VA/DoD Clinical Practice Guideline

Management of Pregnancy

2009



VA/DoD Evidence Based Practice

VA/DoD CLINICAL PRACTICE GUIDELINE FOR PREGNANCY MANAGEMENT

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs (VA) and The Department of Defense (DoD) guidelines are based on the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably and appropriately occur when providers take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

Version 2.0 - 2009 ef

Prepared by:

The Pregnancy Management Working Group

With support from:

The Office of Quality and Performance, VA, Washington, DC

&

Quality Management Directorate, United States Army MEDCOM

Table of Contents

INTRODUCTION	6
ALGORITHM	11
ANNOTATIONS	12
A-0. Organization of Prenatal Care	12
A-1. Confirmed Pregnancy	13
A-2. First Visit with Nurse: Weeks 6 to 8 Assess for Risk Factors	13
A-3. The First Provider Visit: Update Weeks 10-12	16
A-4. Assessment of Risk Factors for Preterm Birth New	20
A-5. Routine Visits: Weeks 16-27	23
A-6. Routine Visits: Weeks 28-41	24
A-7. Postpartum Visit Update	24
Interventions at All Visits	29
I- 1. Screening for Hypertensive Disorders of Pregnancy: Update Weeks (All)	29
I- 2. Breastfeeding Education: Weeks (All)	30
I- 3. Exercise During Pregnancy: Update Weeks (All)	31
I- 4. Influenza Vaccine (Season-Related): Weeks (Any Week)	32
First Visit with Nurse (6-8 Weeks)	33
I- 5. Screening for Tobacco Use – Offer Cessation: Update Weeks 6 - 8	33
I- 6. Screening for Alcohol Use – Offer Cessation: Weeks 6 - 8	34
I- 7. Screening for Drug Use – Offer Treatment: Weeks 6 - 8	35
I- 8. Screening for Blood Type (ABO,Rh) and Antibody Status: Weeks 6 to 8	36
I- 9. Screening for Rubella: Weeks 6 - 8	36
I- 10. Screening for Varicella: Weeks 6 to 8	37
I- 11. Screening for Hepatitis B Virus (HBV): Update Weeks 6 - 8	38
I- 12. Treatment for Hepatitis B Infection: Update Week 36	39
I- 13. Screening for Syphilis Rapid Plasma Reagin (RPR): Weeks 6 - 8	40
I- 14. Screening for Asymptomatic Bacteriuria: Update Weeks 6 - 8	41
I- 15. Screening for Tuberculosis: Update Weeks 6-8	42
I- 16. Screening for HIV – Counsel: Weeks 6 - 8	43
I- 17. Screening for Td and Tdap Booster: Weeks 6 - 8	44
I- 18. Screening for Anemia: New Weeks 6-8	45
I- 19. Screening for Hemoglobinopathies: Update Weeks 6-8	46
I- 20. Screening for Domestic Abuse: Update Weeks 6 - 8	47
I- 21 Screening for Depression: New Weeks 6-8 28 Postpartum visit	49

First Visit With Provider (10-12 Weeks)	51
I- 22. Establishing the Gestational Age: New Weeks 10-12	51
I- 23. Auscultation Fetal Heart Tones: Weeks 10-12, All following visits	53
I- 24. Screening Fundal Height: Weeks 10-12; All following visits	54
I- 25. Assessing (Inappropriate) Weight Gain: Weeks 10-12; All following visits	55
I- 26. Nutritional Supplements: New Weeks 10-12	56
I- 27. Obesity: New Weeks 10-12	58
I- 28. History of Gastric Bypass/Bariatric Surgery: New Weeks 10-12	59
I- 29. Screening for Gonorrhea: Weeks 10-12	60
I- 30. Screening for Chlamydia: Weeks 10-12	61
I- 31. Screening for and Prevention of Cervical Cancer: Update Weeks 10-12	62
I- 32. Screening for HSV: New Weeks 10-12 or onset of symptoms	63
I- 33. Counseling for Cystic Fibrosis Screening: Update Weeks 10-12	64
I- 34. Management of Depression during Pregnancy: New When diagnosed	65
I- 35. Periodontal Disease and Dental Care: New Weeks 10-12	67
I- 36. Prenatal Screening for Fetal Chromosomal Abnormalities: New Weeks 10-12; 16-20	68
Visits During Weeks: 16-27	76
I- 37. Obstetric Ultrasound: Week 16-20	76
I- 38. Education about Symptoms of Preterm Labor: Week-24	79
I- 39. Counseling for Trial of Labor: Update Week 24	81
Visits during Weeks: 28-37	83
I- 40. Screening for Gestational Diabetes: Update Week 28	83
I- 41. Iron Supplement: Update Week 28	85
I- 42. Anti-D Prophylaxis for Rh-Negative Pregnant Women: Week 28	86
I- 43. Assess for Preterm Labor: Weeks 28, 32	87
I- 44. Daily Fetal Movements Counts: Weeks 28; All following visits	88
I- 45. Counseling for Family Planning: Week 32	89
I- 46. Screening for Group B Streptococcus (GBS): Update Week 36	90
I- 47. Assessment of Fetal Presentation: Weeks 36, 38-41	93
Visits During Weeks: 38-41	94
I- 48. Consider Weekly Cervical Check/stripping (sweeping): Update Weeks 38-41	94
I- 49. Term Management: New Weeks 38-41	94
I- 50. Immunization HPV Vaccine: New Prior to discharge; Postpartum visit	96
I- 51. Education - Shaken Baby Syndrome (SBS): New At discharge; Postpartum visit	97

Interventions Not Recommended in Prenatal Care (All Weeks)	99
I- 52. Routine Screening with Fetal Fibronectin: Update Not Recommended	99
I- 53. Routine Cervical Examination: Not Recommended	100
I- 54. Routine Antenatal Pelvimetry: Not Recommended	100
I- 55. Routine Urine Dipstick Test: Not Recommended	101
I- 56. Routine Edema Evaluation: Not Recommended	101
I- 57. Routine Screening for Cytomegalovirus (CMV): Not Recommended	102
I- 58. Rooutine Screening for Parvovirus: Not Recommended	103
I- 59. Routine Screening for Toxoplasmosis: Not Recommended	103
I- 60. Routine Screening for Bacterial Vaginosis: Update Not Recommended	104
I- 61. Immunization – MMR: (measles/mumps/rubella) Not Recommended	105
I- 62. Routine Immunization - Varicella: Not Recommended	105
I- 63. Routine Ultrasound Evaluation of Cervical Length: Update Not Recommended	106
I- 64. Repeat Screening for Anemia, Syphilis, and Isoimmunization: Not Recommended	107
I- 65. Routine Screening for Hypothyroidism: Not Recommended	108
APPENDIX A Guideline Development Process	111
APPENDIX B Screening Items for Self-Administered Questionnaire – First Visit	117
APPENDIX C Hemoglobinopathies	120
APPENDIX D Risk Factors – Preterm Birth	122
APPENDIX E Prenatal Screening for Fetal Chromosomal Abnormalities	125
APPENDIX F Questions for Literature Search	131
APPENDIX G Acronym List	133
APPENDIX H Participant List	136
APPENDIX I Bibliography	139

New The Recommendations are new in Version 2.0 (2009)

INTRODUCTION

The Clinical Practice Guideline for Pregnancy Management (GPM) was developed under the auspices of the Veterans Health Administration (VHA) and the Department of Defense (DoD) pursuant to directives from the Department of Veterans Affairs (VA). VHA and DoD define clinical practice guidelines as:

"Recommendations for the performance or exclusion of specific procedures or services derived through a rigorous methodological approach that includes:

- Determination of appropriate criteria such as effectiveness, efficacy, population benefit, or patient satisfaction; and
- Literature review to determine the strength of the evidence in relation to these criteria."

The intent of the guideline is to:

- Reduce current practice variation and provide facilities with a structured framework to help improve patient outcomes
- Provide evidence-based recommendations to assist providers and their patients in the decision-making process concerning pregnancy
- Identify outcome measures to support the development of practice-based evidence that can ultimately be used to improve clinical guidelines.

2009 UPDATE VERSION OF THE GUIDELINE

In 2003, the first DoD/VA Clinical Practice Guideline for the Management of Uncomplicated Pregnancy was implemented. One of the key components of this CPG was changing from the traditional interval-based visit template (every four weeks in the first and second trimesters) towards a system in which an antenatal visit is planned for a specific gestational age, with each visit having specific well-defined goals and objectives.

The first version of the VA/DoD pregnancy guideline limited its scope of care to women with uncomplicated pregnancies. No recommendations or guidance were given for providers caring for women with common or minor complications of pregnancy. Thus, the guideline was named as the VA/DoD Clinical Practice Guideline for the Management of Uncomplicated Pregnancy (UCP). Women who initially received care according to the guideline simply "exited the guideline" when complications arose. No guidance for even the basic care of these women was provided and the tools, including the medical record materials (flow sheets, mother's handbook, etc.), were deemed non-applicable. However, the UCP guideline materials continued to be used in most institutions and care has been supplemented as needed.

The goal-oriented prenatal care system, first outlined in the 2003 version of the guideline, should be applied to all pregnant women regardless of their risk factors. As such, this guideline encompasses the basic components of prenatal care that will be provided to all pregnant women by low-risk providers (such as Certified Nurse-Midwives, Nurse Practitioners, or Family Practice Care Providers) as well as evidence-based recommendations for advanced prenatal care that should be applied when complications emerge during pregnancy or an increased risk for complications is identified.

However, rather than discard the recommendations for the basic components of prenatal care in women who have been identified with some risk, this version of the guideline includes evidence-based recommendations for routine prenatal care. It also includes additional recommendations suggesting specific and general actions to initiate the appropriate advanced prenatal care for many women with identified risks or complications. Women with specific risk factors, or who develop high-risk conditions complicating the pregnancy, may require additional surveillance (i.e., additional ultrasounds, lab studies, etc.) and/or consultation with advanced prenatal care providers such as Obstetrician/Gynecologists (OB/GYN) specialists or Maternal-Fetal Medicine (MFM) subspecialists.

The recommendations in this guideline may be modified according to local practice conditions and updated scientific evidence. Except in very unusual circumstances, the recommendations outlined in this guideline should serve as a backbone to the supplemental prenatal care that is provided or recommended by advanced prenatal care providers.

The guideline and algorithms are designed to be adapted by individual facilities, considering needs and resources. The algorithm will serve as a guide that providers can use to determine best interventions and timing of care to optimize quality of care and clinical outcomes for their patients. This should not prevent providers from using their own clinical expertise in the care of an individual patient. Guideline recommendations are intended to support clinical decision-making but should never replace sound clinical judgment.

BACKGROUND

Goals of the Guideline

- The primary goal of the Pregnancy Guideline is to improve pregnant woman and provider satisfaction with antenatal care (also referred to in the literature as "prenatal" or "antepartum" care). Approaches include:
 - Outlining antenatal visits for specific gestational ages, with each visit having specific welldefined goals and objectives.
 - Helping ensure both pregnant women and providers are aware of the specific expectations for each visit, thus promoting a partnership with the common goal of a healthy infant and mother. Enhanced patient education will be a hallmark of this healthcare partnership and the goal-oriented prenatal care system.
 - Presenting a standardized care plan in the Pregnancy Guideline that is expected to improve overall patient satisfaction and lessen inter-provider variability, which is often perceived by pregnant women in a negative manner and as a sign of clinical naiveté and uncertainty.
 - Providing a scientific evidence-base for practice interventions and evaluations.

Target population

- The guideline offers best practice advice for antenatal care of pregnant women.
- The guideline will not address specific intra-partum or post-partum needs.

Audiences

The guideline is relevant to primary and secondary healthcare professionals who have direct contact with pregnant women, and make decisions concerning antenatal care.

Development Process

The development process of this guideline follows a systematic approach described in "Guideline-for-Guidelines," an internal working document of VHA's National Clinical Practice Guideline Counsel. Appendix A clearly describes the guideline development process.

The literature was critically analyzed and evidence was graded using a standardized format. The evidence rating system for this document is based on the system used by the U.S. Preventative Services Task Force. (See Appendix A – Development Process.)

Evidence Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.
В	A recommendation that clinicians provide (the service) to eligible patients. At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.
С	No recommendation for or against the routine provision of the intervention is made. At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.
D	Recommendation is made against routinely providing the intervention to asymptomatic patients. At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.
Ι	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Lack of Evidence - Consensus of Experts

Where existing literature was ambiguous or conflicting, or where scientific data were lacking on an issue, recommendations were based on the clinical experience of the Working Group. These recommendations are indicated in the evidence tables as based on "Working Group Consensus."

This Guideline is the product of many months of diligent effort and consensus-building among knowledgeable individuals from the VA, DoD, and academia, and a guideline facilitator from the private sector. An experienced moderator facilitated the multidisciplinary Working Group. The draft document was discussed in two face-to-face group meetings. The content and validity of each section was thoroughly reviewed in a series of conference calls. The final document is the product of those discussions and has been approved by all members of the Working Group.

The list of participants is included in Appendix H to the guideline.

Implementation

The guideline and algorithms are designed to be adapted to individual facility needs and resources. The algorithm will serve as a guide that providers can use to determine best interventions and timing of care for their patients to optimize quality of care and clinical outcomes. This should not prevent providers from using their own clinical expertise in the care of an individual patient. Guideline recommendations are intended to support clinical decision-making but should never replace sound clinical judgment.

Although this guideline represents the state-of-the-art practice at the time of its publication, medical practice is evolving and this evolution will require continuous updating of published information. New technology and more research will improve patient care in the future. The clinical practice guideline can assist in identifying priority areas for research and optimal allocation of resources. Future studies examining the impact of this clinical practice guideline may lead to the development of new practice-based evidence.

Outcomes

- 1. Complete initial screening and intake by the nurse or provider during the first trimester.
- 2. Timely comprehensive screening for risk factors as outlined in the guideline.
- 3. Timely prenatal counseling and education as outlined in the guideline.

Content of the Guideline

The guideline consists of an algorithm that describes the step-by-step process of the clinical decision-making and intervention that should occur, and a summary chart that describes the interventions that should take place throughout the goal-oriented prenatal visits during pregnancy. General and specific recommendations for each visit are included in an annotation section. The links to these recommendations are embedded in the relevant specific steps in the algorithm and the chart describing the overall visits throughout pregnancy.

