Advancing Research in Gestational Lyme Disease: Biobank Establishment and Study Development

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A cross-disciplinary compendium of techniques tailored to probe the intricacies of the Lyme disease bacterium *Borrelia burgdorferi*.

This resource meticulously compiles standard and avant-garde methods, accessible to novices and veteran scientists alike, for robust *in vitro*, *in vivo*, *in situ*, *de novo*, and clinical investigations.

Join us in advancing the frontier of infectious disease methodology.

Chapter 17: Establishing a Pregnancy Lyme Disease Biobank

Stanley J. Naides, MD, FACP, FACR

Chapter 18: Developing a Prospective Gestational Lyme Disease Study

Graham McLennan, Suzanne E. Dale, Laura Gillim, Vivian Weinblatt, Robert Wallerstein, and Stanley J. Naides

Presentation Overview

Introduction to Lyme Disease and Pregnancy:

- Overview of Lyme disease, its incidence, and specific concerns related to pregnancy.

Study Objectives and Design:

- Goals of the study, including maternal and fetal health outcomes, and biobank establishment.

Diagnostic and Sample Collection Methods:

- Serological and molecular diagnostic methods, sample types, and processing protocols.

Biobank Establishment:

- Structure, objectives, and governance of the biobank to support long-term research.

Ethical Considerations:

- Informed consent, privacy, and security issues related to study participants.

Public-Private Partnerships:

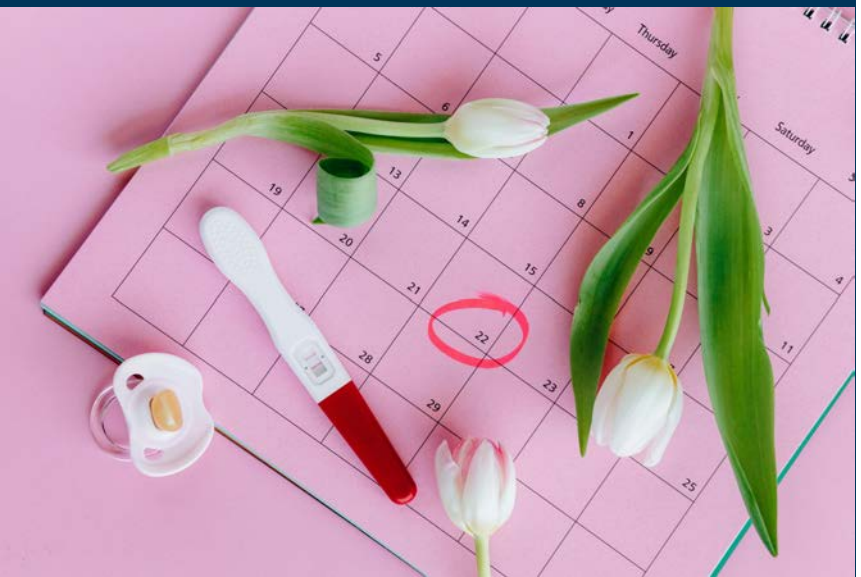
- Importance of collaborations to fund and resource the study and biobank.

Long-Term Impact and Future Directions:

- Potential contributions to Lyme disease research and public health.

1. www.cdc.gov/lyme/stats/index.html,
2. https://icd.who.int/

Introduction to Lyme Disease and Pregnancy



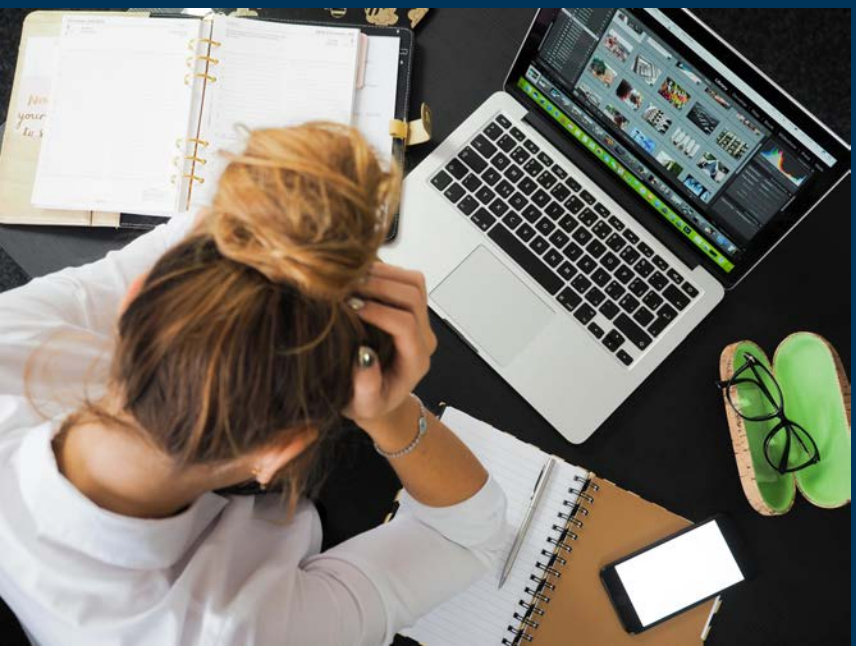
Overview of Lyme Disease:

