

Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is “None”, please specify “None” as your response. “Not applicable” is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** Magee-Womens Research Institute and Foundation
2. **Reporting Period (start and end date of grant award period):** 01/01/2009-12/31/2009
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Cheryl A. Richards, MBA
4. **Grant Contact Person’s Telephone Number:** 412-641-8932
5. **Grant ME Number or SAP Number:** 4100047639
6. **Project Number and Title of Research Project:** Project 2 - Establishment of an Animal Model for Respiratory Infection with Influenza during Pregnancy
7. **Start and End Date of Research Project:** 01/01/2009-12/31/2009
8. **Name of Principal Investigator for the Research Project:** Richard H. Beigi, MD, MSc.
9. **Research Project Expenses.**

9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

\$ 79,270.34

9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
Beigi	Principal Investigator	10	\$24,180.12
Meyn	Statistician	5	\$1,439.95

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
Stefano-Cole	Co-Investigator	5
Reed	Co-Investigator	5
Faith	Co-Investigator	5
Hartman	Co-Investigator	5

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
Implantable animal monitoring chip and monitoring equipment for analysis	This allows the daily monitoring of outcomes in the animals challenged with virus and enables more data capture with less handling of the animals	\$4,681

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes x No

If yes, please indicate the source and amount of other funds:

Department funding of approximately \$10,000

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes x No

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert “not funded” in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Clinical and Pathological Severity of Novel 2009 H1N1 Infection During Pregnancy	<input checked="" type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)	February, 2010	\$275,000.00 in Direct Costs	\$ pending
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify:_)		\$	\$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes No

If yes, please describe your plans:

Having used the Health Research Grants as an excellent foundation to foster our collaboration we plan to continue to apply for influenza-related research in pregnancy in addition to large grants supporting research into other pathogens of high importance and its effects during pregnancy

12. Future of Research Project. What are the future plans for this research project?

This research project will continue with future health research grant funding to expand to influenza challenge in pregnant and non-pregnant ferrets using 2009 H1N1 influenza strains (strain responsible for the current influenza pandemic). This work will hopefully be fostered by the recent R21 submission.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes No

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown				
Total				

	Undergraduate	Masters	Pre-doc	Post-doc
White				

Black				
Asian				
Other				
Unknown				
Total				

14. Recruitment of Out-of-State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes _____ No x _____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes x _____ No _____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

The funding in this project really allowed for an earnest beginning of the collaboratory work that has now fostered a recent R21 submission as well as produced 3 presented abstracts. Perhaps most important is that the scientific relationship has been fostered between the principal investigator and the co-investigators by the foundational support provided. This is a key component of successful collaboration (often overlooked) because it allows for momentum to be gained from a project standpoint, a scientific relationship standpoint and recognition within the institution from senior leadership.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes x _____ No _____

If yes, please describe the collaborations:

The work presented at national meetings has helped to engage other researchers across the country in addition to opening a productive dialogue between our University of Pittsburgh group and the NIH-NIAID/NICHD.

16(B) Did the research project result in commercial development of any research products?

Yes _____ No _____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes _____ No _____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (β) should not

print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

The overall project goals were as follows:

1. Develop a model of collaboration and infrastructure that will allow for ongoing investigation of susceptibility, immunological response and countermeasures to emerging and threatening infectious diseases among pregnant animals.
2. Develop an aerosol delivery challenge model for inhalational influenza among pregnant mice and compare that to non-pregnant mice (controls).
3. Compare whole-body aerosol exposure to nose-only delivery of influenza strain PR/8 (human isolate of seasonal influenza adapted to mice) in pregnant and non-pregnant mice in terms of disease course, clinical signs of morbidity and pathological evaluation at necropsy.
4. Determine the lethal dose (LD₅₀) of a mouse adapted seasonal influenza strain that will kill 50% of the pregnant mouse population and compare to non-pregnant mice. This will be correlated to deposition of influenza virus in the lungs and total body dissemination.

With regard to the first goal, significant strides have been made in terms of developing a collaborative model for aerosol challenge studies of pregnant animals. Funds from the current project have supported investigator effort, actual aerosol challenge studies, equipment to improve data collection and travel to present data at national meetings. These are all developmental components of a successful collaboration between the investigators and is noticed within the University of Pittsburgh leadership. In addition, given our early success in accomplishing our goals and producing abstracts (and manuscripts in progress) the same collaboratory group were able to put a larger R21 grant in to the NIH to expand our investigations into other species using 2009 H1N1 influenza. Goals #2, 3, and 4 were all achieved successfully. These findings will be detailed below.

The project-specific scientific specific aims are listed here:

- 1) Determine the LD₅₀ for aerosolized influenza strain PR/8 in female non-pregnant and pregnant mice
- 2) Compare whole-body aerosol versus nose-only delivery of influenza strain PR/8 in pregnant and non-pregnant mice in terms of disease course and clinical signs.
- 3) Compare deposition and dissemination of influenza in pregnant and non-pregnant mice.