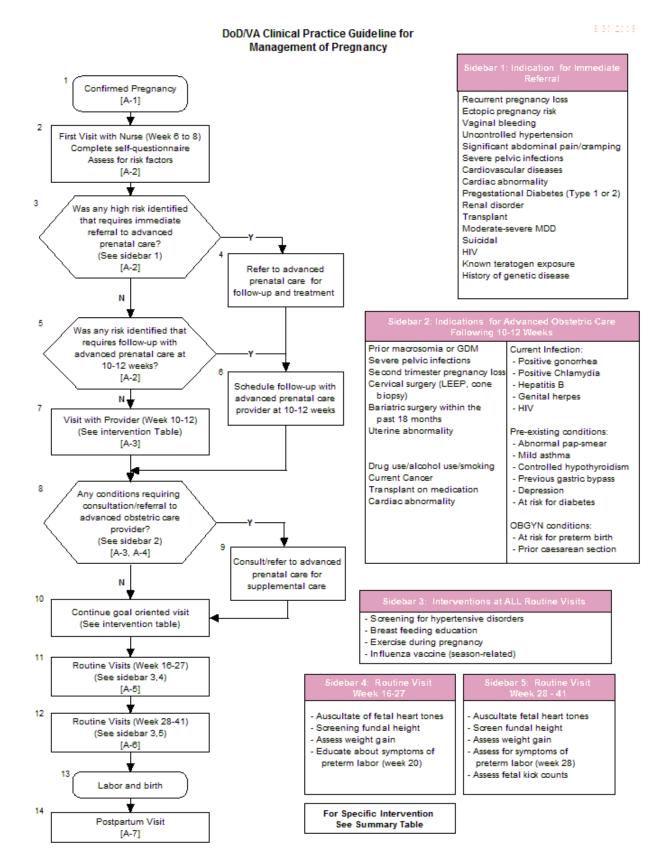
Each annotation includes a brief discussion of the research supporting the recommendations and the rationale behind the grading of the evidence as well as the determination of the strength of the recommendations (SR). A complete bibliography of the references found in this guideline can be found in Appendix I.

Guideline Update Working Group*

VA	DoD
Gwen Garmon, MD, MS	Susan C. Altenburg, RN, BSN, MS, CNM
Connie La Rosa, RN, BSN, MSA	Susan Farrar, LCDR, MD, MPH, MC, USN
Patricia M. Hayes, PhD	Bardett Fausett, Lt Col, MC, USAF
Carla Cassidy, RN, MSN, NP	Trisha Farrell, CDR, CNM, WHNP, NC, USN
	Nancy Hughes, COL, CNM, USA
	Ann Hryshko-Mullen, Lt Col, Ph.D, ABPP, USAF
	Hathryn Kanzler Apolonioo, Capt, Psy.D.
	Mary Kreuger, MAJ, DO, MPH, USA
	Len Kuskowski, CDR, MD, FACOG, MC, USN
	Jason Pates, MAJ, MD, MC, USA
	Mary Wahl, Lt Col, CNM, MSN, NC, USAF
Facilit Oded Sussk	
Quality Management Division, MEDCOM Ernest Degenhardt, COL, MSN, NP, USA Evelyn Patterson, RN, MSN, MBA Marjory Waterman, RN, MN	Healthcare Quality Informatics, Inc. Rosalie Fishman, RN, MSN, CPHQ Joanne Marko, MS, SLP Research Sue Radcliff

^{*} Bolded names are Co-Chair of the Guideline Working Group.
Additional contributor contact information is available in Appendix H.

ALGORITHM



A-0. Organization of Prenatal Care

BACKGROUND

Goal-oriented visits can be provided during individual encounters with OB providers, or can be accomplished in a group setting. Recommendations for reduced visit prenatal care have been instituted at some healthcare facilities. This first DoD/VA Clinical Practice Guideline for the Management of Uncomplicated Pregnancy was implemented in 2003. One of the key components of the clinical practice guideline was changing from the traditional interval-based visit template (every four weeks in the first and second trimesters) towards a system in which an antenatal visit is planned for a specific gestational age, with each visit having specific well-defined goals and objectives.

Group prenatal care has been implemented in many clinical practices in the United States and abroad. Centering Pregnancy® is a group model of prenatal care which provides care in a group setting, integrating assessment support and education at each visit. Studies have shown group prenatal care results in equal or improved perinatal outcomes with no added cost.

Level of care settings:

Throughout this guideline, the term *Routine Prenatal Care* refers to prenatal care generally provided to pregnant women by Family Medicine Physicians, Women's Health Nurse Practitioners, Certified Nurse-Midwives or Obstetrician/Gynecologists. The term *Advanced Prenatal Care* generally refers to care provided to women with complicated pregnancies provided by Obstetrician/Gynecologists and/or Maternal-Fetal Medicine specialists.

Routine Prenatal Care Providers

Individuals qualified to provide routine obstetric care include Family Practice Physicians, Certified Nurse-Midwives, Women's Health Nurse Practitioners, and Obstetrician/Gynecologists. These providers may have varied experience in providing more advanced prenatal care.

Advanced Prenatal Care Providers

Obstetrician-Gynecologist: physician qualified by training and experience to manage complicated pregnancies by virtue of having completed four years of Obstetrics and Gynecology residency training and maintaining currency in the profession.

Maternal-Fetal Medicine (MFM) Specialist: physician who has completed two to three years of Maternal-Fetal Medicine fellowship after completing four years of Obstetrics and Gynecology residency training. Fellowship training provides additional education and practical experience to gain special competence in managing various obstetrical, medical, and surgical complications of pregnancy.

MFM specialists function in collaboration with Family Medicine physicians, Women's Health Nurse Practitioners, Certified Nurse-Midwives and Obstetricians. The relationship and referral patterns between Obstetrician-Gynecologists and MFM specialists will depend on the acuity of the patient's condition and local circumstances.

RECOMMENDATIONS

- 1. Goal-oriented prenatal care system can be delivered to all pregnant women. [B]
- 2. Education should be a central component of prenatal care for all pregnant women. [B]
- 3. Group model of prenatal care, such as the Centering Pregnancy® model, is an acceptable alternative to individual provider appointments. [A]

DISCUSSION

A systematic review published in the Cochrane database concluded that a reduction in the number of antenatal visits with an increased emphasis on the content with regard to services offered at each of the visits could be implemented without an increase in adverse perinatal outcomes (Villar et al., 2001). Partridge & Holman (2005) conducted a study to determine the effects of a reduced number of antepartum visits (as recommended by the 2003 VA/DoD

CPG) on maternal and neonatal outcomes at a military community hospital. The study found that there was no change in perinatal outcomes or patient satisfaction. Application of the prenatal care guideline was associated with a reduction in prenatal visits but a small increase in labor and delivery visits that did not persist after the initial year. No adverse perinatal or patient satisfaction outcomes were noted.

The Centering Pregnancy® Program is a model for delivering prenatal care in a group setting (Rising et al., 2004; Walker et al., 2004). Groups form between 12 to 16 weeks of pregnancy, and continue through the prenatal and postpartum period. Groups are facilitated by the provider or a professional skilled in group leadership. Each group session includes an individual assessment by the provider, as well as education on various pregnancy topics, preparation for childbirth, and early parenting. Women participate in self-care activities such as taking their own blood pressures and weight, and recording them in the chart. The opportunity to meet together for nine or 10 sessions of 90 to 120 minutes each with the same group of expectant parents allows for continued sharing and development of a support network which often extends in to the childrearing period.

A randomized controlled trial was conducted at two university-affiliated hospital prenatal clinics involving 1,047 pregnant women (Ickovics et al., 2007). The results revealed that women assigned to group care were significantly less likely to experience preterm delivery compared with those who received standard individual prenatal care. Women in group sessions were less likely to have suboptimal prenatal care, had significantly better prenatal knowledge, felt more prepared for labor and delivery, and had greater satisfaction with care.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Effect of reduced number of visits	Villar et al., 2001 Partridge, 2005	I	Fair	В
2	Group prenatal care is an acceptable alternative to individual appointments and can result in equal or improved perinatal outcomes	Ickovics et al., 2007 Baldwin et al., 2006	I	Good	A

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

A-1. Confirmed Pregnancy

Confirmation of pregnancy is established by a confirmed positive urine or serum pregnancy test.

A-2. First Visit with Nurse: Update Complete Self-Questionnaire; Assess for Risk Factors

Weeks 6 to 8

BACKGROUND

After confirmation of the pregnancy, the goal of the first prenatal contact is to exchange information and identify existing risk factors that may impact the pregnancy. This initial contact may be accomplished in a group setting or during a one-on-one visit. This encounter provides an opportunity early in the pregnancy to obtain general short-term risk stratification. In this visit, the nurse should identify women who: (1) Need immediate referral to an advanced prenatal care provider (e.g., high risk for ectopic pregnancy); (2) Need to see an advanced prenatal care provider at the first provider visit; or (3) Can have the first provider visit with a low-risk prenatal care provider. **Table 1** contains a checklist of the data collected during the first visit with the nurse and/or obstetric healthcare provider. These data are required to appropriately triage women into one of the three categories noted above. In addition, all active duty pregnant women are required to have an occupational health screening. This referral/consultation with occupational health should be done at this initial encounter.

RECOMMENDATIONS

- 1. Initial assessment by nurse may include the following actions:
 - a. Assure the patient completes the Self-Questionnaire (see Appendix B Screening Items for Self-Administered Questionnaire First Visit)
 - b. Review the patient's completed Self-Questionnaire for issues requiring immediate evaluation or intervention (see Appendix B Screening Items for Self-Administered Questionnaire First Visit)
 - c. Obtain initial prenatal lab tests to be reviewed and documented at the following visit
 - d. Consult with an advanced prenatal care provider regarding advice or instruction to the patient if there are immediate needs (see Table-1)
 - e. Arrange immediate referral to advanced prenatal care for follow-up in cases needing short-term assessment or intervention (see Table-1)
 - f. Provide brief information about options for screening for fetal chromosomal abnormalities and arrange for counseling (See I-36)
 - g. Arrange follow-up with the appropriate provider at 10-12 weeks.

Table 1. Prenatal Risk Assessment by Nurse - Checklist

Risk Assessed by Nurse	Nurse assessment and Questionnaire (see Appendix B)	Laboratory tests	Immediate referral to advanced prenatal care provider	Consult with advanced prenatal care provider	Follow-up with advanced prenatal care: Weeks 10-12
Uncertain dating criteria	$\sqrt{}$	Ultrasound		V	
Late presentation	$\sqrt{}$	Ultrasound		$\sqrt{}$	
Past OB history:					
Recurrent pregnancy loss	$\sqrt{}$				
Ectopic pregnancy risk (prior hx of ectopic, prior tubal surgery, current IUD, hx of tubal infertility, hx PID)	V	Quantitative HCG/ US	V		
Prior macrosomia or prior gestational diabetes mellitus (GDM)	√	Glucola for GDM			
Preterm birth	√			√	
Second-trimester pregnancy loss	V	Ultrasound		√	
Cervical surgery (LEEP, cone biopsy)	V			√	
Bariatric surgery (less than 18 months)	V			√	
Current Problems:					
Vaginal bleeding (current)	$\sqrt{}$		√		
Significant abdominal pain/cramping (current)	√		√		
Prescription, over-the-counter, and herbal medications	√			√	
Drug/alcohol use	$\sqrt{}$				V
Smoking	$\sqrt{}$				$\sqrt{}$
Medical Conditions:					
Cardiovascular diseases	$\sqrt{}$		$\sqrt{}$		\checkmark
Cardiac abnormality	$\sqrt{}$		$\sqrt{}$		
Diabetes mellitus (DM) – Type 1 or 2	$\sqrt{}$	Hgb A1c	$\sqrt{}$		\checkmark
Renal disorder (includes pyelonephritis)	√		\checkmark		
Hypertension	$\sqrt{}$		If not controlled	V	
Thyroid disorders	√	Thyroid function		√	

Gastrointestinal disorders on medications Pulmonary disease Family history of DM in first relative Family history of DM in first relative Glucola for GDM Neurological disorder Autoimmune disorder/Lupus Major mental illness Major mental illness Hepatitis V Hepatitis panel Sexually transmitted disease (STD) Tuberculosis Human immunodeficiency virus (HIV) Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint V To Dentistry To Behavior Health if suicidal or moderate or severe MDD Occupational hazards Hx of infertility √ Transvaginal US	√ √
Family history of DM in first relative Neurological disorder V	√
Neurological disorder	√
Autoimmune disorder/Lupus Major mental illness Blood disorders Hepatitis Hepatitis Sexually transmitted disease (STD) Tuberculosis Human immunodeficiency virus (HIV) Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Coccupational hazards Nomestic violence To Social Work if unsafe Hx of infertility Transvaginal	√
Major mental illness √ Blood disorders √ Hepatitis √ Sexually transmitted disease (STD) √ Tuberculosis √ Human immunodeficiency virus (HIV) √ Rash or viral illness √ Radiation/toxic chemical exposure since becoming pregnant √ Cancer √ Transplant √ Hx of genetic disease or family history of genetic disease or family history of genetic disease √ Dental complaint √ Screen for MDD √ To Behavior Health if suicidal or moderate or severe MDD Occupational hazards √ Homeless √ Domestic violence √ Transvaginal √	√
Blood disorders Hepatitis V Hepatitis panel Sexually transmitted disease (STD) Tuberculosis Human immunodeficiency virus (HIV) Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Screen for MDD Cocupational hazards Hx of infertility To Social Work if unsafe Hx of infertility The patitis panel A Hepatitis panel A Humanimundeficiency virus (HIV) A Humanimundefi	
Hepatitis Sexually transmitted disease (STD) Tuberculosis √ Human immunodeficiency virus (HIV) Rash or viral illness √ Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint ✓ Screen for MDD ✓ To Behavior Health if suicidal or moderate or severe MDD Occupational hazards ✓ To Social Services Domestic violence ✓ Transvaginal ✓ Transvaginal	
Sexually transmitted disease (STD) Tuberculosis Human immunodeficiency virus (HIV) Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Screen for MDD Cocupational hazards V To Dentistry To Public Health Homeless Domestic violence V Transvaginal V Transvaginal V Transvaginal	
Tuberculosis	
Human immunodeficiency virus (HIV) Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Screen for MDD To Behavior Health if suicidal or moderate or severe MDD Occupational hazards Hx of infertility Transvaginal √ Transvaginal	
Rash or viral illness Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Carcer To Behavior Health if suicidal or moderate or severe MDD Occupational hazards To Public Health Homeless Domestic violence To Social Services To Social Work if unsafe Hx of infertility To Infertility Transvaginal	
Radiation/toxic chemical exposure since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint \[\sqrt{\text{To Dentistry}} \] Screen for MDD \[\sqrt{\text{To Behavior Health if suicidal or moderate or severe MDD}} \] Occupational hazards \[\sqrt{\text{To Public Health}} \] Homeless \[\sqrt{\text{To Social Services}} \] Domestic violence \[\sqrt{\text{To Social Work if unsafe}} \] Hx of infertility \[\sqrt{\text{Transvaginal}} \]	√
since becoming pregnant Cancer Transplant Hx of genetic disease or family history of genetic disease Dental complaint Screen for MDD To Behavior Health if suicidal or moderate or severe MDD Occupational hazards Hx of infertility √ Transvaginal √ Transvaginal	√
Transplant Hx of genetic disease or family history of genetic disease Dental complaint Screen for MDD To Behavior Health if suicidal or moderate or severe MDD Occupational hazards To Public Health Homeless To Social Services Domestic violence To Social Work if unsafe Hx of infertility Transvaginal	√
Hx of genetic disease or family history of genetic disease Dental complaint √ To Dentistry To Behavior Health if suicidal or moderate or severe MDD Occupational hazards √ To Public Health Homeless √ To Social Services Domestic violence √ Transvaginal √ Transvaginal	√
of genetic disease □ Dental complaint √ Screen for MDD √ To Behavior Health if suicidal or moderate or severe MDD Occupational hazards √ To Public Health Homeless √ Domestic violence √ To Social Services To Social Work if unsafe Hx of infertility √	
Screen for MDD \[\sqrt{To Behavior Health if suicidal or moderate or severe MDD} \] Occupational hazards \[\sqrt{To Public Health} \] Homeless \[\sqrt{To Social Services} \] Domestic violence \[\sqrt{To Social Work if unsafe} \] Hx of infertility \[\sqrt{Transvaginal} \]	
suicidal or moderate or severe MDD Occupational hazards √ To Public Health Homeless √ To Social Services Domestic violence √ To Social Work if unsafe Hx of infertility √ Transvaginal √ V	
Occupational hazards √ To Public Health Homeless √ To Social Services Domestic violence √ To Social Work if unsafe Hx of infertility √ Transvaginal	
Homeless $\sqrt{}$ To Social Services Domestic violence $\sqrt{}$ To Social Work if unsafe Hx of infertility $\sqrt{}$ Transvaginal	-
·	
Hx of mental illness on medications $\sqrt{}$	
Diet restriction $\sqrt{}$ To Nutrition $\sqrt{}$ Counseling	
Eating disorder $\sqrt{}$	
Body mass index (BMI) > 29 kg/m ² $\sqrt{\frac{\text{Glucola for GDM}}{\text{GDM}}}$	
$BMI < 20 \text{ kg/m}^2 \qquad \qquad $	
Age ($<16 \text{ or } >35$)	
Routine Lab Tests:	
Human immunodeficiency virus (HIV) √	
Complete blood count (CBC) √	
(ABO Rh) blood typing √	
Antibody screen √	
Rapid plasma reagent (RPR) √	
Hepatitis B surface antigen test √	
Rubella test √	
Urinalysis and culture √	

