

April 25, 2006

Elizabeth G. Nabel, Director
National Heart, Lung, and Blood Institute
31 Center Dr., MSC 2486
Bethesda, MD 20892-2486

Dear Dr. Nabel:

I am writing on behalf of our more than 1 million members and supporters to ask that the NHLBI not extend its grant (HL077128) to Dr. Kathleen O'Hagan for her study "Uterine Circulatory Response to Exercise in Pregnancy," in which she measures the blood flow of pregnant rabbits exercised on a motorized treadmill. We have reviewed the protocol for this experiment and contrasted its claims with the relevant literature, expert opinions, and basic common sense. Our findings show that Dr. O'Hagan's study suffers from a number of flaws, both particular to her experimental design and general to animal models of blood flow in pregnancy.

The problems with Dr. O'Hagan's study stem largely from differences between humans and rabbits. In human placentation, for example, there is a more pervasive and intimate apposition between maternal and fetal tissue, affecting, among other things, the nature of blood flow between the mother and fetus. There are also clear differences in term length, number of fetuses, stages of fetal development, uterine structure, and other factors that are significant to studies of pregnancy. In addition to gestational differences, there are physiological differences, such as the fact that humans are bipedal and rabbits are quadrupeds. This changes the forces acting on blood flow, the spatial relationship between the fetus and key organs such as the heart, and how the fetus moves during physical activity.

Dr. O'Hagan's experiment also suffers from the difficulties of studying animals in laboratories. Physiological data, particularly heart rate and blood pressure, are unpredictably affected by the stress and fear of laboratory life. These effects make studies on hypertension particularly unreliable, which may be why Dr. O'Hagan's earlier work on blood pressure and renal sympathetic nerve activity baroreflex in pregnant and nonpregnant rabbits has produced contradictory findings (O'Hagan 2001). Furthermore, because she is studying exercise, it should be noted that laboratory confinement presents an irremedial confounding variable—confined rabbits receive deficient levels of exercise between their exercise trials. It is the equivalent of strapping women in bed and letting them up only to run on a treadmill a handful of times over their nine-month pregnancy.

In Dr. O'Hagan's grant application, she claims, "For ethical and technical reasons, it is difficult to directly investigate the uterine blood flow response



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PEOPLE FOR THE ETHICAL
TREATMENT OF ANIMALS

501 FRONT ST.
NORFOLK, VA 23510
757-622-PETA
757-622-0457 (FAX)

PETA.org
Info@peta.org

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to exercise in pregnant women.” This claim is false. A literature review using the NIH’s PubMed database shows that uterine blood flow is regularly measured in women during clinical studies using safe and effective Doppler ultrasound technology. In fact, there are many studies that specifically measure the effects of exercise on uterine blood flow in women. These studies, not animal research, have conclusively proved that exercise is safe and beneficial in normal pregnancy. The success of Doppler in more than 20 years of clinical research contrasts sharply with the dearth of successful research in animal models.

Our general supposition—that animal models of blood flow in pregnancy are inadequate—is supported by the NHLBI. The NHLBI Working Group on Research on Hypertension During Pregnancy reported in 2001, “Animal models are of limited benefit because of significant differences in placentation among mammals, as well as differences in length of gestation and perhaps even posture between mammalian models and humans.” In light of this observation, the group has said that clinical studies are the key to advancements in obstetric care. However, it also said, “There are few obstetrician/gynecologists trained in rigorous clinical research, and even fewer formal training programs.”

There is no justification for ignoring NHLBI experts by continuing to fund animal experimentation at the expense of clinical studies and clinical training for ob/gyns. We respectfully ask that you not extend Dr. O’Hagan’s current grant. We also ask that the NHLBI refrain from funding future grant applications by Dr. O’Hagan that involve animals and that it set appropriate funding priorities that direct money toward clinical investigation and away from animal research.

Thank you for taking the time to consider our requests. If you have any questions, please contact me at 757-962-8326. We look forward to hearing from you.

Sincerely,

A handwritten signature in cursive script that reads "Matthew Mongiello".

Matthew Mongiello
Research Associate