Specific Aim 1: This was done using 2 serial challenge experiments (same methods, two different batches of mice). Both were aerosol challenge studies using both pregnant and non-pregnant mice and A/PR/8 (mouse-adapted). As proposed in the grant 3 successive doses were used in order to approximate and bracket the true LD₅₀ for the experiments. Both serial investigations produced very similar and important results summarized here:

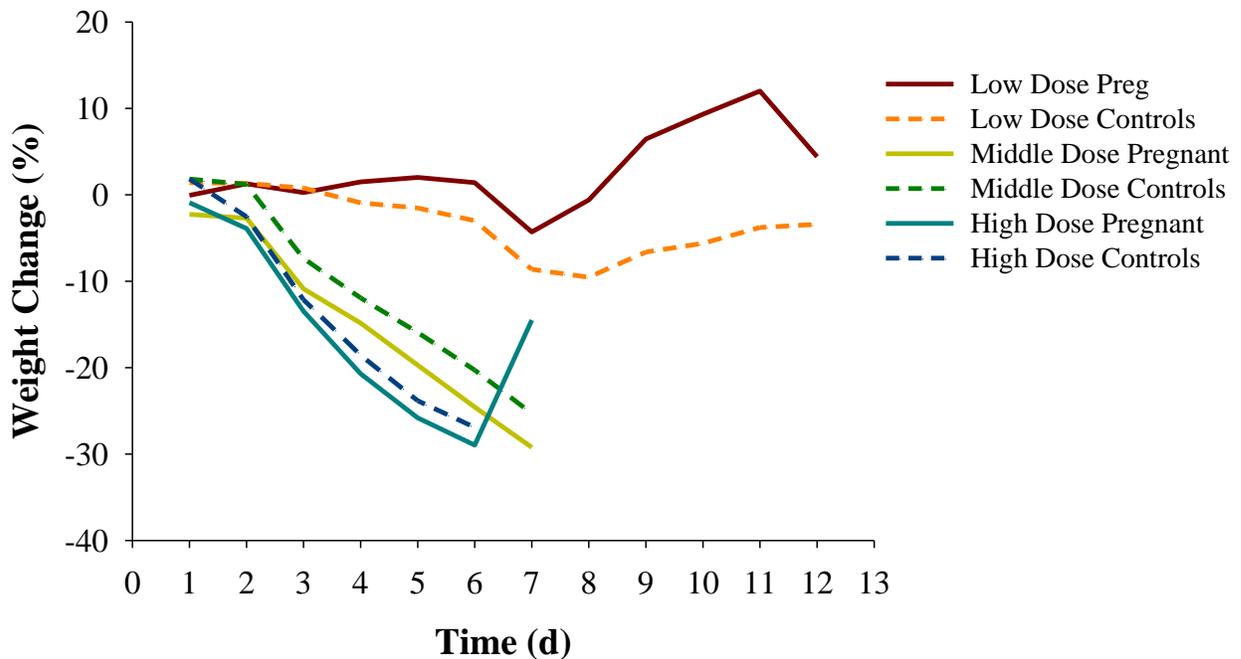
- Pregnant mice and non-pregnant mice had the same LD₅₀ values and thus no apparent differences in susceptibility to severe infection.
- Pregnant and non-pregnant mice had the same clinical course of disease at the same dose
- The LD₅₀ for the aerosol technique was approximately 10-fold lower than what has been reported for intranasal inoculation in the literature.

The first challenge used a total of 60 mice, of which 30 were sent as pregnant and presumed to be pregnant. As an example of the actual successive doses used, see the table highlighting experiment #1:

CHALLENGE DOSE IN PLAQUE FORMING UNITS (pfu)

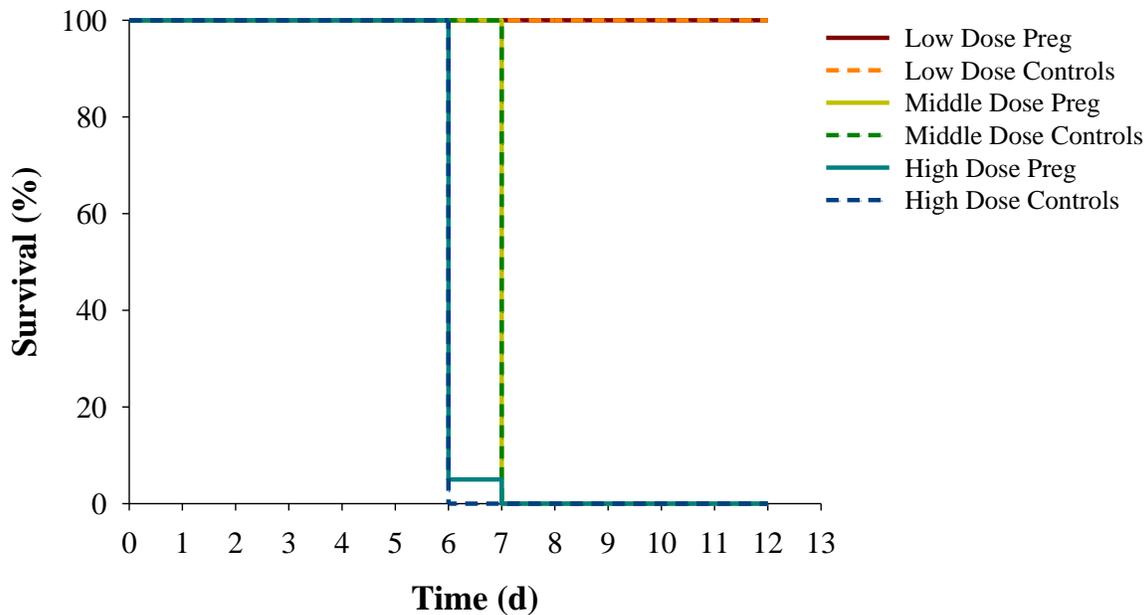
Group	Low	Middle	High
Pregnant	14.7	179.3	1680.1
Non-pregnant	15.9	197.3	1827.9