Additional Information:			
Religion	√		
Language barrier	\checkmark		
Currently or previously deployed or family member	V		
Born outside the United States	V		
Lives with cats	V		
Wears seat belts	V		
Planned pregnancy	V		
Highest level of education	V		

A-3. The First Provider Visit: Update

Weeks 10-12

BACKGROUND

The first provider visit offers an opportunity for the provider to review the information obtained through the Self-Questionnaire and the results of the initial laboratory studies and to note any salient issues previously identified at the initial 6-8 week nurse's visit. The provider also has an opportunity to further investigate notable issues, complete a physical examination, address/document fetal viability, confirm the gestational age and address any complications that may have arisen in the interval since the initial nurse's visit.

The provider will outline the plan of care based on the information gathered from this and the initial nurses' visit. The plan for the ongoing prenatal care should be based on the backbone of routine prenatal care outlined in this guideline and then individualized by addressing any currently identifiable risks/complications and outlining any indicated supplemental prenatal interventions. The outline of care may involve referring the patient to, or consulting with, an advanced prenatal care provider. (See Annotation A-0 for Level of Care Settings)

RECOMMENDATIONS

- 1. At the first provider visit, a complete medical history and physical examination (including thyroid, breast and pelvic examination) should be obtained. Information from the previous visit(s) and laboratory studies should be reviewed and significant problems/risks should be assessed.
- 2. At the first provider visit, the provider should outline an individualized plan of prenatal care that includes guideline-based routine prenatal care and consultation with advanced prenatal care providers or other medical specialty care services if needed.
- 3. The following are conditions not addressed by this guideline that will require supplemental care that might be best provided by routine or advanced obstetric care providers and/or behavioral health providers depending on the individual circumstances and local conditions:
 - Current mental illness requiring medical therapy
 - Substance use disorders
 - Eating disorders.
- 4. The following are among conditions that require supplemental prenatal care or consultation with or referral to an advanced prenatal care provider (Table 2):
 - General
 - Body mass index (BMI) <16.5 or >30
 - Age (<16 or > 34 years at delivery)

- At risk for diabetes
- b. Infections:
 - Hepatitis B or C (see I-11)
 - Human Immunodeficiency virus (HIV)
 - Syphilis (positive RPR)
 - Cytomegalovirus (CMV)
 - Toxoplasmosis
 - Primary Herpes
 - Rubella
 - Parvovirus
 - Positive gonorrhea (see I-29)
 - Positive Chlamydia (see I-30)
 - Genital herpes (see I-32)
 - Recurrent urinary tract infections/stones
- c. Pre-existing medical conditions:
 - Abnormal pap smear (see I-31)
 - Controlled hypothyroidism
 - Previous gastric bypass/bariatric surgery (see I-28)
 - Mild depression (I- 21 & 34)
 - Cardiovascular disease
 - High blood pressure
 - Familial hyperlipidemia
 - Pregestational diabetes
 - Kidney disease (including pyelonephritis)
 - Inflammatory bowel disease
 - Bronchio pulmonary disease including asthma
 - Autoimmune diseases including Anticardiolipin Antibody Syndrome, and Systemic Lupus Erythematosis
 - Thromboembolic disease, current or historical
 - Cancer
 - Seizure disorders
 - Hematologic disorders (including anemia, thrombocytopenia)
 - Genetic disease with known effect on pregnancy
- d. Obstetric conditions:
 - Vaginal bleeding
 - Isoimmunization
 - Placenta previa—symptomatic or present beyond 28 weeks

- Placental abruption
- At risk for preterm birth (see A-4)
- Prior cesarean section (see I-39)
- Previous uterine or cervical surgery
- Intrauterine fetal demise
- Preterm labor
- Preterm ruptured membranes
- Recurrent pregnancy loss
- Suspected or documented fetal growth abnormalities (intrauterine growth restriction [IUGR] or macrosomia)
- Abnormalities of amniotic fluid including oligohydramnios, polyhydramnios
- Fetal anomaly(s)
- Multiple gestation
- Surgical condition during pregnancy (e.g., appendectomy, ovarian cystectomy, cerclage)

Table 2. Conditions Requiring Supplemental Care

Risk Assessed by Routine Prenatal Care Provider	Referral/Consult with Advanced Prenatal Care Provider	Consider Referral/Consult with Advanced Prenatal Care Provider
GENERAL CONDITIONS		1101100
Genetic condition potentially affecting fetus	٧	
Body Mass Index (BMI < 16.5 or >30)		٧
Age < 16 or > 34		V
Genetic condition affecting patient or spouse		٧
OBSTETRIC CONDITIONS (current or historical)		
Recurrent pregnancy loss	٧	
Ectopic pregnancy	٧	
Significant abdominal pain/cramping	٧	
Vaginal bleeding	٧	
Second-trimester pregnancy loss	٧	
Preterm labor (current) or birth (history)	٧	
Cervical surgery (LEEP, cone biopsy)	٧	
Uterine abnormality	٧	
Short (<2.5 cm) cervix (< 36 weeks)	٧	
Pregnancy induced hypertensive disorders	√ .	
Gestational diabetes mellitus (GDM)	√	
Malpresentation (> 36 weeks)	٧	
Placenta Previa (symptomatic or beyond 28 weeks)	√	
Abnormal amniotic fluid: oligo/poly hydramnios	√	
Preterm ruptured membranes	٧	
Fetal growth abnormality (<10, >90 %tile) Known or suspected fetal anomaly	√ √	
Multiple gestation	V √	
Isoimmunization	V √	
Abnormal prenatal screening result (aneuploidy risk)	√	
Abnormal prenatal screening result (ONTD risk)	√	
Intrauterine fetal demise	√	
Teratogenic exposure including drugs or radiation	•	٧
Placental abruption		√
Prior cesarean section		٧
Intrapartum complications		٧
GYNECOLOGIC, MEDICAL, SURGICAL CONDITIONS		
Current need for surgery	V	
Bariatric surgery (< 18, > 36 months ago)	V √	
Diabetes mellitus (DM) – Type 1 or 2	V √	
Hematalogic disorders (except mild anemia)	√	
Gastrointestinal disorders on medication	√	
Chronic hypertension	٧	
Cardiovascular disease	٧	
Pulmonary disease including asthma	٧	
Cancer (current or recent)	V	
Neurological disorders including epilepsy	V	

Risk Assessed by Routine Prenatal Care Provider	Referral/Consult with Advanced Prenatal Care Provider	Consider Referral/Consult with Advanced Prenatal Care Provider
Renal, urinary tract disorder	V	
Autoimmune disorder including Lupus	٧	
Antiphospholipid syndrome	٧	
Hyperlipidemia prior to pregnancy	٧	
Transplant	٧	
Abnormal pap smear		٧
Breast abnormality		٧
Pelvic surgery for infertility or infection		٧
Illicit drug, alcohol, or tobacco use		٧
Thyroid disorders		٧
INFECTIOUS DISEASES		
Severe pelvic infections	٧	
Hepatitis	٧	
Tuberculosis	٧	
HIV	٧	
TORCH infection	٧	
Sexually transmitted disease (STD)		٧
PSYCHOSOCIAL CONDITIONS		
Major depressive disorder (MDD)	To Mental Health if suicidal or moderate or severe MDD	٧
Domestic violence	To Social Work if unsafe environment	٧
Homeless	To Social Service	٧

A-4. Assessment of Risk Factors for Preterm Birth New

BACKGROUND

Preterm birth is the second leading cause of neonatal mortality in the United States. Although many preterm births are due to the development of obstetric complications, over 70 percent result from *spontaneous* preterm birth which includes deliveries related to idiopathic preterm labor, preterm rupture of membranes, and cervical insufficiency. Demographic or historical risk factors for spontaneous preterm birth delivery may be discovered at the initial nursing intake or provider visit. Other risk factors develop as a woman's pregnancy progresses and include certain symptoms or physical examination and imaging findings. Although the prediction and prevention of spontaneous preterm birth remain challenging, continual surveillance for these risk factors may be beneficial as effective therapeutic options are developed. Some risk factors only require annotation in the obstetric record and routine surveillance as indicated in this pregnancy guideline. The identification of other risk factors should prompt increased surveillance in the form of consultation with an advanced prenatal care provider or ancillary testing and imaging studies.

To date, no single test or sequence of tests has an optimal sensitivity or predictive value for preterm birth. Fetal fibronectin testing and cervical length measurement by transvaginal ultrasound appear to be useful in the management of some women meeting the criteria for increased surveillance. Most studies have shown that these tests have limited utility when used in the asymptomatic woman at low risk for preterm delivery. Importantly,

modalities such as salivary estriol levels, bacterial vaginosis screening and home uterine activity monitoring are generally not effective at predicting preterm birth regardless of risk status.

Recent data suggest that the administration of progesterone intramuscularly or intravaginally beginning early in pregnancy in women at high risk for preterm birth significantly reduces the rate of preterm delivery. Specifically, women with a prior spontaneous birth at less than 37 weeks' of gestation and asymptomatic women with a shortened cervical length in the 2nd trimester appear to benefit from the administration of progesterone beginning early in pregnancy. Progesterone therapy is typically begun early in the 2nd trimester and continued until approximately 36 weeks. Both intramuscular 17 alpha hydroxyprogesterone caproate (250 mg, administered weekly) and vaginal progesterone suppositories (100 to 200mg, administered once daily) have been described in the literature.

Despite the apparent benefits of progesterone in high-risk populations and its growing use, the ideal progesterone formulation and long-term safety of the drug must be confirmed by additional studies. Progesterone supplementation for the prevention of preterm birth should still be considered investigational.

The identification of women at risk for preterm birth now increases in importance in light of the expanded availability of and indications for progesterone therapy for the prevention of preterm birth.

RECOMMENDATIONS

Assessment of preterm birth

- 1. Women should be assessed for preterm birth risk as early as possible in the pregnancy in order to optimize maternal and newborn outcomes.
- 2. Screening for preterm birth risk factors should continue up to 37 weeks estimated gestational age.
- 3. Women at increased risk but meeting the criteria for normal surveillance should have the risk factor(s) documented in the medical record to increase awareness of the risk but may continue to be followed in accordance with the routine management of the pregnancy guideline.
- 4. Routine care providers should consult with an advanced prenatal care provider whenever a woman meets the criteria for increased surveillance for preterm birth.
- 5. Women requiring increased surveillance should be considered for ancillary studies and other additional intervention. Progesterone supplementation should be considered in these women (see A-4).
- 6. Routine screening of fetal fibronectin (fFN) in asymptomatic or low-risk women is not recommended (see I-52). fFN testing in symptomatic or high-risk women between 24 and 34 6/7 weeks' gestation may be useful in guiding management.
- 7. The measurement of cervical length by transvaginal ultrasound may be useful in some patients requiring increased surveillance for preterm labor. Sonographic cervical length measurement is not recommended as a routine screening or prediction tool in women only requiring normal surveillance.
- 8. The determination of salivary estriol levels, bacterial vaginosis screening and home uterine activity monitoring are not recommended as a means to predict preterm birth.

Progesterone therapy

- 9. It is reasonable to offer antenatal progesterone therapy to women at high-risk for preterm delivery and who meet the generally accepted inclusion criteria. [B]
- 10. Progesterone may be administered intramuscularly on a weekly basis or intravaginally on a daily basis. [B]
- 11. Progesterone therapy should only be initiated after consultation with an advanced prenatal care provider (obstetrician or maternal-fetal medicine specialist). [C]

Table 3. Risk Factors for Preterm Birth Stratified by Those Requiring either Normal or Increased Surveillance *

^{*}Women with multiple risk factors in the Normal Surveillance category may require individualized assessment and warrant consultation with an advanced prenatal care provider.

DISCUSSION

Several methods of identifying women at high risk for preterm delivery have been evaluated in recent years. Numerical scoring systems using historical risk factors have generally failed to identify most women who deliver preterm. Vaginal probe ultrasonographic cervical assessment (I-63) appears to increase the ability to predict spontaneous preterm birth in high-risk women, but currently has a limited role in the screening of normal-risk women. The fetal fibronectin immunoassay (see I-52) performed on cervical secretions obtained from the posterior fornix has a high negative predictive value for delivery within seven days of testing in women presenting with signs and symptoms of preterm labor. Other methods for identifying women at high risk for preterm labor include: home uterine activity monitoring, salivary estriol, screening for periodontal disease, and bacterial vaginosis (I-60) testing. However, the efficacy of these modalities has not been clearly demonstrated and their use remains controversial.

Historically, the lack of an effective treatment to prevent preterm birth has rendered any prediction scheme impotent. The ability of cervical cerclage to prevent preterm birth or lengthen gestation likewise remains questionable with conflicting reports of efficacy in the obstetric literature. Antimicrobial therapy, including treatment of bacterial vaginosis, does not appear to meaningfully reduce the preterm birth rate. Tocolysis of preterm labor with various agents remains unproven in the prevention of preterm delivery but is often used to prolong latency to allow the administration of antenatal corticosteroids.