- **Incidence in Europe and the United States:**
  - Lyme disease incidence in Europe ranges from 20-40 per 100,000, with higher rates in endemic areas (Smith et al., 2002).
  - In the U.S., about 476,000 cases are estimated annually, though only 30,000 are officially reported (CDC, 2023).
- **Risk Factors and Symptoms:**
  - Lyme disease is transmitted by ticks (e.g., *Ixodes scapularis*) and manifests as erythema migrans (bull's-eye rash), fever, fatigue, and joint pain (Stanek et al., 2012).

Impact on Pregnancy:

- **Potential Risks to Pregnant Women and Fetuses:**
  - Risks include spontaneous abortion, stillbirth, congenital anomalies, and developmental issues (Lakos & Solymosi, 2010).
- **Current State of Research:**
  - Limited studies focus on gestational Lyme disease, with most being case reports or small series (Maraspin et al., 2010).

Rationale for the Study



Existing Gaps in Research:

- **Limited Data on Gestational Lyme Disease:**
  - Few comprehensive studies; most data comes from small case series, limiting generalizability (Maraspin et al., 2010).
- **Need for Comprehensive Population-Based Studies:**
  - Large-scale prospective studies are needed to establish accurate incidence, risk factors, and outcomes (Leavey et al., 2016).

Importance of the Proposed Study:

- **Addressing Unanswered Questions in Maternal and Fetal Health:**
  - This study aims to fill the knowledge gap on the effects of *Borrelia* infection during pregnancy and long-term outcomes for children (Smith et al., 2002).

Study Objectives

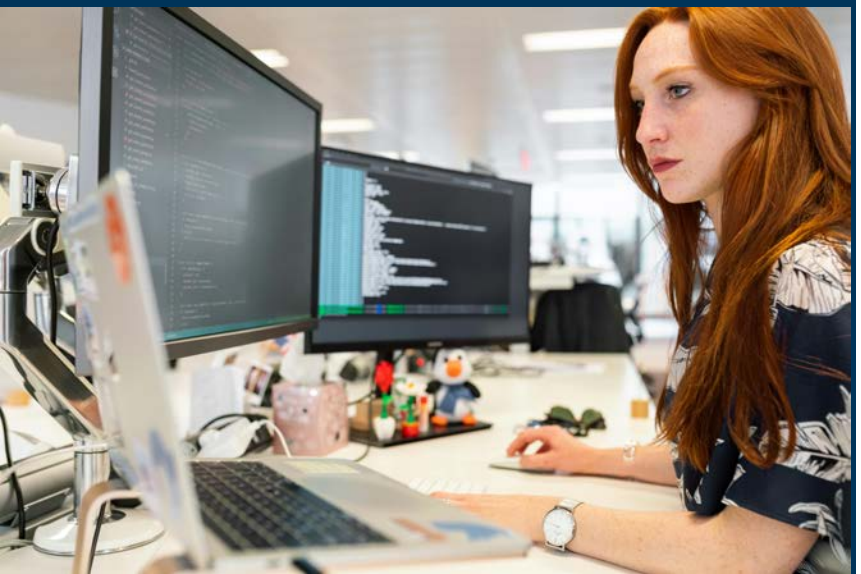
Primary Goals:

- **Assess Maternal and Fetal Outcomes:**
  - Monitor pregnancy outcomes, including potential complications and developmental delays in offspring (Lakos & Solymosi, 2010).
- **Long-Term Follow-Up of Offspring:**
  - Children will be monitored until age 5 to assess developmental milestones and potential chronic conditions (McLennan et al., 2024).

Secondary Goals:

- **Detection of Borrelia Species and Other Tick-Borne Pathogens:**
  - Use serological, microscopic, culture, and molecular techniques for comprehensive pathogen detection (McLennan et al., 2024).
- **Establishment of a Biobank for Future Research:**
  - Create a biorepository to store biospecimens for ongoing and future research on Lyme disease and pregnancy (McLennan et al., 2024).