The data for weight gain/loss (as a marker for disease effects) after challenge is demonstrated in the figure below:



(Data is group average % change in weight for each animal at each time-point)

Below is a figure that shows the survival and time to death (or euthanasia); mice were euthanized when moribund by CO2 intoxication



-The actual LD₅₀ (no difference between pregnant & non-pregnant) for the 1st round of experiments was: 55 pfu. Similar data was accumulated after the 2nd round of challenges, with the LD₅₀ from that round at 15 pfu. These are in the same range of doses and validate the assertion that the LD₅₀'s after aerosol challenge are approximately 10-fold lower than intranasal inoculation.

-Median time to death was 6.5 days (compared to 7-10 days with intranasal inoculation).

- Of the batch that were supposed to be pregnant, only 12 were. Our plan at that point after this round of experiments was to challenge at a later point in pregnancy moving forward (14-16 days gestation instead of @ 10 days) so that pregnancy can be visually confirmed prior to challenge. This approach also had the added benefit of later in gestation (approximates 3rd trimester in mice) when most of the untoward maternal outcomes seem to peak in human influenza infection.

Specific Aim #2: No direct comparison between intranasal and aerosol challenge was done given the fact that by the time the experiments for this grant started the investigators had developed a strong comfort level with aerosol challenges using the current system and were confident that aerosol was a more efficient manner of introducing infection. Instead, aerosol challenges were solely performed and then the LD₅₀ values were compared using published historical controls for the intranasal inoculation. Given our above findings, validation that aerosol challenge is a more efficient manner of introducing inhalational infection in animals has been achieved. This system was also designed in an attempt to simulate real-life exposure more closely. Moving forward we will continue to use the aerosol methodology for numerous reasons.

Specific Aim #3: Part of the preliminary work in this grant included deposition studies using inert particles to investigate into differences between pregnant and non-pregnant mice. In order to assess this endpoint we used inert fluorescent, 1 μ m latex microspheres (Invitrogen) as the inhalation product. The steps were as follows:

1. 36 presumed pregnant (day 11 gestation, guaranteed pregnant) 8-10 week old Balb/c mice were used.
2. Non-pregnant controls used from those found not to be pregnant from experiments of original 36. The actual breakdown was 24 pregnant and 12 non-pregnant.
3. Whole-body aerosol exposure using Collison 3-jet nebulizer (AeroMP) was used to aerosolize fluorescent 1 μ m latex microspheres (Invitrogen)
4. Three groups, given increasing numbers of microspheres by inhalation (1×10^3 , 1×10^4 , 1×10^5)
5. At 2 hrs, 24 hrs, and 48 hours, three mice taken from each group & necropsied
6. Lungs homogenized in PBS; supernatants passed over cell strainer to remove debris
7. Analyzed on FACS Aria with beads from bacterial counting kit (Invitrogen)