In contrast to these controversial or minimally effective treatments, recent data suggest that the administration of progesterone (see A-4) intramuscularly or intravaginally beginning early in pregnancy in women at high risk for preterm birth significantly reduces the rate of preterm delivery. The possibility of preventing preterm birth, as the availability of progesterone treatment expands, raises the importance of identification of women at high risk for preterm delivery.

The identification of any of the risk factors for preterm birth should be documented clearly in the obstetric record to facilitate potential intervention. Generally, any such intervention should be logically based upon the plausible

strength of association between the risk factors for preterm birth and the ability of the intervention to mitigate such risks. For instance, a history of prior preterm birth places a woman at higher risk for preterm delivery than simply a maternal age younger than 17 years, though both are known risk factors.

The use of predictors of spontaneous preterm birth permits identification of a group of women for whom increased surveillance and possible intervention may be tested. By stratifying women at low risk for preterm birth to normal surveillance, unnecessary, costly, and potentially hazardous intervention might be avoided. As various combinations of risk factors may be present in any one woman, the Working Group recommends a simple approach by which women are stratified according to the normal or increased requirements of surveillance as early as possible in the pregnancy. The appropriate intervention or referral may then be made based on these categorizations.

For discussion and summary of risk factors see Appendix D.

EVIDENCE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Offer progesterone therapy to women at risk for recurrent preterm birth	Da Fonseca et al., 2003 Fonseca et al., 2007 Meis et al., 2003	I	Fair	В
2	Progesterone may be administered intramuscularly or intravaginally	ACOG, 2003 Da Fonseca et al., 2003 Fonseca et al., 2007 Meis et al., 2003	III I I	Poor Good Fair Good	В
3	Progesterone should be initiated after consultation with obstetrician or MFM specialist	ACOG, 2003 Working Group Consensus	III	Poor	С
1	Surveillance and intervention based on risk stratification for preterm birth	Working Group Consensus	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

A-5. Routine Visits: Weeks 16-27

Visits during this period should include the following:

- Auscultation of fetal heart tones if negative, elevate care
- Screening fundal height
- Screening for hypertensive disorders
- Assessing weight gain
- Education about symptoms of preterm labor (week 20)

For specific interventions see Prenatal Care Interventions – Weeks 16-27.

A-6. Routine Visits: Weeks 28-41

Visits during this period should include the following:

- Auscultation of fetal heart tones if negative, elevate care
- Screening fundal height
- Screening for hypertensive disorders
- Assessing weight gain
- Assessing for symptoms of preterm labor (week 28, 32)
- Assessing fetal kick counts

For specific interventions see Prenatal Care Interventions – Weeks 28-41.

A-7. Postpartum Visit Update

BACKGROUND

The postpartum visit provides the opportunity for providers to interact with the new mother and her infant through interview, exam, and testing. The timing and the content of the postpartum visit have often been topics for debate. Recent literature helps the provider to answer these questions based on the evidence. The maternal postpartum visit should occur approximately eight weeks after delivery. Eight weeks is the optimal time to decrease the rate of false positive cervical smears.

RECOMMENDATIONS

- 1. The following should be included in the postpartum visit:
 - Pelvic and breast examinations. [B]
 - Cervical smear should be completed as indicated by cervical cancer screening guidelines (see I-31). [A]
 - Initiate or continue the HPV vaccine series for women age < 26 years (see I-50). [C]
 - Screening for postpartum depression (see I-21). [B]
 - Screening for domestic violence (see I-20). [B]
 - Diabetes testing for patients with pregnancies complicated by gestational diabetes. The two-hour 75g oral glucose tolerance test (GTT) is recommended but a fasting glucose can also be done. [B]
 - Education about contraception, infant feeding method, sexual activity, weight, exercise and the woman's assessment of her adaptation to motherhood. Pre-existing or chronic medical conditions should be addressed with referral for appropriate follow-up as indicated. [I]

DISCUSSION

The optimal timing of the postpartum visit is approximately eight weeks after delivery. This time is chosen primarily due to the decreased rate of abnormal cervical smears observed at eight weeks (28 percent) verses the rate at six (32 percent) or four (59 percent) weeks. There were no differences in the distribution of abnormal Pap smears at the repeat smear done three months after the postpartum examination (Rarick & Tchabo, 1994) though this data does not take into account the use of liquid-based cytology and the most current recommendations for frequency of Pap smears. Some providers may choose to perform the visit at six weeks for convenience of the woman who is returning to work before the eight-week time frame. As facilities switch to liquid-based cytology, new studies will be needed to evaluate the number of false positives at six versus eight weeks postpartum to optimize visit timing.

The postpartum Pap smear is of value in identifying a significant yield of dysplasia. The sensitivity of the prenatal Pap test may be less than desired. The rate of abnormal postpartum smears in pregnant women with normal prenatal smears ranges from 2.8 (Londo et al., 1994) to over 5 percent (Weiss et al., 1989). These studies are challenged by a smaller study by Jazayeri and colleagues, who found that in patients without risk factors for cervical intraepithelial neoplasia and a normal Pap smear during pregnancy, there was no significant difference between their prenatal and postpartum smears (Jazayeri et al., 1999).

Women with a history of GDM are at increased risk of developing diabetes. Some women will be diagnosed shortly after pregnancy, suggesting they had pre-existing diabetes. Although the ADA advocates use of fasting blood glucose determination, the oral GTT will more accurately identify those women with impaired glucose tolerance. Unfortunately, the incidence of postpartum screening in women with GDM is poor.

There is no evidence to recommend for or against discussion of specific topics at the post partum visit. Topics to be addressed at this visit are ultimately based on the discretion of the provider and the needs of the woman.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Postpartum visit at eight weeks	Rarick & Tchabo, 1994	I	Good	В
2	Tests traditionally performed at this visit include the cervical smear, pelvic exam, and breast exam. The Pap smear may be deferred in women without a history of abnormal Pap smears and whose Pap smear remains current	Jazaveri et al., 1999 Londo et al., 1994 Weiss et al., 1989	II	Fair	В
3	Diabetes screening in women whose pregnancies were complicated by GDM	ACOG, 2001 Conway, 1999	II	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

INTERVENTIONS

Prenatal care for all pregnant women should include the interventions listed in the following Summary Table. Each intervention should be completed by the indicated week (NOTE: Between weeks 38-41, weekly visits may be needed). Intervention marked with * only apply if the risk/condition has been identified/diagnosed.

Summary Table: Prenatal Care Interventions

	Trimester	Fir	rst	Sec	cond		Third		Post Date	Post- partum
	INTERVENTION Week:	6-8	10-12	16-20	24	28	32	36	38-41	PP
I-1	Screening for hypertensive disorders	ব	ব	র	I	I	র	র	I	
I-2	Breastfeeding education	4	4	র	<u> </u>	<u> </u>	<u> </u>	র	<u> </u>	
I-3	Exercise during pregnancy	4	⊴	র	র	র্	⊴	4	র্	
I-4	Influenza vaccine (season-related)	4	⊴	র	র	র্	⊴	4	র্	
I-5	Screening for tobacco use - offer cessation	I								
I-6	Screening for alcohol use - offer cessation	র্								
I-7	Screening for drug abuse - offer cessation	র্								
I-8	Screening for Rh status	র								
I-9	Screening for rubella	র্								
I-10	Screening for varicella	র								
I-11	Screening for hepatitis B	র								
I-12	Treatment for hepatitis B *							র	র	
I-13	Screening for syphilis (Rapid Plasma Reagin)	র								
I-14	Screening for asymptomatic bacteriuria	র্								
I-15	Screening for tuberculosis	র								
I-16	Screening for HIV – counsel	র								
I-17	Immunization – Td booster (first trimester)	র								
I-18	Screening for anemia	র								
I-19	Screening for hemoglobinopathies *	র								
I-20	Screening for domestic abuse	র				র				<u> </u>
I-21	Screening for depression					4				<u> </u>
I-22	Establishing the gestational age		র							
I-23	Auscultation fetal heart tones		⊴	ব	র	র্	⊴	র	র্	
I-24	Screening fundal height		<u> </u>	র	র্	র্	<u> </u>	র	র্	
I-25	Assessing weight gain (inappropriate)		⊴	ব	<u> </u>	<u> </u>	⊴	⊴	<u> </u>	

	Trimester:	Fii	rst	Sec	cond		Third		Post Date	Post- partum
	INTERVENTION Week:	6-8	10-12	16-20	24	28	32	36	38-41	PP
I-26	Nutritional supplement		র্							
I-27	Management of obesity *		র্							
I-28	Gastric bypass consideration *		<u> </u>							
I-29	Screening for gonorrhea		₫							
I-30	Screening for Chlamydia		র							
I-31	Screening for cervical cancer		র্							
I-32	Screening for HSV and prophylaxis		র							
I-33	Counseling for cystic fibrosis screening		র							
I-34	Management of depression *		র			ব				ব
I-35	Assessment of periodontal disease		₫							
I-36	Education about Prenatal Screening									
	- Screening test 1st trimester		₫							
	- Counseling and test 2nd trimester			র						
I-37	Obstetric ultrasound			ব						
I-38	Education about preterm labor				র					
I-39	Counseling for trial of labor *				<u> </u>					
I-40	Screening for gestational diabetes					4				
I-41	Iron supplementation *					₫				
I-42	Anti-D prophylaxis for Rh-negative women *					₫				
I-43	Assess for preterm labor					₫	Q			
I-44	Daily fetal movement counts					₫	Q	4		
I-45	Counseling for family planning						a			
I-46	Screening for Group B Streptococcal (GBS)							র		
I-47	Assessment of fetal presentation							4	4	
I-48	Consider Weekly cervical check/stripping								⊴	
I-49	Term management								4	
I-50	Immunization HPV vaccine *									4
I-51	Education on Shaken Baby Syndrome									⊴

Inte	rventions Not Recommended In Routine Prenatal Care	(All Weeks)	
I-52	Screening with fetal fibronectin	M	_
I-53	Cervical examination	\sqrt	
I-54	Antenatal pelvimetry	M	
I-55	Urine dipstick test	\sqrt	
I-56	Edema evaluation	\sqrt	
I-57	Screening for cytomegalovirus (CMV)	\sqrt	
I-58	Screening for parvovirus	\sqrt	
I-59	Screening for toxoplasmosis	\sqrt	
I-60	Screening for bacterial vaginosis	\sqrt	
I-61	Immunization – MMR	\sqrt	
I-62	Immunization – Varicella	M	
I-63	Ultrasound (US) evaluation of cervical length at week 24	M	
I-64	Repeat screening for anemia, syphilis, and isoimmunization	M	
I-65	Screening for hypothyroidism	\(

Interventions at All Visits

I- 1. Screening for Hypertensive Disorders of Pregnancy: Update

Weeks (All)

BACKGROUND

Hypertension in pregnancy can be defined as either a diastolic pressure greater than 90 mmHg or systolic pressure greater than 140 mmHg recorded on two separate occasions more than six hours apart, at any time during the gestation. Hypertension detected before the 20th week of gestation in the absence of gestational trophoblastic disease or high-order multiple gestation is generally considered indicative of chronic hypertension. Gestational hypertension is defined as isolated hypertension in the absence of proteinuria occurring after 20 weeks' gestation. Hypertension occurring in conjunction with proteinuria beyond 20 weeks' gestation is classified as preeclampsia. Proteinuria is defined as >300 mg in a 24-hour urine collection in the absence of evidence of a urinary tract infection. Regardless of the etiology or specific diagnosis, all hypertensive disorders of pregnancy are associated with an increased risk for adverse perinatal outcome and require supplemental monitoring and care beyond the routine care outlined in this guideline.

RECOMMENDATIONS

- Recommend measuring blood pressure of all pregnant women at each prenatal visit, following the guidelines of the National High Blood Pressure Education Program and the VA/DoD Clinical Practice Guidelines for Hypertension. [B]
- 2. Women diagnosed with hypertension during pregnancy should be managed by, or in consultation with, an advanced prenatal care provider. [C]
- 3. Korotkoff 5 sound (disappearance of sound) will be used to determine the diastolic pressure. [C]

DISCUSSION

The risks of untreated preeclampsia and chronic hypertension in pregnancy are many. Potential maternal complications include placental abruption, renal failure, cerebral hemorrhage, disseminated intravascular coagulation, pulmonary edema, circulatory collapse, eclampsia, and death. Fetal complications may include hypoxia, low birth weight, premature delivery, or perinatal death (Chesley, 1984; Cunningham & Lindheimer, 1992; National Institutes of Health [NIH] Working Group on High Blood Pressure in Pregnancy, 2000). There are no clinical tests or signs that remotely and accurately predict outcomes of the various hypertensive disorders of pregnancy; thus, any woman demonstrating persistent hypertension during pregnancy should be considered at increased risk for adverse perinatal outcomes and monitored appropriately.

The best screening strategy for hypertension in pregnancy appears to be early detection of hypertension through routine screening at each prenatal encounter. Although there is no direct proof that regular blood pressure screening reduces maternal or perinatal morbidity or mortality, it is unlikely that ethical concerns will allow a study to withhold blood pressure screening or treatment from a control group. Since the screening test is simple, inexpensive, and acceptable to women, screening is indicated on an empirical basis (United States Preventive Services Task Force [USPSTF], 1996; NIH Working Group on High Blood Pressure in Pregnancy, 2000). There are no updated consensus reports from either the USPSTF or NIH.

The collection of meaningful blood pressure data requires consistent use of correct technique and a cuff of appropriate size. The woman should be in the sitting position and the blood pressure should be measured after the woman has rested for five minutes. The blood pressure cuff should be appropriately sized for the woman's arm and placed at the level of the heart (National High Blood Pressure Education Program, 1990). Korotkoff 5 sound (disappearance of sound) will be used for determining the diastolic pressure (NIH Working Group on High Blood Pressure in Pregnancy, 2000).

While the overall recommendations contained in this section are graded as Level III quality of evidence, it is important to recognize that these expert consensus recommendations are actually based on evidence-based information spanning the spectrum of scientific validity from level I through III. Providers are referred to the appropriate most current documents for further descriptions and discussion (USPSTF, 1996; ACOG, 2001; NIH Working Group on High Blood Pressure in Pregnancy, 2000). Also, see VA/DoD guidelines for Hypertension in Primary Care.

It should be noted here that there is emerging, albeit controversial, data regarding antiplatelet therapy in patients with hypertensive disorders of pregnancy. There are ongoing studies investigating the positive role of low-dose aspirin administration in patients at risk for developing preeclampsia. While the current body of literature, including a Cochrane review, provides evidence of no increased risk of perinatal complications with the use of low-dose aspirin in the second and third trimester, there is a paucity of information regarding which women are most likely to benefit, when treatment is best started and at what dose (Askie et al., 2007; Duley et al., 2007; Kozer et al., 2003).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine blood pressure screening at each prenatal visit	ACOG, 2001 NIH Working Group on High Blood Pressure in Pregnancy, 2000 USPSTF, 1996	III	Good	В
2	Women diagnosed with hypertension may require a higher level of care	ACOG, 2001 Cunningham & Lindheimer, 1992 NIH Working Group on High Blood Pressure in Pregnancy, 2000	III	Poor	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 2. Breastfeeding Education:

Weeks (All)

BACKGROUND

Between 50 and 90 percent of expectant mothers decide how they will feed their babies either before conceiving or very early in pregnancy (Bailey & Sheriff, 1992; Dix, 1991). Prenatal breastfeeding education is a key opportunity to educate expectant mothers on the benefits and methods associated with successful breastfeeding during the time they are making their decision on choice of infant feeding method.

