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The goal of this study was to determine the effect of PFDA on hepatic glucose transport in perfused rat livers using a paired-tracer first-pass extraction technique. This work was performed in collaboration with LCDR John Wyman, Ph.D. of the Naval Medical Research Institute, Wright-Patterson AFB. Carol learned the perfusion techniques, coordinated all aspects of the data acquisition, and was solely responsibile for data processing. This project was described in detail in the Annual Report for AFOSR-90-0148 which was submitted January 5, 1994. Therefore, only a very brief discussion of the work is given herein.

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Technical Report for AASERT Grant #F49620-92-J-0218DEF

Principal Investigator: Nicholas V. Reo, Ph.D.
Institution: Wright State University, Dayton, OH
Report Period: June 1, 1993 to May 31, 1994

Submitted: June 6, 1994

Since June 1992 this AASERT grant has provided support for Carol M. Goecke as a full-time student in the Biomedical Sciences Ph.D. program at Wright State University. During the current reporting period, Carol was in her last year of study and was not enrolled in classes. She was engaged full-time in laboratory research and writing her Ph.D. dissertation. Carol successfully defended her dissertation on March 22, 1994 and completed the requirements for the Ph.D. degree.

Carol was a co-author of two publications and three scientific abstracts this past year. She submitted an abstract and attended the Fifth North American Meeting of the International Society for the Study of Xenobiotics (ISSX) in Tucson, Arizona on October 17-21, 1993. The ISSX committee organized an evaluation process for attending graduate students whereby all student abstracts (39 total) were evaluated by a distinguished panel of judges and four awards were presented. Carol received an award for the *Best Abstract and Presentation* by a graduate student.

The following is a list of publications and abstracts for the reporting period.

N. V. Reo, C. M. Goecke, L. Narayanan, and B. M. Jarnot. "Effects of Perfluoro-*n*-octanoic Acid, Perfluoro-*n*-decanoic Acid, and Clofibrate on Hepatic Phosphorus Metabolism in Rats and Guinea Pigs *in Vivo*." *Toxicol. Appl. Pharmacol.* 124, 165-173 (1994).

C.M. Goecke, B.M. Jarnot, and N.V. Reo. "Effects of the Peroxisome Proliferator, Perfluoro-n-decanoic Acid, on Hepatic Gluconeogenesis and Glycogenesis: A ^{13}C NMR Investigation." *Chem. Research Toxicol.* 7, 15-22 (1994).

C.M. Goecke, N.V. Reo, J. Wyman and B. M. Jarnot: "Effects of Perfluoro-*n*-Decanoic Acid on Hepatic Glucose Transport." *The Toxicologist* (in press). Society of Toxicology, Annual Meeting, Dallas, TX, March 1994.

N. V. Reo, L. Narayanan and C. M. Goecke: "Induction of Liver Phospholipase C Activity by the Peroxisome Proliferator, Perfluorodecanoic Acid." International Society for the Study of Xenobiotics, *ISSX Proceeding*, 4, 103 (1993). Presented at the Fifth North American ISSX Meeting, Tucson, AZ, October 1993.

C. M. Goecke, L. Narayanan, B. M. Jarnot and N. V. Reo: "Effects of the Peroxisome Proliferator Perfluorodecanoic Acid on Hepatic Glucose and Alanine Metabolism." International Society for the Study of Xenobiotics, *ISSX Proceeding*, 4, 166 (1993). Presented at the Fifth North American ISSX Meeting, Tucson, AZ, October 1993. Received student award for Best Scientific Abstract and Presentation.

Laboratory Research

During the period from June 1993 to January 1994, Carol performed experiments designed to assess the effects of perfluorodecanoic acid (PFDA) on hepatic glucose transport. From January through March she was engaged full-time in preparing and writing her Ph.D dissertation.

The goal of this study was to determine the effect of PFDA on hepatic glucose transport in perfused rat livers using a paired-tracer first-pass extraction technique. This work was performed in collaboration with LCDR John Wyman, Ph.D. of the Naval Medical Research Institute, Wright-Patterson AFB. Carol learned the perfusion techniques, coordinated all aspects of the data acquisition, and was solely responsible for data processing. This project was described in detail in the Annual Report for AFOSR-90-0148 which was submitted January 5, 1994. Therefore, only a very brief discussion of the work is given herein.

Treated male F-344 rats received a single ip. injection of PFDA (50 mg/kg) while pair-fed controls received an equal volume of vehicle solution. At 5 days post-treatment, livers were perfused with tracer amounts of [^{14}C]3-O-methylglucose (^{14}C-3-OMG) and the extracellular marker, [^{3}H-fructose]sucrose. Effluent samples were collected at 2 sec. intervals and hepatic extraction of ^{14}C-3-OMG was calculated.

The data reveal that PFDA causes a significant decrease in glucose transport activity ($p = 0.02$). Control rats yield a *ca.* 1.8-fold greater percent hepatic glucose extraction (mean ± SE) compared to PFDA rats, 27.1 ± 3.6 versus 15.5 ± 2.2, respectively. These studies clearly demonstrate that the inhibition in hepatic glycogen synthesis, which was observed in earlier ^{13}C NMR experiments following PFDA treatment, is predominately due to a severe dysfunction in glucose transport. A manuscript is currently being prepared for submission to *Chemical Research in Toxicology*.

Current Status of AASERT Program

Upon Carol Goecke's graduation in March 1994, the student stipend provided by the AASERT grant was terminated. I had intended to provide support for another Ph.D. student in my laboratory, Mehdi Adinehzadeh, beginning this June. Mehdi, however, has decided to take a leave-of-absence from the graduate program until September 1994. Therefore, no student is being supported at present. In September 1994 I anticipate that Mehdi Adinehzadeh will return to the laboratory and, additionally, attempts will be made to attract new graduate students into the program.