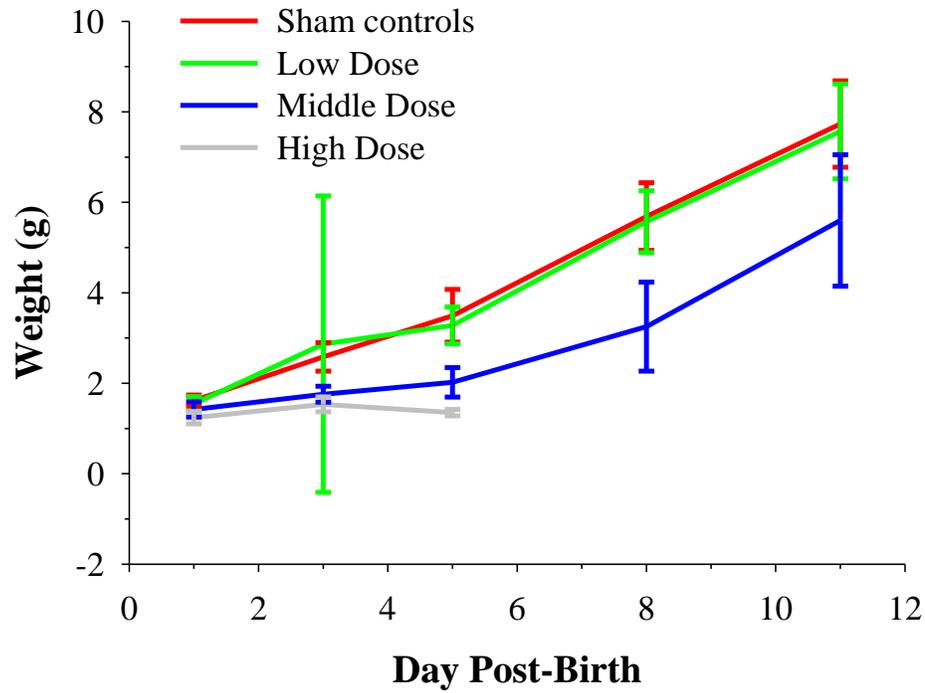
The findings of this experiment demonstrated that in both pregnant and non-pregnant mice, the amount of microspheres deposited and retained in the lungs was proportional to the amount aerosolized. Moreover, there was no difference noted between pregnant and non-pregnant mice in terms of either amount deposited or length of time the microspheres were retained. This suggests that for the current experimental model, pregnant and non-pregnant mice will inhale, be compartmentally exposed to, and retain similar amounts of viral particles when challenged with the same dose.

Conclusion: There is no significant difference in deposition or retention between pregnant & non-pregnant mice of inhaled particles.

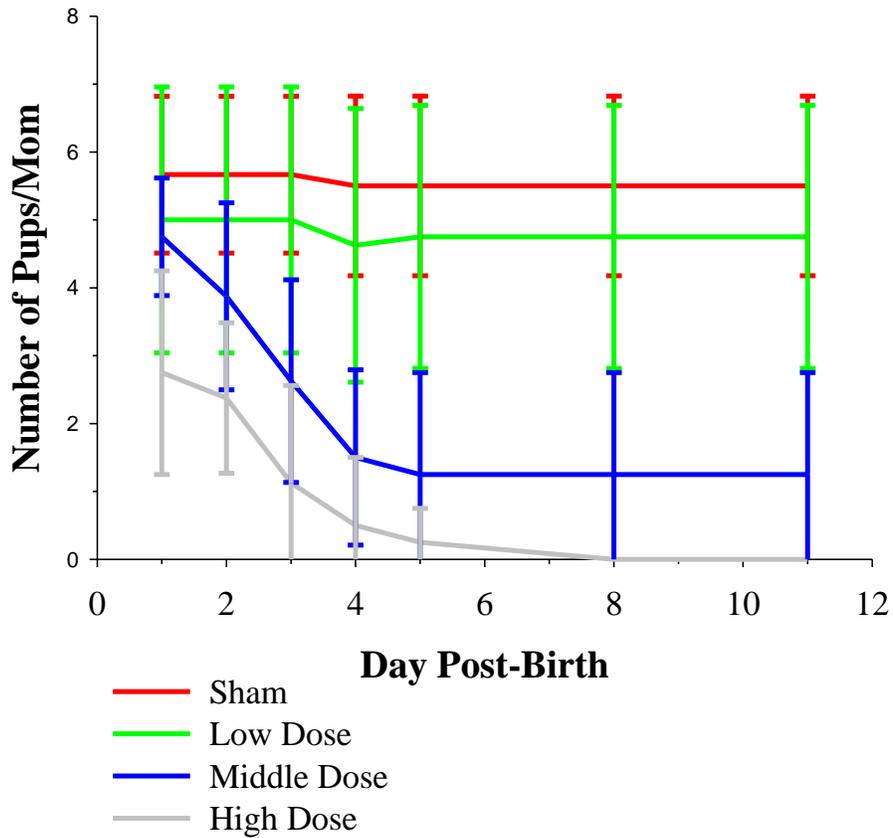
Separate from the original 3 specific aims noted above, interesting observations were made in terms of the effects of the influenza exposure and infection in the mother upon the offspring. This was noted in the 2nd progress report, but will be reported briefly upon here as well. In addition, these new findings with regards to effects on the offspring will also be investigated in future projects, including the R21 that has just been submitted for review to the NIH/NIAID.

Four days after infection with A/PR/8/34, all pregnant mice delivered their pups (day 18 of gestation). It was immediately evident that differences in the number of mice born to each pregnant mouse corresponded with the dose of A/PR/8/34. This is noted in the next 2 figures. Overall it was noted that influenza challenges had statistically significant effects not only on the size of the litter, but also on the weight of pups at birth, and weight gain of neonatal pups over the first week of life. These noted effects on pups demonstrated a dose-response relationship to the influenza challenge dose. These are very interesting findings and bring up new considerations about the effects in-utero of maternal influenza infection. This line of investigation will be explored more intensively in the coming years.