RECOMMENDATIONS

- 1. Recommend offering breastfeeding education to all pregnant women during the first visit with the provider. [B]
- 2. Recommend asking pregnant women, "What do you know about breastfeeding?" rather than, "Do you plan on breast or bottle feeding?" to provide an open opportunity for education. [B]
- 3. Recommend continuing education throughout pregnancy for those pregnant women who express a desire to breastfeed or for those who are still undecided on feeding method. [C]
- 4. Recommend including family/significant others in breastfeeding education. [B]

DISCUSSION

Breastfeeding is the most nutritious form of feeding the human infant, offering such immunologic benefits as lowering the incidence of otitis media (Duncan et al., 1993) and gastrointestinal tract disease (Howie et al., 1990). Breastfeeding mothers also benefit with less postpartum blood loss, faster return to prepartum weight (Dewey et al., 1993) and decreased incidence of both ovarian (Gwinn et al., 1990) and breast cancers (Layde et al., 1989). Providers caring for pregnant women are ideally positioned to educate these women about the multiple benefits of

breastfeeding. Care should be taken to approach the topic with sensitivity to engender a supportive environment for questioning. The BEST Start Program is one that focuses on asking the woman for information regarding her beliefs about breastfeeding, rather than focusing just on her infant feeding method of choice (Bryant & Roy, 1990). Use of this method has been associated with a 50 percent increase in breastfeeding in the general population, with more marked effects in teenagers. At the first prenatal visit, a woman is asked, "What do you know about breastfeeding?" instead of "Are you going to breastfeed or bottle feed this baby?" The program elicits and acknowledges the mother's concerns and then educates her about the benefits of breastfeeding. This is repeated at each prenatal visit. Appropriate prenatal breastfeeding education is instrumental in helping the mother to establish realistic expectations, which, in turn, will prevent premature weaning. Use of anticipatory guidance has been shown to positively influence the breastfeeding process. Including the mother's significant other is helpful, since positive, knowledgeable support promotes increased breastfeeding satisfaction and duration. Education provided over the course of the pregnancy should be personalized for each woman with particular attention being paid to those women who have had prior breast surgery or who have noticed no change in breast size over the course of the pregnancy. These women should be provided additional information by a provider well acquainted with breastfeeding education or by a lactation consultant.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Breastfeeding inquiry	Hartley & O'Connor, 1996	II-2	Fair	В
2	Breastfeeding education	Hill & Humenick, 1993 Hill, 1991	III II-3	Fair	В
3	Longitudinal breastfeeding education	Berens, 2001	III	Fair	С
4	Family/significant other participation in breastfeeding education	Berens, 2001 Humenick et al., 1997	III II-1	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 3. Exercise During Pregnancy: Update

Weeks (All)

BACKGROUND

Attitudes toward exercise during pregnancy have changed markedly in recent decades. The underlying concern has revolved around fears that the exercise-induced increases in maternal body temperature, circulating stress hormones, and biomechanical stress, coupled with the decreased visceral blood flow, could have adverse effects on multiple aspects of the course and outcome of pregnancy. Only recently has a substantial amount of research been completed to support the idea that it is both safe and beneficial to exercise during pregnancy. Currently, there is no evidence to suggest that regular maternal exercise is associated with fetal compromise or unexplained fetal death. Furthermore, regular exercise improves maternal fitness, reduces the usual musculoskeletal complaints associated with pregnancy, enhances feelings of well being, improves body image, and decreases maternal weight gain and fat deposition in late pregnancy.

RECOMMENDATIONS

- 1. Strongly recommend all healthy, pregnant women perform regular mild to moderate exercise sessions, three or more times per week. [A]
- 2. Recommend individualized exercise programs for all pregnant women, based on their pre-pregnancy activity level. [I]
- 3. Recommend against high-altitude (>10,000 feet) activities, scuba diving, and contact sports during pregnancy. [I]

DISCUSSION

A meta-analysis by Kramer and McDonald (2006) combined results from 11 studies and found that regular exercise in pregnancy improves or maintains physical fitness without negative effects on the mother or fetus. Hatch et al. (1993) and Clapp et al. (2000) found that for low-risk women, maternal exercise enhanced fetoplacental growth and was not associated with adverse maternal or fetal outcomes. Cycling and swimming are currently considered the safest form of exercise during pregnancy, but walking seems to be the most frequent form of exercise (43 percent) actually chosen by pregnant women. At present, there is no published literature on the effect of weight training on the course and outcome of pregnancy (Clapp, 2001). Several randomized controlled trials (RCTs) and numerous prospective observational studies by Clapp have looked at the effects of exercise on low-risk women. Some of these women led sedentary lifestyles prior to pregnancy and began a formal exercise program during the first trimester, and others were trained athletes who continued to exercise at training levels throughout the duration of their pregnancies. Neither group of women demonstrated associated adverse maternal, fetal, or neonatal effects and there were varying degrees of benefit.

On the other hand, pregnancy complications are much higher and birth weights significantly lower at altitudes above 10,000 feet, which suggests that exposure to the additional physiologic stress produced by exercising at high altitudes may not be wise (Alderman et al., 1995). Similarly, pregnant women who dive recreationally to levels requiring decompression on a regular basis, demonstrate a three- to six-fold increase in the incidence of spontaneous abortion, congenital malformation, intrauterine growth restriction, and preterm labor (Camporsei, 1996). Common sense dictates that contact sports or any activity where there is a reasonable risk of abdominal trauma (e.g., kickboxing, hockey, football, skydiving, soccer, and horseback riding) should be avoided during pregnancy (Hammer et al., 2000).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Regular exercise for all pregnant women	ACOG, 1994 Campbell & Mottola, 2001 Clapp et al., 1999, 2000, 2001 Kramer & McDonald, 2006 Morris & Johnson, 2005 Sady et al., 1989 Sternfeld et al., 1995	I	Good	A
2	Individualized exercise programs, based on the woman's pre-pregnancy activity level	ACOG, 1994 Clapp et al., 1999 Sternfeld et al., 1995	II-2	Good	В
3	High altitude, contact sports and scuba diving (not recommended)	Alderman et al., 1995 Camporsei, 1996 Hammer et al., 2000	II-2	Good	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 4. Influenza Vaccine (Season-Related):

Weeks (Any Week)

BACKGROUND

Women who acquire influenza during pregnancy may experience an increase in morbidity and mortality during an epidemic, with a possible increased abortion rate. Most recent CDC guidelines suggest that immunization of pregnant women for influenza has been found to be safe for both the mother and the fetus regardless of gestational age.

RECOMMENDATIONS

1. Recommend immunizing all pregnant women for influenza during the epidemic season. [B]

DISCUSSION

Maternal immunization can enhance passive immunity of infants to pathogens that cause life-threatening illnesses. In most instances, immunization during pregnancy will provide important protection for the woman, as well as for her infant (Englund et al., 1998).

Influenza vaccination may be offered to anyone who wishes to reduce the chance of becoming ill with influenza, to include pregnant women who will be in the second or third trimester during epidemic season. Pregnant women with medical problems should be offered the influenza vaccination before the influenza season regardless of stage of pregnancy (ACOG #305, 2004).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Influenza immunization	ACOG, 2004 Englund et al., 1998	II	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

First Visit with Nurse (6-8 Weeks)

I- 5. Screening for Tobacco Use - Offer Cessation: Update

Weeks 6 - 8

BACKGROUND

Tobacco use in pregnancy is associated with decreased birth weight, as well as risk for spontaneous abortion and preterm labor. Newborns exposed to environmental tobacco smoke experience an increased incidence of upper respiratory infections and deaths from Sudden Infant Death Syndrome (SIDS). Behavioral and pharmacologic methods for smoking cessation are both safe and effective in pregnancy.

RECOMMENDATIONS

- 1. Strongly recommend routine screening for tobacco use in pregnancy at the initial prenatal visit. For patients who smoke, recommend assessment of smoking status at each subsequent prenatal visit. [A]
- 2. If the screening is positive, cessation should be strongly recommended. [A]
- 3. There is insufficient data to recommend for or against pharmacologic therapy for tobacco cessation in pregnancy. [I]

DISCUSSION

A Cochrane review (Lumley et al., 2004) found that all nicotine replacement therapy (NRT) products are Category D and not recommended for use by pregnant women. Despite the absence of data on safety, efficacy, and effectiveness, the use of pharmacologic agents in pregnancy is becoming increasingly considered, given the increased awareness of the harm from smoking in pregnancy and the benefits of pharmacotherapy (Benowitz et al., 2000). Dempsey et al. (2001) recommend that doses of prescribed nicotine in pregnancy should be similar to a smoking dose, and that intermittent forms of NRT (gum, spray, inhaler) are preferred to continuous use formulations as the total dose of nicotine will be less. All NRT trials in pregnancy to date are of nicotine patches (continuous use formulations). As there are still too few trials to assure safe use in pregnancy, and animal studies suggest nicotine

may be toxic to the developing central nervous system, Dempsey et al. (2001) recommend registries of women using NRT be established to gather more outcome data. Certainly, if nicotine replacement therapy results in smoking cessation and subsequent cessation of the nicotine replacement therapy, the overall dose of nicotine to the fetus would be less than if the woman continues to smoke.

Bupropion is Category C, but no trials for smoking cessation in pregnancy have been reported (Oncken, 2003). Chantix (varenicline) is Category C, but has not been studied in pregnant women. Animal studies reported low fetal weights and fertility problems in offspring (package insert).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening for tobacco use	Dolan-Mullen et al., 1991 Lumley et al., 2004	I	Good	A
2	Cessation of tobacco use	Dolan-Mullen et al., 1994 Panjari et al., 1999 Wisborg et al., 2000	I	Good	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 6. Screening for Alcohol Use - Offer Cessation:

Weeks 6 - 8

BACKGROUND

Alcohol is a known teratogen with adverse effects on fetal facial and central nervous system development. Maternal alcohol consumption is a leading preventable cause of birth defects and childhood disabilities in the United States (Centers for Disease Control [CDC], 1995). While there is a clear dose-dependent effect, numerous observational studies have failed to delineate a threshold level for safe alcohol consumption during pregnancy.

RECOMMENDATIONS

- 1. Recommend routine screening for alcohol consumption using a standardized tool (refer to the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders). [B]
- 2. If the screening is positive, cessation should be strongly recommended. [B]
- 3. There is insufficient evidence regarding which cessation intervention tool is the most effective. [I]

DISCUSSION

One screening and treatment study showed good identification of pregnant drinkers with the T-ACE tools, but no difference with a brief counseling intervention (i.e., one-hour session with a trained counselor) (Chang et al., 1999).

Two smaller RCTs of brief interventions showed modest reductions in alcohol use (Handmaker et al., 1999; Reynolds et al., 1995). No evidence was found showing the effect of any interventions on maternal or neonatal morbidity or mortality.

There are several brief alcohol screening questionnaires available for routine office use. The T-ACE questionnaire with a cut-off of tolerance of >2 drinks/day and the TWEAK questionnaire with a cut-off of >1 drink/day seem to have the highest sensitivities for alcohol use (Chang et al., 1998; Bradley et al., 1998). The standard ACOG antepartum record questions are not useful for detecting alcohol consumption in pregnant women (Budd et al., 2000).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening for evidence of problem drinking, using a standardized tool	Chang et al., 1999 Handmaker et al., 1999 Reynolds et al., 1995	I	Fair	В
2	If the screening is positive, recommend cessation	Chang et al., 1999 Handemaker et al., 1999 Reynolds et al., 1995	I	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 7. Screening for Drug Use - Offer Treatment:

Weeks 6 - 8

BACKGROUND

Up to one in ten babies may be exposed to illegal drugs during pregnancy. Use of these drugs may be harmful to the health and growth of the fetus, particularly early in pregnancy. Drug use later in pregnancy increases the risk for preterm delivery and fetal growth restriction. Risks to the mother include HIV, hepatitis, and addiction.

RECOMMENDATIONS

- 1. Recommend routine screening for illicit drug use using a self-report method. [C]
- 2. Recommend pregnant women identified as abusing drugs be offered treatment and receive care in consultation with or referral to an advanced prenatal care provider. (See also VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders.) [C]

DISCUSSION

One systematic review and two cohort studies were identified. One study recommended screening for drug use by using a self-report method (Howell et al., 1999). Ask the question: "Are you currently using or have you used recreational/illicit drugs during this pregnancy?" (Horrigan et al., 1996). No systematic reviews or trials evaluating a screen-and-treat strategy for substance abuse were found.

A low-quality but inclusive qualitative systematic review of variable quality trials revealed benefits to different drug abuse treatment programs for pregnant women. Benefits included improved treatment retention rates, increased birth weights, decreased drug use, and increased knowledge of issues surrounding drug abuse (Howell et al., 1999).

The diagnosis of substance abuse is hampered by the potential for adverse socio-economic consequences pertaining to discovery of the abuse.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine screening for illicit drug use	Horrigan et al., 1996	II-2	Fair	С
2	If the screening is positive, offer treatment	Howell et al., 1999	II-3	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 8. Screening for Blood Type (ABO,Rh) and Antibody Status:

Weeks 6 to 8

BACKGROUND

Since the introduction of anti-D (Rhogam) immune globulin injections during and after pregnancy in women who are D antigen negative, the incidence of isoimmunization has fallen from 10 cases to 1.3 cases/1,000 live births. Testing and identification of pregnant women with non-anti-D antibodies allows for early treatment of infants, which may improve fetal outcomes.

RECOMMENDATIONS

- 1. Recommend evaluation of maternal ABO and Rh blood type and blood antibody status at the initial prenatal visit. [B]
- 2. Pregnant women with positive antibody screens should be referred for consultation to assist with further management. [C] (see I-42)
- 3. There is insufficient evidence to recommend for or against routine repeat testing at 28 weeks' gestation. [I]

DISCUSSION

No systematic reviews or prospective studies were found comparing a regimen of "expanded" antibody testing to ABO and Rh testing only. Descriptive studies of isoimmunization and complication rates for non-Rh (D) antibodies show that there are increasingly comparable rates of morbidity and mortality associated with non-D as well as with D isoimmunization. Conventional Indirect Antiglobulin (Coombs') Testing appears to detect the majority of these cases. The overall burden of disease is low, but is similar to anti-D isoimmunization (Bowell et al., 1986; Howard et al., 1998).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Antibody screening	Bowell et al.,	II-2	Good	В
2	Rh status screening	Howard et al., 1998	II-2	Fair	С
3	Repeat screening at 28 weeks	Working Group Consensus	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 9. Screening for Rubella:

Weeks 6 - 8

BACKGROUND

Congenital Rubella Syndrome (CRS) is a constellation of findings in newborns exposed to the rubella virus prior to 16 weeks' gestation. The syndrome includes hearing loss, developmental delay, and ocular and cardiac defects. The incidence of CRS has declined dramatically since the advent of rubella vaccination in 1969. Identification of women lacking rubella immunity during the preconception period allows for immunization before pregnancy. Identification of non-immune women during pregnancy allows for risk counseling and immunization postpartum.