Study Design Overview



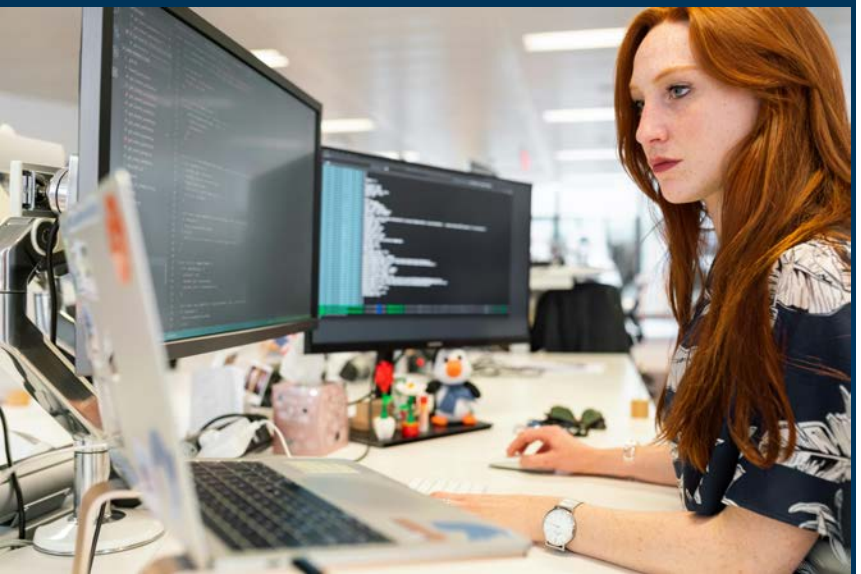
Recruitment Strategy:

- **Inclusion of Obstetrical Practices in Endemic and Non-Endemic Areas:**
  - Recruit participants from a variety of geographic regions to capture a wide range of exposure risks (Lakos & Solymosi, 2010).
- **Targeting Early Pregnancy for Enrollment:**
  - Enrollment begins as early as possible in the first trimester to track the full course of pregnancy (WHO, 2023).

Study Cohorts:

- **Comparison of Infected vs. Non-Infected Pregnant Women:**
  - Establish cohorts for comparative analysis of pregnancy outcomes between infected and non-infected participants (Maraspin et al., 2010).
- **Considerations for Geographic and Demographic Variability:**
  - Adjust for variables such as local *Borrelia* species, socioeconomic status, and access to healthcare (Leavey et al., 2016).

Study Design Overview



Participant Engagement:

- **Recruitment Methods: Social Media, Patient Support Groups, Direct Advertising:**
  - Utilize diverse channels to maximize participant enrollment and retention (Leavey et al., 2016).

- **Ensuring a Representative Sample:**
  - Focus on recruiting a demographically diverse participant pool to enhance generalizability of findings (Maraspin et al., 2010).

Diagnostic Methods

Serological Testing:

- **Two-Tier Testing Algorithm:**
  - Initial ELISA test followed by a Western blot for confirmation; standard protocol recommended by CDC (CDC, 1995).
- **Challenges and Limitations in Pregnant Women and Neonates:**
  - Potential for false positives/negatives; maternal antibodies may affect neonatal testing accuracy (Smith et al., 2002).

Molecular and Non-Serological Testing:

- **PCR, Microscopy, Culture, and Other Methods:**
  - PCR for direct detection of *Borrelia* DNA; microscopy and culture for further confirmation (CDC, 2021).
- **Importance of Accurate Diagnosis for Maternal and Fetal Health:**
  - Early and accurate diagnosis is critical to prevent adverse pregnancy outcomes (Smith et al., 2002).

Case Definitions for Lyme Disease:

- **Criteria for Diagnosing in Pregnant Women, Fetuses, and Neonates:**
  - Standardized definitions are needed for consistent diagnosis and treatment across populations (CDC, 2021).

Biospecimen Collection and Processing

Types of Biospecimens Collected:

- **Maternal and Cord Blood, Amniotic Fluid, Placental Tissue, etc.:**
  - Specimens collected throughout pregnancy for serological and molecular analysis (McLennan et al., 2024).

Processing and Storage Protocols:

- **Ensuring Sample Integrity and Standardization:**
  - Standardized protocols for collection, transport, and storage to maintain sample viability (WHO, 2023).
- **Use of Biospecimens for Ongoing and Future Research:**
  - Biospecimens will be stored in the biobank for use in current and future research initiatives (McLennan et al., 2024).

Challenges in Sample Collection:

- **Addressing Logistical Issues and Ensuring High-Quality Samples:**
  - Develop solutions for timely collection and transport, particularly from remote areas (McLennan et al., 2024).

Establishing the Pregnancy Lyme Disease Biobank

Objectives and Scope:

- **Support for the Study and Broader Research Community:**
  - Provide high-quality biospecimens for Lyme disease research and other related studies (McLennan et al., 2024).
- **Long-Term Storage and Management of Biospecimens:**
  - Ensure samples are preserved under optimal conditions for extended research use (NIH, 2023).

Governance and Oversight:

- **Structure of the Executive Committee:**
  - Committee responsible for the biobank's operations, policies, and strategic direction (McLennan et al., 2024).
- **Roles and Responsibilities of Committees:**
  - Various subcommittees to manage biobank operations, data security, and ethical compliance (NIH, 2023).

