrenal hyperplasia treated prenatally with dexamethasone.” J Clin Endocrinol Metab.

2007; 92:542-8; and [b] Trautman, PD, Meyer-Bahlburg HF, Postelnek J, New MI. “Effects of early prenatal dexamethasone on the cognitive and behavioral development of young children: results of a pilot study.” Psychoneuroendocrinology 1995; 20:439-449.

v

□ Frias J, Levine L, et al. “American Academy of Pediatrics Technical Report: Congenital Adrenal Hyperplasia.” Pediatrics 2000;106:6:1511-18.

vi

□ “DEX-exposed CAH girls will show. . . decreased masculinized gender-role behavior,” from the hypotheses section of Dr. New’s 1996 grant renewal application to the National Institutes of Health, National Institute of Child Health and Human Development, grant #3R37HD000072 1996:2, via FOIA request by Advocates for Informed Choice. “The overall objective is to fill the gap of knowledge about the long-term consequences of early-prenatal DEX treatment on childhood development on the one

hand, and the success of DEX in suppressing behavioral masculinization in the sub-sample of girls with definitive congenital adrenal hyperplasia on the other. [...] The spectrum of behavioral effects ranges from mild or marked tomboyish behavior of childhood to increased adolescent/adult bisexuality and lesbianism..." [emphasis added] New grant renewal application 1996:60.

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□ <http://www.newchf.org/testing.php>.

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□ Frias J, Levine L, et al. "Reply: Prenatal Treatment of Congenital Adrenal Hyperplasia: Author Differs with Technical Report." *Pediatrics* 2001:107:4:804.

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□ Complaint, US v. WCMC (S.D.N.Y. 2005) (No. 03 Civ. 6761); Determination Letter from the OHRP to Dr. Antonio M. Gotto, Jr., Provost for Medical Affairs and Dean of the Medical College and Dr. Jeffery M. Cohen, Associate Dean, Weill College of Medicine of Cornell University (May 24, 2004).

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□ Elton, C. A Prenatal Treatment Raises Questions of Medical Ethics, *Time*, June 18, 2010, <http://www.time.com/time/health/article/0,8599,1996453,00.html>; Nature Medicine, Clitoroplasty and Dex Studies Scrutinized by Bioethicists, *A Spoonful of Medicine*, June 28, 2010, http://blogs.nature.com/nm/spoonful/2010/06/clitoroplasty_and_dex_studies_1.html; Begley, S., The Anti-Lesbian Drug, *Newsweek*, July 2, 2010, <http://www.newsweek.com/2010/07/02/the-anti-lesbian-drug.html>.

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□ Yang J, and Poppas D. Nerve Sparing Ventral Clitoroplasty: Analysis of Clitoral Sensitivity and Viability. *Journal of Urology*, Vol. 178, 1598-1601, October 2007.

xii

□ Lee, P.A., Houk, C., Ahmed, S.F., et al. Consensus Statement on Management of Intersex Disorders. *Archives of Disease in Childhood*. 2006:91; 554-63.

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□ Dreger, A. and Feder, E. K., Bad Vibrations, *Bioethics Forum: Diverse Commentary on Issues in Bioethics*, a service of The Hastings Center, June 16, 2010; Nature Medicine, Clitoroplasty and Dex Studies Scrutinized by Bioethicists, *A Spoonful of Medicine*, June 28, 2010, http://blogs.nature.com/nm/spoonful/2010/06/clitoroplasty_and_dex_studies_1.html; Battan, C., Leading Cornell Doctor Performing Genital Cutting, *The Nation*, June 21, 2010, <http://www.thenation.com/blog/36481/leading-cornell-doctor-performing-genital-cutting>