RECOMMENDATIONS

- 1. Recommend all pregnant women have a serum screen for rubella status at the initial prenatal visit. [B]
- 2. Recommend seronegative pregnant women be counseled to avoid exposure. [B]
- 3. Recommend seronegative pregnant women be vaccinated in the immediate postpartum period. [B]

Rubella in the first 16 weeks of pregnancy causes miscarriage, abortion, stillbirth, and CRS. The most common manifestations of CRS are hearing loss, developmental delay, growth retardation, and cardiac and ocular defects. Approximately 20 percent of infants born to mothers infected with rubella during the first three months of pregnancy have signs of CRS at birth, most commonly cataracts and congenital heart disease (McElhaney et al., 1999). No treatment for rubella is mentioned in the literature. Vaccination prior to pregnancy shows that greater than 90 percent have protection against clinical rubella illness, and seropositivity is long lasting. Due to concerns about possible teratogenicity, a measles/mumps/rubella (MMR) or measles vaccination is not recommended during pregnancy (Chang et al., 1970; Horstmann et al., 1985). Hemagglutination-Inhibition tests, associated with both false positive and false negative results, have been replaced by enzyme immunoassay and latex agglutination with sensitivities of 92 to 100 percent and specificities of 71 to 100 percent (Steece et al., 1985).

Postpartum vaccination demonstrates >90 percent protection against clinical rubella infection and seropositivity is long lasting. Vaccinating healthy women of childbearing age provides protection for the women from adult onset rubella and for their future children from Congenital Rubella Syndrome (CRS).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Serum screening for rubella status at the initial prenatal visit	McElhaney et al., 1999	II-2	Fair	В
2	Counseling seronegative pregnant women to avoid exposure	Working Group Consensus	III	Poor	В
3	Vaccinating seronegative pregnant women in the immediate postpartum period	Horstman et al., 1985	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 10. Screening for Varicella:

Weeks 6 to 8

BACKGROUND

Varicella infection during pregnancy may lead to poor outcomes for both mother and fetus. The incidence of varicella in pregnancy is less than one in 1,000. Most adults are immune to varicella due to previous exposure. In women who report no history of infection, 85 percent are found to have positive antibody titers. Identification of non-immune persons through screening with subsequent immunization may decrease the incidence of varicella.

RECOMMENDATIONS

- 1. Recommend routine screening for varicella through history. [B]
- 2. If negative/unsure history, obtain a varicella titer. [B]
- 3. Recommend offering vaccination postpartum, if varicella is non-immune. [B]

DISCUSSION

A single systematic review was identified. The CDC (2007) recommends that all adults be immunized, if seronegative. Among U.S. women of childbearing age, the mean incidence of varicella is 2.16/1,000 per year. Maternal infection in the first half of the pregnancy has been associated with congenital varicella syndrome. In addition, varicella infections during pregnancy may result in higher rates of complications from the infection, such as varicella pneumonia and death (Smith et al., 1998). Varicella disease during the first two trimesters of pregnancy might infect the fetus and result in congenital varicella syndrome. Therefore, routine antenatal screening for

evidence of immunity and postpartum vaccination for those without evidence of immunity is now recommended (CDC, ACIP 2007).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine varicella screening	Smith et al., 1998	I	Good	В
2	Postpartum varicella immunization in seronegative pregnant women	CDC, 2007	I	Good	В

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 11. Screening for Hepatitis B Virus (HBV): Update

Weeks 6 - 8

BACKGROUND

Each year in the United States an estimated 22,000 infants are born to women with chronic hepatitis B virus (HBV). The incidence of acute hepatitis B in pregnancy is 1 to 2/1,000 and the prevalence of chronic hepatitis B is 5-15/1,000. Certain groups including Southeast Asians, Pacific Islanders, Alaskan Native Americans, drug addicts, transfusion recipients, women on dialysis and those with tattoos have an increased prevalence of infection (Duff, 1998).

However, these risk factors will only identify 60 percent of women with HBV infection. Perinatal transmission of hepatitis B virus occurs if the mother has an acute infection, particularly during late pregnancy or the early postpartum period, or if the mother is a chronic hepatitis B antigen carrier.

The risk of vertical transmission (mother to infant) can be greatly reduced (>90 percent) if the infectious status of the mother is known and therapy is given to the baby shortly after delivery. The risk of vertical transmission may also be reduced by maternal therapy during the last month of pregnancy.

RECOMMENDATIONS

- 1. Recommend routine laboratory screening for hepatitis B surface antigen at the initial prenatal visit. [A]
- 2. Repeat laboratory screening of pregnant women with identification of hepatitis risk factors during the pregnancy (e.g., healthcare worker, intravenous (IV) drug use, exposure to hepatitis, visit for evaluation or therapy for sexually transmitted infections, and new tattoos and blood transfusions). [C]
- 3. Vaccinate pregnant women with hepatitis risk factors who have not been previously vaccinated. [B]
- 4. Women at risk for HBV infection in pregnancy should be counseled concerning additional methods to prevent HBV infection. [C]

DISCUSSION

Universal laboratory screening of all pregnant women for hepatitis B is recommended in early in pregnancy (ACOG, 2007). Screening strategies using only risk factors would fail to identify 40 percent of infected women (Mast et al., 2005). The mortality risk for adults contracting HBV is one percent. Most (85 to 90 percent) women infected with HBV will clear the infection completely and the remainder will be chronic carriers. In those 10 to 15 percent who become chronic carriers, 15 to 30 percent will have persistent hepatitis and cirrhosis with associated sequelae.

In contrast to adults, 85 to 95 percent of neonates who contract HBV will become chronic carriers and 25 to 30 percent will suffer serious complications or die from the disease. The vertical transmission rate is lowest with maternal disease in the first trimester (10 percent) and highest in the third trimester (90 percent).

Vaccination is effective in preventing maternal infection. Prenatal therapy for mothers and postnatal therapy for infants reduces the vertical transmission rate by more than 90 percent. Thus, prevention and therapeutic strategies can have a large impact in preventing neonatal infection in at-risk pregnancies.

Two single antigen vaccines for HBV are currently available and are 95 percent effective in producing seroconversion in recipients. An effective hepatitis A and B vaccine is also available and highly effective.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screen for hepatitis B at first prenatal visit	ACOG, 2007	I	Good	A
2	Rescreen pregnant women with risk factors for hepatitis	Duff, 1998	III	Fair	С
3	Vaccinate pregnant women with hepatitis risk factors who have not been previously vaccinated	Mast et al., 2005	II	Good	В
4	Pregnant women at risk for HBV infection during pregnancy should be counseled concerning other methods of preventing HBV infection	Mast et al., 2005	III	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 12. Treatment for Hepatitis B Infection: Update

Week 36

BACKGROUND

Perinatal transmission of hepatitis B virus occurs if the mother has an acute infection, particularly during late pregnancy or the early postpartum period, or if the mother is a chronic hepatitis B antigen carrier.

Vertical transmission of infection occurs in 90 percent of pregnancies where the mother is hepatitis B e antigen positive and in about 10 percent of surface antigen positive, e antigen negative mothers. Most (85 to 95 percent) of infected infants become chronic carriers. Infants born to infectious mothers treated by both hepatitis vaccination and hepatitis B-specific immunoglobulin are 90 percent less likely to become infected than untreated infants.

There is also evidence that treating the mother in the last month of pregnancy with lamivudine or hepatitis B immunoglobulin may further reduce the transmission rate if she is highly infectious (HBV-DNA $>1.2 \times 10^9$ geq/mL).

RECOMMENDATIONS

- 1. Treat all infants born to hepatitis B positive mothers with Hepatitis B immunoglobulin and initiate hepatitis B vaccination within 12 hours of birth. [A]
- 2. Strongly consider treating infants born to women at high risk for hepatitis B who have not been vaccinated or whose infectious status is unknown. [B]
- 3. Consider treating women who have high copy numbers of HBV-DNA with lamivudine during the last month of pregnancy. [B]
- 4. Women with HBV infection should be taught, and encouraged to implement, strategies to decrease transmission to non-infected intimate contacts. [B]

Universal laboratory screening of all pregnant women for hepatitis B is recommended early in pregnancy (ACOG, 2007). Repeat screenings are also recommended for women who are, or become, high risk for acquiring hepatitis B infection during pregnancy. Such a strategy will identify approximately one percent of the overall population as being HBV positive during pregnancy.

The likelihood of vertical transmission is highest in the third trimester and around the time of birth. A combination of passive and active immunization of infants born to hepatitis B surface antigen-positive mothers affords very good protection to the infected infants (Sangfelt et al., 1995; Michielsen & Van Damme, 1999).

Randomized trials have demonstrated a reduction in late pregnancy vertical transmission by maternal therapy with lamivudine and with hepatitis B immune globulin (HBIG).

However, follow-on studies leave some uncertainty regarding the cost effectiveness of using HBIG alone to prevent vertical transmission (Yuan et al., 2006).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Active and passive immunization of neonates born to HBV-positive mothers within 12 hours of birth	Sangfelt et al., 1995; Michielsen & Van Damme, 1999 ACOG, 2007 #86	I	Good	A
2	Strongly consider treating infants born to women at high risk for hepatitis B who have not been vaccinated or whose infectious status is unknown	ACOG, 2007 #86	II	Good	В
3	Consider treating women who have high copy numbers of HBV-DNA lamivudine during the last month of pregnancy	Ahu et al., 2003 Li et al., 2004 Van Zonneveld et al., 2003 Xu et al., 2004	I	Good	В
4	Teach and encourage women with HBV to implement strategies to decrease transmission to non-infected intimate contacts	ACOG, 2007 #86 Mast et al., 2005	II	Fair	В

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 13. Screening for Syphilis Rapid Plasma Reagin (RPR):

Weeks 6 - 8

BACKGROUND

Syphilis is a sexually transmitted disease that can cause significant mortality and morbidity in both the mother and fetus. The disease is acquired through either sexual or congenital transmission and can be effectively treated using broad-spectrum antibiotics. Screening for maternal syphilis, treating, and tracking all confirmed cases, can prevent congenital syphilis.

RECOMMENDATIONS

- 1. Recommend routine screening for syphilis using serologic testing (i.e., RPR or Venereal Disease Research Laboratory [VDRL]) at the initial prenatal visit. [B]
- 2. Recommend a confirmatory test using a more specific treponemal assay (FTA-ABS, MHA-TP, HATTS) for pregnant women who test positive. [B]

- 3. Strongly recommend therapy with penicillin G antibiotic for pregnant women who have confirmed syphilis, as recommended by other sexually transmitted disease (STD) guidelines. [A]
- 4. Recommend appropriate medical and legal mandates follow-up and state/service branch reporting requirements for pregnant women screening positive. [I]

Three cohort studies identified strong association between untreated maternal syphilis and premature birth as well as a wide variety of severe abnormalities (Donders et al., 1993; Dorfman & Glaser, 1990). A number of variables are associated with asymptomatic syphilis: large urban areas or southern states, a history of STDs, low socioeconomic status, black race or Hispanic heritage, and a history of prostitution or IV drug use (CDC, 1998). Serologic tests have a sensitivity of 62 to 76 percent in primary syphilis and near 100 percent in secondary syphilis. Treponemal tests should not be used as initial screening tests (Hart, 1986). Maternal antibiotic therapy prevents nearly all congenital syphilis.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine syphilis screening	Donders et al., 1993 Dorfman & Glaser, 1990	II-3	Fair	В
2	Confirmatory syphilis testing in pregnant women with positive screens	Hart, 1986	II-2	Fair	В
3	Treatment of confirmed positive	CDC, 1998	II-2	Fair	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 14. Screening for Asymptomatic Bacteriuria: Update

Weeks 6 - 8

BACKGROUND

Bacteriuria occurs in two to seven percent of pregnant women. Asymptomatic bacteriuria (ASB) in pregnant women is an established risk factor for serious complications including pyelonephritis, preterm delivery, and low birth weight.

RECOMMENDATIONS

- 1. Strongly recommend screening for ASB at initial obstetrical visit via urine culture and sensitivity. [A]
- 2. There is insufficient evidence to recommend for or against repeat screening throughout the remainder of pregnancy. [I]
- 3. Strongly recommend a three to seven-day course of appropriate antibiotics based on positive culture and sensitivity, and woman's history of medication allergies. [A]
- 4. There is insufficient evidence to recommend for or against a test of cure (TOC) after completion of antibiotic therapy, except in pregnant women with ASB-Group B Strep. [I]

DISCUSSION

The USPSTF recommends screening for asymptomatic bacteriuria with urine culture for pregnant women at 12 to 16 weeks' gestation or at the first prenatal visit (Grade A) on the basis of good evidence that treatment for asymptomatic bacteriuria reduces the incidence of symptomatic urinary tract infections, low-birth-weight children, and preterm delivery (USPSTF, 2008).

Pregnant women with ASB have a 13 to 27 percent chance of developing pyelonephritis. They also have a 1.5 to 2-fold increased risk of preterm delivery or delivery of a low-birth-weight infant compared to women without ASB (Smaill, 2001).

Treatment of ASB in pregnancy reduces the risk of maternal pyelonephritis (numbers-needed-to-test [NNT]=7) and the risk of preterm delivery and/or low birth weight infants (NNT=21) compared to no treatment or placebo (Smaill, 2001).

The risks of pyelonephritis and preterm delivery/low-birth-weight infants are reduced by similar degrees with either short-term treatment (three to seven days) or continuous treatment until delivery. There are no differences in cure rates for bacteriuria or rates of recurrent ASB between single-dose and short-course therapy, but the data for this outcome are heterogeneous; the data regarding pyelonephritis and preterm delivery are too limited to be definitive (Smaill, 2001).

Dipstick urine tests, microscopic examination for pyuria and bacteriuria, and rapid enzymatic screening tests do not accurately detect ASB in pregnancy (Millar et al., 2000).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening for ASB at the initial prenatal visit by urine culture	Romero et al., 1989 Smaill, 2001 USPSTF, 2008	I	Good	A
2	Repeat screening throughout pregnancy	Working Group Consensus	III	Poor	I
3	A three- to seven-day course of appropriate antibiotics based on positive culture and sensitivity, and woman's history of medication allergies	Smaill, 2001	I	Good	A
4	TOC after completion of antibiotic therapy	Working Group Consensus	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 15. Screening for Tuberculosis: Update

Weeks 6-8

BACKGROUND

The incidence of tuberculosis has increased in the United States. Most new cases occur in cities with at least 500,000 people and in women in higher risk groups. High-risk groups for tuberculosis include individuals who:

- Have HIV infection
- Live in close contact with individuals known or suspected to have tuberculosis
- Have medical risk factors known to increase risk of disease if infected
- Are born in a country with high tuberculosis prevalence
- Are medically underserved
- Have a low income
- Are alcoholics
- Are intravenous drug users
- Are residents of long-term care facilities (e.g., correctional institutions, mental institutions, nursing homes and facilities)
- Are healthcare professionals working in high-risk healthcare facilities.