Average Pup Weight Gain



Average number of pups



The work from this project has led to 3 abstracts that have been or will be presented at national meetings this year:

1. **Beigi RH**, Faith S, Hattemer A, Hartman A, Reed DS, Stefano-Cole K. Development of a pregnant animal model for aerosol infection with influenza. Oral presentation at the Aerobiology in Biodefense III Conference, Cumberland, MD, July, 2009.
2. Reed D, Faith S, Cole K, Hartman A, Hattemer A, **Beigi RH**. Small-particle aerosolization enhances the virulence and time to death of mouse-adapted influenza viruses in Balb/c mice. Poster presentation at the American Society of Microbiology, Biodefense Meeting, Washington D.C, March, 2010.
3. **Beigi RH**, Faith S, Hattemer A, Hartman A, Reed DS, Stefano-Cole K. Aerosolized Influenza Infection During Murine Pregnancy & the Effects on the Offspring. Poster Presentation: Society For Gynecologic Investigation Annual Meeting, Orlando, FL, March 2010.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be “No.”

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

Yes
 No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

Yes
 No

If “Yes” to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both “No.”)

18(C) How many hospital and health care professionals were involved in the research project?

_____ Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____ Number of subjects originally targeted to be included in the study

_____ Number of subjects enrolled in the study

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:

_____ Males
_____ Females
_____ Unknown

Ethnicity:

_____ Latinos or Hispanics
_____ Not Latinos or Hispanics
_____ Unknown

Race:

_____ American Indian or Alaska Native
_____ Asian
_____ Blacks or African American
_____ Native Hawaiian or Other Pacific Islander
_____ White
_____ Other, specify: _____
_____ Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?

_____ Yes
_____ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?

_____ Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the “Cognition and MRI in Older Adults” research project (Project 1), and two publications for PI Zhang for the “Lung Cancer” research project (Project 3), the filenames should be:

- Project 1 – Smith – Publication 1 – Cognition and MRI
- Project 1 – Smith – Publication 2 – Cognition and MRI
- Project 3 – Zhang – Publication 1 – Lung Cancer
- Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
2.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
3.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes No

If yes, please describe your plans:

We plan to combine data from at least 2 of the 3 abstracts and submit for peer-reviewed publication within the next 3 months.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.

Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. **DO NOT DELETE THESE INSTRUCTIONS.** There is no limit to the length of your response.

The results of our studies suggest that late pregnancy influenza infection may be directly detrimental to the offspring, which was not previously recognized. It has been known for some time that pregnancy increases the risk of bad outcomes from influenza infection (this again was validated in the recent and ongoing 2009 H1N1 influenza pandemic). However, the full effects on the offspring of influenza in pregnancy have never been fully elucidated. The data derived herein suggests that late term influenza infection may have direct effects on the offspring in terms of many markers of well-being (litter size, birth weight, early neonatal growth and early neonatal survival). This was found using a relatively benign mouse-adapted seasonal strain (A/PR/8). This suggests such effects may be even more pronounced from infection with more aggressive pandemic strains (such as 2009 H1N1 and others). This will be explored in future research.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment.

Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. **DO NOT DELETE THESE INSTRUCTIONS.** There is no limit to the length of your response.

The main “new prevention discovery” noted herein is the potential effects of influenza infection in pregnancy upon the offspring (murine pups) as noted above in answer 21. This has important potential prevention implications because encouraging vaccination of pregnant women has growing evidence in favor of direct fetal and neonatal benefit, and the data herein suggests potentially more support for this concept (in addition to what was already known).

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes _____ No x _____

If “Yes” to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is “No.”)

- a. Title of Invention:
- b. Name of Inventor(s):
- c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):
- d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes _____ No _____

If yes, indicate date patent was filed:

- e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes _____ No _____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

- f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes _____ No _____

If yes, how many licenses were granted? _____

- g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes ___ No ___

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes _____ No x _____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

Biosketch for Richard H. Beigi, MD, MSc.

A. Positions and Honors.

Positions:

1/2004 – 7/2006: CASE School of Medicine, Assistant Professor, Reproductive Biology, Department of Obstetrics and Gynecology, Metro Health Medical Center
8/2006 – Current University of Pittsburgh SOM, Assistant Professor, Reproductive Sciences, Department of Obstetrics/Gynecology /RS, MWH of UPMC

Honors:

Department Excellence in Resident Education Award	2009
APGO: Departmental Excellence Medical Student Teaching Award	2008
ACOG Annual Meeting: Mentoring Research Award Ceremony	2007
Alpha-Omega-Alpha (AOA) Inductee - Resident Teaching Distinction	2001
Senior Resident Research Award – Cleveland OB/GYN Society	2001

Service:

11/2009 – Current	CDC-COCA Critical Care Conference Call Invited Expert: Critical Care of H1N1 in Pregnancy
10/2009 – Current	ACOG Representative to the National Vaccine Advisory Committee (NVAC) Working Group
03/2009	NICHD/NIAID : Invited Expert: Pregnancy and Contraception in Microbicide Development Meeting
02/2009 – Current	CDC : Invited Expert: Advisory Work-Group to the ACIP: Pertussis (Tdap) Vaccination during Pregnancy
10/2008	CDC : Advisory Committee on Immunization Practices (ACIP). Recommendations from the Anthrax Vaccine in Pregnancy Work-Group
09/2008	NIH/NICHD – Biodefense Expert Working Group Meeting. Rockville, Maryland September 8-9, 2008
05/2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Antibiotic and Antivirals use in Pregnancy
05-2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Radiation Exposures in Pregnancy
05-2008 – Current	NIH/NICHD – Invited Expert: Biodefense – Infectious Diseases Working Group: Vaccine use in Pregnancy
05-2008 – Current	CDC – Invited Advisory group to ACIP: Anthrax vaccine in pregnancy
04/2008 – Current	CDC – Invited Expert Working Group: Pandemic Influenza & Pregnancy
04/2007	NIH/NICHD : Invited Study Section Reviewer: HIV Maternal-Child AIDS Network Sites

B. Selected Peer-reviewed Publications (Selected from a list of 31)

1. **Beigi RH.** Pandemic Influenza and Pregnancy: A Call for Preparedness Planning. *Obstet Gynecol* 2007; 109:1193-6.

2. Tabery J, Mackett CW and the University of Pittsburgh Medical Center Pandemic Influenza Task Force's Triage Review Board (**Beigi RH**). Ethics of Triage in the Event of an Influenza Pandemic. *Disaster Med Public Health Preparedness* 2008; 2:114-8.
3. Farrell RM, **Beigi RH**. Pandemic Influenza and Pregnancy: An Opportunity to Assess Maternal Bioethics. *Am J Pub Health*. *Am J Pub Health* 2009 2009; 99:S231-S235.
4. **Beigi RH**, Davis G, Hodges J, Akers A. Preparedness Planning for Pandemic Influenza Among Large United States Maternity Hospitals. *Emerging Health Threats* 2009;2:e2.doi:10.3134/ehth.09.002.
5. Rasmussen SA, Jamieson DJ, MacFarlane K, Cragan JD, Jennifer Williams J, on behalf of the Pandemic Influenza and Pregnancy Working Group...(**Richard Beigi**). Pandemic Influenza: Special Considerations for Pregnant Women – Summary of a Meeting of Experts. *A J Pub Health* 2009; 99:S248-S254.
6. **Beigi RH**, Switzer GE, Meyn LA. Acceptance of a pandemic avian influenza vaccine in pregnancy. *J Reprod Med* 2009; 54:341-46.
7. Lee BY, Bailey RR, Wiringa AE, Assi TM, **Beigi RH**. Anti-viral Medications for Pregnant Women for Pandemic and Seasonal Influenza: An economic computer model. *Obstet Gynecol* 2009; 114(5):971-980.
8. Broughton DE, **Beigi RH**, Switzer GE, Raker CA, Anderson BL. Obstetrical Healthcare support staff attitudes and beliefs regarding influenza vaccination in pregnancy. *Obstet Gynecol* 2009; 114(5):981-7.
9. **Beigi RH**, Wiringa AE, Bailey R, Assi TM, Lee BY. Economic value of seasonal and pandemic influenza vaccination during pregnancy. *Clin Infect Dis* 2009; 49(12):1784-92.

D. Research Support.

1. U01-AI-068633-01: Microbicide Trials Network 4/2008 – Ongoing
NIH/NIAID/NICHD
Protocol Chair: MTN-002: First ever study to be conducted among pregnant women of a topical microbicide for the prevention of HIV. This is a Pharmacokinetic and Placental Transfer evaluation of Term Gravidas undergoing cesarean section.
2. U01-AI-068633-01: Microbicide Trials Network 9/2008 – Ongoing
NIH/NIAID/NICHD
Protocol Co-Chair: MTN-016: HIV Prevention Agent Exposure Registry: EMBRACE Protocol. This is an international pregnancy exposure registry for all women enrolled in HIV prevention investigations.
3. U10-HD-047905-06: Obstetric-Fetal Pharmacology Research Units: 1/2010 – Ongoing
NIH/NICHD:
Site Co-Investigator: Currently we are conducting an investigation of the pharmacokinetics of oseltamivir in pregnancy through this research network that is charged with the investigation of the pharmacokinetics and pharmacodynamics of therapeutic agents in pregnancy
4. ACOG RESEARCH AWARD 4/2007 – 4/2008
Co-Principal Investigator & Mentor

Title: Developing a Comprehensive Immunization Program: Surveying Vaccination Needs and Patient Interest at an Academic Women's Medical Center.

Biosketch for Kelly Stefano-Cole, Ph.D.