Sample Provenance and Ownership:

- **Policies for Access to Samples and Data:**
  - Clear guidelines on who can access the biobank's resources and under what conditions (McLennan et al., 2024).
- **Ensuring Ethical Use of Stored Biospecimens:**
  - Adherence to ethical guidelines in the use of samples for research (NIH, 2023).

Ethical Considerations

Informed Consent Process:

- **Special Considerations for Pregnant Women, Fetuses, and Neonates:**
  - Consent procedures must be tailored to protect vulnerable populations and ensure fully informed participation (OHRP, 2023).

Data Privacy and Security:

- **Compliance with HIPAA and Other Regulations:**
  - All data handling must comply with HIPAA and other relevant regulations to protect participant privacy (HIPAA, 1996).
- **Strategies for De-Identification and Secure Data Management:**
  - Implement robust data de-identification protocols to ensure confidentiality (McLennan et al., 2024).

Human Subjects Protection:

- **Oversight by Institutional Review Boards (IRBs):**
  - Regular IRB reviews to ensure ethical conduct throughout the study (OHRP, 2023).
- **Addressing Ethical Issues in Vulnerable Populations:**
  - Special attention to the rights and protections of pregnant women, fetuses, and neonates (McLennan et al., 2024).

Public-Private Partnerships

Role of Collaborations:

- **Importance of Public-Private Partnerships for Funding and Resources:**
  - Essential for securing necessary resources, expertise, and funding for the study (NIH, 2023).
- **Examples of Successful Models (e.g., Alzheimer's Disease Neuroimaging Initiative):**
  - ADNI as a model of effective public-private collaboration for large-scale studies (ADNI, 2023).

Potential Partners and Funding Sources:

- **Government Agencies, Foundations, Universities, Pharma, Diagnostic Labs:**
  - Potential partners include NIH, CDC, pharma companies, and foundations (NIH, 2023).

Building and Sustaining Partnerships:

- **Strategies for Long-Term Collaboration and Resource Sharing:**
  - Establish clear goals, regular communication, and mutual benefit frameworks to maintain partnerships (McLennan et al., 2024).

Long-Term Impact and Future Directions

Research and Clinical Implications:

- **Contributions to Understanding Gestational Lyme Disease:**
  - Potential to establish new guidelines for diagnosis and treatment of Lyme disease in pregnancy (CDC, 2023).
- **Development of New Diagnostic Tools and Treatments:**
  - Research findings may lead to the development of new diagnostic assays and therapeutic approaches (McLennan et al., 2024).

Expansion of the Biobank:

- **Opportunities for Additional Research Initiatives:**
  - Biobank can support a wide range of research projects beyond Lyme disease (McLennan et al., 2024).
- **Long-Term Value to the Scientific Community:**
  - Providing a valuable resource for ongoing and future research (CDC, 2023).

Future Research Directions:

- **Potential Studies Leveraging the Biobank and Study Data:**
  - Studies on co-infections, long-term outcomes, and new diagnostic markers (McLennan et al., 2024).
- **Enhancing Collaboration Across Research Disciplines:**
  - Cross-disciplinary studies could yield innovative approaches and insights (McLennan et al., 2024).

Conclusion

Summary of Key Points:

- **Comprehensive Approach to Studying Gestational Lyme Disease:**
  - Integrating prospective study design with biobank establishment.
- **Importance of the Biobank for Future Research:**
  - Essential for advancing understanding and treatment of Lyme disease.

Final Thoughts:

- **Call to Action for Continued Support and Collaboration:**
  - Encourage partnerships and funding to ensure study success.
- **Emphasizing the Impact on Public Health:**
  - Highlight the potential for significant public health benefits.

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RECRUITING

Pregnancy and Early Neurodevelopmental Outcomes Following In Utero Lyme Disease Exposure

ClinicalTrials.gov ID NCT06026969

Sponsor Children's National Research Institute

Information provided by Children's National Research Institute (Responsible Party)

Last Update Posted 2023-09-07

RECRUITING

Navigating Pregnancy and Parenthood With Lyme Disease

ClinicalTrials.gov ID NCT06397794

Sponsor Children's National Research Institute

Information provided by Children's National Research Institute (Responsible Party)

Last Update Posted 2024-05-03

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Children's National Research Institute

Collaborators

- Clinical Trials Network for Lyme and Other Tick-Borne Diseases
- Steven & Alexandra Cohen Foundation

Investigators

- Principal Investigator: Sarah B. Mulkey, MD, PhD, Children's National Research Institute

https://clinicaltrials.gov/search?cond=Lyme%20Disease&term=Pregnancy&viewType=Card

https://lymediseaseassociation.org/category/lyme-tbd/pregnancy-and-lyme/

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