RECOMMENDATIONS

- 1. All pregnant women from one or more high-risk groups should be screened for tuberculosis with a Mantoux test with purified protein derivative (PPD) soon after the pregnancy is diagnosed. [C]
- 2. Pregnant women with a positive PPD with known conversion in the last two years and no clinical or X-ray evidence of disease should be treated with isoniazid (300 mg per day) starting after the first trimester and continuing for nine months. [C]
- 3. For pregnant women with a positive PPD whose time of conversion is unknown and who have no clinical or X-ray evidence of disease present, consider delaying therapy until after the pregnancy. [C]
- 4. Pregnant women with active tuberculosis should be treated with multi-drug therapy including isoniazid and rifampin, supplemented by ethambutol if isoniazid drug resistance is suspected. [C]

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	All pregnant women from one or more high-risk groups should be screened for tuberculosis with a Mantoux test with purified protein derivative (PPD) soon after the pregnancy is diagnosed	ACOG Guidelines for Perinatal Care, 1998 ATS/CDC, 2000 ACOG, 2006	III	Fair	С
2	Pregnant women with a positive PPD with known conversion in the last two years and no clinical or X-ray evidence of disease should be treated with isoniazid (300 mg per day) starting after the first trimester and continuing for nine months	ACOG Guidelines for Perinatal Care, 1998 ATS/CDC, 2000	II, III	Fair	С
3	For pregnant women with a positive PPD whose time of conversion is unknown and who have no clinical or X-ray evidence of disease present, consider delaying therapy until after the pregnancy	ACOG Guidelines for Perinatal Care, 1998 ATS/CDC, 2000	II	Fair	С
4	Pregnant women with active tuberculosis should be treated with multi-drug therapy including isoniazid and rifampin, supplemented by ethambutol if isoniazid drug resistance is suspected	ACOG Guidelines for Perinatal Care, 1998 ATS/CDC, 2000	III	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 16. Screening for HIV – Counsel:

Weeks 6 - 8

BACKGROUND

During the past decade, HIV infection became a leading cause of morbidity and mortality among women. As the incidence of HIV infection has increased among women of childbearing age, increasing numbers of children have become infected through perinatal transmission.

RECOMMENDATIONS

- 1. Strongly recommend routine testing for HIV infection at the initial prenatal visit. [A]
- 2. Pregnant women who test positive for HIV should be referred for treatment and counseling. [I]
- 3. Recommend retesting all high-risk pregnant women during the early third trimester and offer repeat testing for patients who refused the first test. [B]

DISCUSSION

Several studies have indicated that counseling and testing strategies that offer testing only to those women who report risk, fail to identify up to 50 to 70 percent of HIV-infected women (CDC, 1995). A policy of routine screening for all pregnant women with their consent is recommended on the grounds of easier implementation and greater sensitivity than risk profile screening (AAP/ACOG, 1995).

A randomized placebo controlled trial demonstrated that a regimen of zidovudine started by 14 to 34 weeks' gestation and continued through six weeks postpartum reduced vertical transmission of HIV from 25 to 8.3 percent. Zidovudine has had a low incidence of severe side effects in the mother and infants studied, but long-term effects are unknown (Connor et al., 1994).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine HIV screening	AAP/ACOG, 1995 CDC, 1995	I	Good	A
2	Retest high-risk women	Higgins et al., 1991 Tookey et al., 1998	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 17. Screening for Td and Tdap Booster:

Weeks 6 - 8

BACKGROUND

Tetanus and diphtheria were serious causes of infectious morbidity and mortality of people of all ages prior to the advent of widespread effective active immunization programs. The majority of cases of diphtheria and tetanus occur in adults who have not received adequate vaccination, and fatality rates for diphtheria are approximately 10 percent and 25 percent for tetanus. The tetanus-diphtheria (Td) vaccine is made up of bacterial toxins that cause the production of antibodies against the live bacterium when administered to an individual. Unfortunately, the immune response is not lifelong, thus periodic revaccination is required to ensure immunity. Since the vaccine is made up of inactive bacterial particles and not live bacteria, pregnancy is not a contraindication to providing indicated preventive services such as tetanus booster vaccination.

RECOMMENDATIONS

- 1. Strongly recommend routine screening for Tdap booster status at the initial prenatal visit. [A]
- 2. If there is no documentation of Td booster within the last 10 years: [A]
 - a. Provide Tdap in the immediate postpartum period before discharge from the hospital or birthing center
 - b. May provide Tdap at an interval as short as two years since the most recent Td vaccine
 - c. Provide Td during pregnancy for tetanus and diphtheria protection when indicated, or defer the Td vaccine indicated during pregnancy to substitute Tdap vaccine in the immediate postpartum period if the woman is likely to have sufficient protection against tetanus and diphtheria.

- 3. Td booster should be provided if indicated. There are no contraindications other than a previous severe reaction to Td vaccination, such as anaphylaxis, generalized uriticaria, or angioedema. [A]
- 4. If the pregnant woman is an immigrant and it is unclear that she ever received the primary vaccination series, she should be given a primary series with an initial dose, a second dose a month later, and a third dose 12 months later. [B]

Effective antibody response is 95 to 100 percent in healthy adults after primary vaccination series. Immunity wanes over the years and the precise duration of immunity is unknown for specific individuals, but generally lasts at least a decade for small inoculum of tetanus encountered in a small or minor wound. For any other wound, it is recommended that a tetanus booster be administered unless the patient has received a Td booster within the previous five years. Neonates receive passive immunization from maternal antibodies until their immune system is adequate to provide an antibody response to neonatal vaccinations.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening for Td booster status at the first prenatal visit	USPSTF, 1996	II-1	Good	A
2	If no documentation of Td booster within the last 10 years, provide Td booster; there are no contraindications other than documented allergies to administration of Td during pregnancy	Fingar et al., 1998 ICSI, 2001 USPSTF, 1996	II-1	Good	A
3	Pregnant women deemed unlikely to have received initial three-dose vaccination (immigrants from underdeveloped countries) should receive an initial three dose series	Fingar et al., 1998 ICSI, 2001 USPSTF, 1996	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 18. Screening for Anemia: New

Weeks 6-8

BACKGROUND

Anemia occurs in two to four percent of pregnant women. It is defined as a hemoglobin or hematocrit concentration less than the fifth percentile of a healthy pregnant population and varies during the trimesters of pregnancy and in African versus non-African populations. Non-African women with a hematocrit less than 33, 32 and 33 percent in the first, second and third trimesters, respectively, are anemic. The threshold for anemia in the African-American population is two percent lower. Severe anemia, defined as a hemoglobin < 6 gm/dL is associated with adverse pregnancy outcomes due to inadequate fetal oxygenation. Iron deficiency and acute blood loss are the most common causes of anemia. Anemia can be categorized by the size of the red blood cell (microcytic, normocytic and macrocytic), the mechanism of the anemia, or by whether the anemia is acquired or inherited. Certain ethnic groups are at increased risk for inheritable causes of anemia and should be screened for such (see Appendix C - Screening for Hemoglobinopathies). Iron deficiency anemia is usually microcytic (Mean Corpuscular Volume <80 fL), can be confirmed by laboratory findings of diminished stores, and responds to iron supplementation. Iron deficiency anemia during pregnancy has been associated with an increased risk of low birth weight, preterm delivery, and perinatal mortality. There is also an association between maternal iron deficiency anemia and postpartum depression and poor results in mental and psychomotor performance testing in offspring.

RECOMMENDATIONS

- 1. All pregnant women should be screened for anemia during pregnancy with a hematocrit or hemoglobin measurement during the first visit. [C]
- 2. Pregnant women with anemia should be further evaluated to define the cause of the anemia and given nutrient supplementation if deficient (e.g. iron, B12 or Folate). [C]
- 3. Red blood cell transfusion should be considered for pregnant women with severe anemia. [C]
- 4. Iron sucrose transfusion should be considered for pregnant women with iron deficiency anemia who fail to respond to oral iron supplementation after eliminating modifiable causes of malabsorption. [C]

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	All pregnant women should be screened for anemia during pregnancy with a hematocrit or hemoglobin measurement in the first and third trimester	ACOG, 2008 #95 CDC, 1998	III	Fair	С
2	Pregnant women with anemia should be further evaluated to define the cause of the anemia and given nutrient supplementation if deficient (e.g. iron, B12 or Folate)	ACOG, 2008 #95 Institute of Medicine, 1993 Reveiz et al., 2007	II, III	Fair	С
3	Red blood cell transfusion should be considered for pregnant women with severe anemia	ACOG, 2008 #95	II	Fair	С
4	Iron sucrose transfusion should be considered for pregnant women with iron deficiency anemia who fail to respond to oral iron supplementation after eliminating modifiable causes of malabsorption	ACOG, 2008 #95 Faich & Strobos, 1999 Bhandal & Russell, 2006	III	Fair	С

 $\overline{LE = Level \ of \ Evidence; \ QE = Quality} \ \overline{of \ Evidence; \ SR = Strength} \ of \ Recommendation (See Appendix A)$

I- 19. Screening for Hemoglobinopathies: Update

Weeks 6-8

BACKGROUND

The hemoglobinopathies are a heterogeneous group of single-gene disorders that includes the structural hemoglobin variants such as sickle cell disease and thalassemia. More than 270 million people worldwide are heterozygous carriers of hereditary disorders of hemoglobin, and at least 300,000 affected homozygotes or compound heterozygotes are born each year. Sickle cell disease and the thalassemias are discussed below.

RECOMMENDATIONS

- 1. Carrier screening should be offered to individuals of African, Southeast Asian, and Mediterranean descent. [A]
- 2. A complete blood count and hemoglobin electrophoresis are the recommended tests to screen for hemoglobinopathies. [B]

Genetic screening can identify couples at risk for offspring with hemoglobinopathies and allow them to make informed decisions regarding reproduction and prenatal diagnosis. Individuals of African, Southeast Asian, and Mediterranean ancestry are at a higher risk for being carriers of hemoglobinopathies and should be offered carrier screening. Ethnic groups considered to be at low risk for hemoglobinopathies include northern Europeans, Japanese, Native Americans, Inuit (Eskimo), and Koreans. If both parents are determined to be carriers, genetic counseling is recommended. It should be noted that ethnicity is not always a good predictor of risk because individuals from at-risk groups may marry outside their ethnic group. A CBC and hemoglobin electrophoresis should be performed for screening patients at risk. Solubility tests alone are inadequate for screening because they fail to identify important transmissible hemoglobin gene abnormalities affecting fetal outcome. Couples at risk for having a child with sickle cell disease, thalassemia or sickle-thalassemia disease should be offered genetic counseling to review prenatal testing and reproduction options. Prenatal diagnosis of hemoglobinopathies is best accomplished by DNA analysis of cultured amniocytes or chorionic villi.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Offer carrier screening to individuals of African, Southeast Asian, and Mediterranean descent	ACOG, 2007 Angastiniotis et al., 1998 Davies et al., 2000	I	Good	A
2	A complete blood count and hemoglobin electrophoresis are the recommended tests to screen for hemoglobinopathies	ACOG, 2007	III	Good	В

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 20. Screening for Domestic Abuse: Update

Weeks 6 - 8

BACKGROUND

Domestic violence is an epidemic problem that may be first identified during pregnancy. Unfortunately, high-quality evidence-based documentation does not exist regarding the benefits of specific interventions to decrease domestic violence. Healthcare providers need to be aware that a woman's decision to leave an abusive relationship may result in an escalation of violence.

RECOMMENDATIONS

- 1. Recommend routine screening for domestic abuse at the first visit, week 28, and the post partum visit, using the following three simple/direct questions: [B]
 - o Within the last year, have you been hit, slapped, kicked, or otherwise physically hurt by someone?
 - o Since you've been pregnant, have you been hit, slapped, kicked, or otherwise physically hurt by someone?
 - o Within the last year, has anyone forced you to engage in sexual activities?
- 2. There is insufficient evidence to recommend for or against specific interventions for identified domestic abuse in pregnancy. [I]
- 3. If the screening is positive, follow appropriate medical/legal mandates for reporting requirements for state/branch of service. [C]

Domestic violence is a common problem, estimated to occur in up to 20 percent of pregnancies (Gazmararian et al., 1996). The few observational studies that have assessed the relationship between abuse during pregnancy and maternal or fetal outcomes have not found consistent associations.

One poor-quality non-randomized trial found a decreased frequency and severity of violence at six and 12 months postpartum for women offered three one-on-one 30-minute counseling sessions with a trained nurse, as part of their prenatal care. The intervention and control groups were not comparable prior to intervention, making the results difficult to interpret (Parker et al., 1999).

A second non-randomized trial of poor quality found no difference when abused women were given simple written information or offered unlimited access to a professional counselor during prenatal care, with or without additional support from a "mentor mother." Because the study had significant methodological flaws, it is possible that a clinically significant benefit from the intervention could have been missed (McFarlane et al., 2000).

There are several studies validating multiple screening tools for the occurrence of domestic violence (McFarlane et al., 1995; Norton et al., 1995). The recommendation for the utilization of three simple/direct questions is based on the only study that addressed domestic violence and the pregnant population (McFarlane et al., 1992).

Renker (2007) conducted a survey of 519 women postpartum who had been screened with a computer-based program for domestic abuse. The computer-based interviews offer an alternative approach to screening and women who are hesitant to disclose domestic violence to a provider may be more likely to report it on the computer survey.

Three simple questions by a primary provider during a prenatal visit will detect abuse approximately as effectively as a well-validated research instrument (McFarlane et al., 1992).

Higher rates of detection are achieved if providers ask about abuse at several prenatal visits, rather than asking a single time (Covington et al., 1997).

A systematic review evaluating the available evidence on interventions aimed at preventing abuse or reabuse of women found that no study has examined, in a comparative design, the effectiveness of screening when the end point is improved outcomes for women (as opposed to identification of abuse). No high-quality evidence exists to evaluate the effectiveness of shelter stays to reduce violence. Among women who have spent at least one night in a shelter, there is fair evidence that those who received a specific program of advocacy and counseling services reported a decreased rate of reabuse and an improved quality of life. The benefits of several other intervention strategies in treating both women and men are unclear, primarily because of a lack of suitably designed research measuring appropriate outcomes (Wathen & Macmillan., 2003).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine screening during pregnancy for domestic abuse	Gazmararian et al., 1996	II-2	Fair	В
2	Routine screening for domestic abuse with three simple/direct questions at weeks 8, 24, and 32, possibly using a computerized interview	McFarlane et al., 1992 Renker et al., 2007	II-2	Fair	В
3	Specific interventions after identifying domestic abuse in pregnancy	McFarlane et al., 2000 Parker et al., 1999 Wathen & Macmillan , 2003	III	Poor	I

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

BACKGROUND

Depression in pregnancy in general, and in the peripartum period in particular, is a well-recognized problem. Although estimates vary, in the first three months after childbirth, 14.5 percent of women have a new episode of major or minor depression, and 10 percent to 20 percent of mothers are believed to suffer with depression sometime during their postpartum course, making postpartum depression the most common serious postpartum disorder. In addition, it is an under-recognized entity, with 50 percent of cases undetected. This rate of under-detection can be reduced by the use of a screening instrument, administered during the course of pre- and postnatal visits. This detection can lead to further diagnostic interviews and to appropriate treatment, lessening the deleterious effects of depression on both the mother and child. When a woman is diagnosed with depression, treatment should follow (see I-34).