B. Positions and Honors:

Positions and Employment:

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| 1994-1998 | Postdoctoral Research Associate, University of Pittsburgh School of Medicine, Department of Molecular Genetics and Biochemistry, Pittsburgh, PA. |
| 1999-2001 | Research Instructor, University of Pittsburgh School of Medicine, Department of Molecular Genetics and Biochemistry, Pittsburgh, PA. |
| 2002-2006 | Assistant Professor, University of Pittsburgh School of Medicine, Department of Medicine, Division of Infectious Diseases, Pittsburgh, PA. |
| 2006-2009 | Assistant Professor, University of Pittsburgh School of Medicine, Department of Immunology, Pittsburgh, PA. |
| 2007-present | Associate Director, Regional Biocontainment Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, PA |
| 2009-present | Associate Professor, University of Pittsburgh School of Medicine, Department of Immunology Pittsburgh, PA. |

Honors:

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| 2003 | University of Pittsburgh School of Medicine, Dept. of Medicine Junior Faculty Research Award |
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C. Selected Peer-Reviewed Publications (from a list of 40)

1. **Cole KS**, Alvarez M, Elliott DH, Lam H, Rowles JL, Clements JE, Murphey-Corb M, Montelaro RC, Robinson JE. Rhesus monoclonal antibodies to simian immunodeficiency virus define nine binding domains on the surface envelope glycoprotein. *Virology* 2001; 290:59-73.
2. **Cole KS**, Steckbeck JD, Rowles JL, Czajak SC, Desrosiers RC, Montelaro RC. Removal of N-linked glycosylation sites in the V1 region of SIV gp120 results in redirection of B-cell responses to V3. *J Virol* 2004; 78:1525-1539.
3. McBurney SP, Young KR, Nwaigwe CI, Soloff AC, **Cole KS**, Ross TM. Lentivirus-like particles without reverse transcriptase elicit efficient immune responses. *Curr. HIV Res.* 2006; 4:475-484.
4. Steckbeck JD and **Cole KS**. Dissecting the humoral immune response to simian immunodeficiency virus: mechanisms of antibody-mediated virus neutralization. *Imm. Res.* 2006; 36:51-60.
5. Milush JM, **Cole KS**, Schmidt K, Durudas A, Pandrea I, Sodora DL. Mucosal innate immune response associated with a timely humoral immune response and slower disease progression after oral transmission of simian immunodeficiency virus to rhesus macaques. *J Virol* 2007; 81: 6175-6186.
6. Milush JM, Reeves J, Gordon SM, Zhou D, Muthukumar A, Kosub DA, Chacko E, Giavedoni LD, Ibegbu CC, **Cole KS**, Miamidian JL, Paiardini M, Barry AP, Staprans S, Silvestri G, Sodora DL. Virally induced CD4⁺ T cell depletion is not sufficient to induce AIDS in a natural host. *J Immunol* 2007; 179: 3047 - 3056.

Mechanisms of SIV Neutralization

This study focused on defining the mechanisms of antibody-mediated neutralization of SIV using a unique panel of rhesus monoclonal antibodies.

Role: Principal Investigator

Biosketch for Doug Reed, Ph.D.

B. Positions and Honors.

2008–present Aerobiology Manager, Regional Biocontainment Laboratory, University of Pittsburgh, Pittsburgh, PA

2007–2008 Chief, Department of Animal Studies, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

2005-2007, Team Leader, Department of Animal Studies, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

1999–2005, Microbiologist, Center for Aerobiological Sciences, USAMRIID, Fort Detrick, Frederick, MD

2000-present Member, American Association of Immunologists

2008-present Member, American Society of Microbiology

Army Research & Development Award recipient in 2003

U.S. Army Achievement Medal for Civilian Service, 2005

C. Peer-reviewed publications or manuscripts in press (in chronological order).

1. McElroy, A.K., Bray, M., **Reed, D.S.**, and Schmaljohn, C.S. 2002. Andes virus infection of cynomolgus macaques. *J Infect Dis.* 186:1706-12.
2. Geisbert T., Hensley, L.E., Larsen, T., Young, H.A., **Reed, D.S.**, Geisbert, J.B., Scott, D.P., Kagan, E., Jahrling, P.B., and Davis, K.J. 2003. Pathogenesis of Ebola hemorrhagic fever in cynomolgus macaques: evidence that dendritic cells are early and sustained targets of infection. *Am J Pathol* 163(6):2347-2370.
3. **Reed, D.S.**, Hensley, L., Geisbert, J., Jahrling, P.B., and Geisbert, T. 2004. Depletion of peripheral blood T lymphocytes and NK cells during the course of Ebola hemorrhagic fever in cynomolgus macaques. *Viral Immunology* 17(3): 390-400.
4. **Reed, D.S.**, Lind, C.M., Sullivan, L.J., Pratt, W., and Parker, M. 2004. Aerosol infection of cynomolgus macaques with enzootic strains of Venezuelan Equine Encephalitis. *J Infect Dis.* 189:1013-7.
5. **Reed, D.S.**, Lind, C.M., Lackemeyer, M., Sullivan, L.J., Pratt, W., and Parker, M. 2005. Genetically engineered, live attenuated vaccines protect nonhuman primates against aerosol challenge with a virulent IE strain of Venezuelan equine encephalitis virus. *Vaccine*: 23(24) pp. 3139-3147.
6. **Reed, D.S.**, Larsen, T., Sullivan, L.J., Lind, C.M., Lackemeyer, M.G., Pratt, W.D., and Parker, M.D. 2005. Aerosol exposure to western equine encephalitis virus causes fever and encephalitis in cynomolgus macaques. *J Infect Dis.* 192(7):1173-82
7. **Reed, D.S.**, Lackemeyer, M.G., Garza, N.L., Norris, S., Gamble, S., Sullivan, L.J., Lind, C.M., Raymond, J.L. 2007. Severe encephalitis in cynomolgus macaques exposed to aerosolized Eastern Equine Encephalitis virus. *J Infect Dis.* 196:441-450.

8. Rubins, K. H., Hensley, L.E., Wahl-Jenson, V., Daddario, K.M., Young, H., **Reed, D.S.**, Jahrling, P.B., Brown, P.O., Relman, D.A., Geisbert, T.W. 2007. The temporal program of peripheral blood gene expression in the response of non-human primates to ebola hemorrhagic fever. *Genome Biology* 8(8)R174:1-14.
9. Fritz, E.A., Geisbert, J.B., Geisbert, T.W., Hensley, L.E., **Reed, D.S.** 2008. Cellular immune response to Marburg virus infection in cynomolgus macaques. *Viral Immunol.* 21(3):355-64.
10. Geisbert, T.W., Daddario-Dicaprio, K.M., Geisbert, J.B., **Reed, D.S.**, Feldmann, F., Grolla, A., Stroher, U., Fritz, E.A., Hensley, L.E., Jones, S.M., Feldmann, H. 2008. Attenuated recombinant vaccines protect nonhuman primates against aerosol challenge with Ebola and Marburg viruses. *Vaccine.* 26(52):6894-6900.
11. Rossi, C.A., Ulrich, M., Norris, S., **Reed, D.S.**, Pitt, M.L.M., Leffel, E.K. 2008. Identification of a surrogate marker for infection in the african green monkey model of inhalational anthrax. *Infect Immun.* 76:5790-5801.
12. Martin, S.S., Bakken, R.R., Lind, C., **Reed, D.S.**, Price, J.L., Koehler, C., Parker, M.D., Hart, M.K., Fine, D.L. 2009. Telemetric analysis to detect febrile responses in mice following vaccination and challenge with Venezuelan equine encephalitis virus. *Vaccine* 27:6814-23
13. Roy, C.J., **Reed, D.S.**, Wilhelmsen, C., Hartings, J., Norris, S., Geisbert, J., Jahrling, P., Steele, K.E. 2009. Pathogenesis of aerosolized Eastern Equine Encephalitis virus in guinea pigs. *Virology J.* 6:170.
14. Alves, D.A., Glynn, A.R., Lackemeyer, M.G., Garza, N.L., Buck, J.G., **Reed, D.S.** 2010. Aerosol exposure to the Angola strain of Marburg virus causes lethal viral hemorrhagic fever in cynomolgus macaques. *Vet Pathol.* In Press.

D. Research Support.

Ongoing Research Projects:

1. S1008576. Cell Mediated Immunity following LVS vaccination in Mice. 2009-2010. Study Director. 20% effort. Tularemia Vaccine Development Team, NIAID subcontract through Dynport Vaccine Company

2. Completed Research Projects:

1. H.H.0003_07_RD_B. Development of replicon-based vaccines for alphaviruses. Co-Investigator. 2004-2008. NIH/DOD funded. Project objective: evaluate the efficacy of replicon based alphavirus vaccines against aerosol challenge with 3 alphaviruses.
2. X.X.009_06_RD_B. Animal models of aerosol infection with filoviruses. Principal Investigator. 2006-2008. DOD funded. Objective of project was to develop rodent and nonhuman primate models for use in efficacy studies to evaluate vaccines or therapeutics for protection against aerosol challenge with Marburg or Ebola virus
3. H.H.0002_07_RD_B. Live Attenuated WEE and EEE Viruses for a Combined Equine Encephalitis Vaccine. Co-Investigator. 2001-2008. DOD funded. Project objective was to evaluate the efficacy of live, attenuated alphaviruses as vaccines against aerosol

challenge with three alphaviruses (Venezuelan, Western, and Eastern equine encephalitis) in animal models.

4. W81XWH-06-C-0390. Novel viral biowarfare agent identification & treatment. Principal Investigator. 2006-2008. Congressional/DOD funded. Develop novel therapeutics for treatment of Venezuelan equine encephalitis.