RECOMMENDATIONS

- 1. Women should be screened for depression during their first contact with obstetric healthcare services, at week 28 and at the postpartum visit. [B]
- 2. Depression screening should be performed using a standardized screening tool such as the Edinburgh Postnatal Depression Scale (EDPS) or the PHQ-2. [B]
- 3. Women should be asked early in pregnancy if they have had any previous psychiatric illnesses, and if they had a past history of serious psychiatric disorder they should be referred for a psychiatric assessment during the antenatal period. [B]

RATIONALE

Early detection of depression during pregnancy is critical because depression can adversely affect birth outcomes and neonatal health and, if left untreated, can persist after the birth. Untreated postpartum depression can impair mother-infant attachments and have cognitive, emotional, and behavioral consequences for children. The best studied of these screening instruments is the Edinburgh Postnatal Depression Scale (EDPS).

EVIDENCE STATEMENTS

- Women are at elevated risk for depression during the antenatal and post-partum periods. The point prevalence of depression is seven to 15 percent during pregnancy and five to greater than 31 percent in the post-partum period (AHRQ, 2005; Bennett et al., 2004; Gaynes et al., 2005).
- In addition to adverse effects on the mother, depression has adverse effects on the fetus and infants (Epperson et al., 1999). The presence of maternal depressive symptoms at a critical time for infant and family has additional adverse effects, such as marital distress (Beck, 2001), problems with mother-infant interaction and attachment (Righetti-Veltema et al., 2003) and adverse behavioral and cognitive effects in the child (Grace et al., 2003).
- In a systematic review of the evidence for depression screening during pregnancy, only one study reported on screening accuracy in a population, with six patients with major depression and 14 patients with either major or minor depression. For major depression, sensitivities for the Edinburgh Postnatal Depression Scale (EPDS) at all thresholds evaluated (12, 13, 14, 15) were 1.0, underscoring the markedly small number of depressed patients involved; specificities ranged from 0.79 (at EPDS >12) to 0.96 (at EPDS >15). For major or minor depression, sensitivity was much poorer (0.57 to 0.71), and specificity remained fairly high (0.72 to 0.95) (Gaynes et al., 2005).
- For postpartum depression screening, a systematic review reported that the small number of depressed patients involved in the studies precluded identifying an optimal screener or an optimal threshold for screening. "Our ability to combine the results of different studies in a meta-analysis was limited by the use of multiple cut-offs and other differences in the studies that would have made the pooled estimate hard to interpret. Where we were able to combine the results through meta-analysis, the pooled analysis did not add to what one could conclude from individual studies." (Gaynes et al., 2005.)

- Three systematic reviews evaluated screening tools for postpartum depression, used either in the prenatal or postpartum period.
 - The first review (Austin & Lumley, 2003) included 16 studies evaluating screening tools prenatally. Outcome assessments used the Edinburgh Postnatal Depression Scale (EPDS) or standardized diagnostic psychiatric interviews, or both. However, most of the studies were small only four studies had adequate sample sizes to assess the sensitivity and specificity of postpartum depression screens. In the two largest population-based studies the positive predictive value was low. The authors concluded that no screening instruments were appropriate for prenatal prediction of postpartum depression.
 - A second review (Boyd et al., 2005) included 36 studies of self-reported scales for postpartum depression screens two weeks after labor. Out of eight tools that have been evaluated, the results suggested that the EPDS is the most extensively studied postpartum measure with moderate psychometric soundness. However, as in the other reviews, most of the studies included had small sample sizes.
 - The evidence report/technology assessment (Gaynes et al., 2005) also looked at the predictive value of different screening tools for detecting depression during the perinatal period. Although the EPDS and the PDSS seemed to have higher sensitivities than the BDI (with estimates ranging from 0.75 to 1.0 at different thresholds), the author questioned the external validity of the studies and the accuracy given the small sample sizes in several studies.
- A review of the literature (Gjerdingen et al., 2007) concluded that postpartum depression screening improves recognition of the disorder but that additional studies with large, representative samples are needed to help identify the ideal postpartum depression screening tool.
- Although there are no published reports on the validity of the PHQ-9 in screening for postpartum depression it has been used as a screen in obstetrics/gynecology practices that include both women of childbearing age and older women. The PHQ-2 was studied in eight primary care clinics and seven obstetrical/gynecology clinics, where construct and criterion validity were found to be very good, and sensitivity and specificity high (83 and 92 percent, respectively) (Kronke et al., 2003). A single study (done in Europe and with no control group) showed that a two-item questionnaire, substantially the same as the PHQ-2, performs comparably to longer instruments (Jesse et al., 2005).
- Administering the EPDS by phone at six to eight weeks postpartum is an efficient and accurate way to
 identify women at high-risk for postpartum depression within the first six months after delivery (Hanusa,
 2008).
- Studies that have addressed postpartum depression screening demonstrate that screening is feasible in the outpatient setting and can improve the rates of detection and treatment (Georgiopoulos et al., 2001; NICE, 2007).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Women are at increased risk for depressive disorders during pregnancy and postpartum periods	Gaynes et al., 2005	I	Good	A
2	Depression screening improves detection during pregnancy and in postpartum	Georgiopoulos et al., 1999 Gjerdingen et al., 2007 NICE, 2007	I	Good	A
3	PHQ-2 is a sensitive screen for depression in postpartum women	Kronke et al., 2003	II I	Fair	В
4	EDPS is a sensitive and valid screen for depression in the antepartum and postpartum period	Adouard et al., 2005 Boyd et al., 2005 Evins et al., 2000 Peindl et al., 2004 Hanusa et al., 2008	П	Good	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

First Visit With Provider (10-12 Weeks)

I- 22. Establishing the Gestational Age: New

Weeks 10-12

BACKGROUND

Establishing accurate pregnancy dating impacts the management of normal and abnormal pregnancies and thus is one of the most important responsibilities of prenatal care providers. Accurate dating is essential for timing tests such as prenatal screening tests for an euploidy, assessment of proper fetal growth and maturity and management of the pregnancy past the due date. Common usage of the term gestational age refers to menstrual age that equals conceptional age plus 14 days.

Currently, the gestational age is assessed by menstrual history, clinical examination, ultrasound or by a known conceptional date. Gestational age is most accurately established by a certain conception date as occurs with reproductive technologies, single intercourse associated conceptions and basal body temperature records, each of which is highly predictive of conceptional age. The next most accurate assessment of menstrual age is by a six to eleven-week crown-rump length measurement by ultrasound followed by a certain last menstrual period in women with regular cycles, then by early second-trimester sonographic examinations and then first trimester followed by second-trimester physical examination. Dating the pregnancy by menstrual history or clinical examination is subject to considerable error. The mother's initial detection of fetal movements and late pregnancy ultrasound are too unreliable to be useful for accurate assessment of the gestational age.

RECOMMENDATIONS

- 1. Establish the gestational age-based estimated delivery date (EDD) prior to 20 weeks' gestational age. [B]
- Various information and methods for dating a pregnancy may be available for consideration. EDD should be based on the most accurate information/method available for the individual pregnancy (see Table 4. Accuracy of Pregnancy Dating Information/Modalities (Prioritized List). [B]
- 3. Gestational age permitting, first-trimester ultrasound should be used to establish the gestational age and EDD **if** there is any uncertainty regarding the EDD due to: a pelvic examination discrepancy (> +/- two weeks), an unknown or uncertain last menstrual period (LMP), or irregular menstrual cycles. [B]

- 4. When a first-trimester dating ultrasound has not been previously performed a dating ultrasound at 16 to 22 weeks should be obtained. This examination can be combined with a basic screening anatomy ultrasound. [B]
- 5. Situations with abnormal fetal biometric ratios (e.g., head / abdominal circumference [HC/AC], biparietal diameter /femur length [BPD/FL]) limit the accuracy of biometric measurements for pregnancy dating and may signal fetal anomalies or karyotype abnormalities. Such circumstances require individualized assessment by an advanced prenatal care provider to establish dating and recommend ongoing assessment(s) and management. [C]
- 6. When clinical decisions late in pregnancy necessitate gestational age information and the dates have not been established prior to the 29th week, fetal maturity may be assumed when one of the following criteria are met: [C]
 - a. 20 weeks of audible fetal heart tones by a non-electronic method
 - b. 30 weeks of audible fetal heart tones by an electronic method
 - c. 36 weeks from a positive pregnancy test in a reliable laboratory.

Table 4. Accuracy of Pregnancy Dating Information/Modalities (Prioritized List)

- 1. In vitro fertilization (+/- 1 day).
- 2. Ovulation induction, artificial insemination, a single intercourse record, ovulation predictor assay or basal body temperature measurement (+/- 3 days).
- 3. First-trimester sonographic assessment (6-11 weeks) (+/- 8%).
- 4. Reported LMP, if reliable.
- 5. Twelve to 22-week second-trimester sonographic examination (CRL or BPD, HC, AC and FL) if the LMP is unknown or uncertain or if the LMP is more than 8 percent discordant from the sonographic examination.
- 6. Twenty-three to 28-week second-trimester sonographic examination (BPD, HC, AC, FL) confirmed by a second examination 3-6 weeks later demonstrating normal interval growth (+/- 8%).
- 7. Third-trimester sonographic evaluation (+/-8%).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Establish the gestational age-based due date (EDD) prior to 20 weeks' gestational age	Mongelli et al., 1996 Wilcox et al., 1993	Ш	Good	В
2	Base the due date on the most accurate data available	Mongelli et al., 1996, 2005 Peek et al., 1994	II	Good	В
3	Gestational age permitting, first-trimester ultrasound should be used to establish the gestational age if there is any uncertainty in the EDD	Mongelli et al., 1996 Peek et al., 1994 Sladkevicius et al., 2005	II	Good	В
4	When a first-trimester dating ultrasound has not been previously performed a dating ultrasound combined with an anatomy ultrasound at 16 to 22 weeks should be obtained	Geirsson et al., 1993 Gardosi et al., 1997 Mul et al., 1996	II	Good	В
5	The presence of abnormal fetal biometric ratios limit the accuracy of biometric measurements for dating, may signal fetal anomalies, and require individualized assessment by an advanced prenatal care provider	Watson et al., 2007 ACOG, Practice Bulletin #98, 2008	III	Fair	С
6	When clinical decisions late in pregnancy necessitate gestational age information and the dates have not been established, fetal maturity may be assumed based on well-established clinical grounds	ACOG ,1999	III	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 23. Auscultation Fetal Heart Tones:

Weeks 10-12, All following visits

BACKGROUND

No studies show improved perinatal outcome from identifying fetal heart tones, but expert opinion concurs that an occasional fetal demise may be found (with no other signs or symptoms) or an occasional cardiac anomaly might be detected. The primary indication for identifying fetal heart tones is the enormous psychological benefit to parents.

RECOMMENDATIONS

1. Recommend assessing fetal heart tones at each prenatal visit, starting at 10 to 12 weeks. [C]

DISCUSSION

This intervention has not been specifically researched, though studies can be found that correlate fetal heart tones with confirmation of fetal viability. Auscultation of fetal heart tones is an easy and inexpensive way to document fetal health. It has no known risk and offers significant psychological benefit and reassurance to both expectant parents and healthcare providers alike. Additionally, routine auscultation of fetal heart tones assists in early

identification of fetal demise which may otherwise be asymptomatic, and affords the opportunity to initiate appropriate counseling and treatment.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Auscultation of fetal heart tones	Engstrom, 1985 Jimenez et al.,1983 Working Group Consensus	III	Poor	С

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 24. Screening Fundal Height:

Weeks 10-12; All following visits

BACKGROUND

Fundal height is commonly used as an indicator of fetal growth. A discrepancy between fundal height and gestational age in weeks, particularly between weeks 20 and 36, may indicate abnormal growth and/or abnormalities in amniotic fluid volume. Timely detection and treatment of these abnormalities may improve fetal outcomes.

RECOMMENDATIONS

- 1. Recommend measuring fundal height in all pregnant women at each visit during the second and third trimesters. [B]
- 2. There is insufficient evidence to recommend for or against measuring fundal height after 36 weeks' gestation. [I]

DISCUSSION

Fundal height measurement is inexact and subject to inter- and intra-observer errors. However, the screening maneuver is simple, inexpensive, and widely used during prenatal care. Women should always be placed in the same position for the measurement, lying supine with the legs extended. All studies of the reliability and validity of fundal height measurements have used this position (Engstrom & Work, 1992). The measurement, taken between the symphysis pubis and the fundus, should approximate the gestational age in weeks within three centimeters; any difference greater than three centimeters may warrant further investigation, particularly between weeks 20 and 36. Several studies have shown good sensitivity and specificity for predicting low birth weight for gestational age (Mathai et al., 1987; Pearce & Campbell, 1987; Wise & Engstrom, 1985). Fundal height measurements after 36 weeks' gestation continue to be of benefit despite lower yield in accuracy, especially among multiparous women.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Fundal height measurement at 20 to 36 weeks	Calvert et al., 1982 Engstrom & Work, 1992 Jimenez et al., 1983 Lindhard et al., 1990 Mathai et al., 1987 Pearce & Campbell, 1987 Quaranta et al., 1981 Wise & Engstrom, 1985	I	Good	В
2	Fundal height measurement after 36 weeks	Working Group Consensus	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 25. Assessing (Inappropriate) Weight Gain:

Weeks 10-12; All following visits

BACKGROUND

Pregnant women who experience inappropriate weight gain may be at risk for a number of complications. Excessive weight gain may increase the risk for macrosomic infants, shoulder dystocia, operative delivery and postpartum obesity. Inadequate weight gain is associated with preterm delivery, intrauterine growth restriction, and low birth weight. Screening for inappropriate weight gain allows for early intervention to prevent these complications.

Obesity is defined as a BMI of 30 kg/m² or greater and affects approximately one-third of adult women. Obese women are at increased risk for several pregnancy complications (see I-27).

RECOMMENDATIONS

- 1. Recommend assessing and documenting body mass index (BMI) of all pregnant women at the initial visit. [B]
- 2. Pregnant women found to have a BMI <20 kg/m² should be referred for nutrition counseling and considered at increased risk for fetal growth restriction. [B]
- 3. Recommend screening for inappropriate weight gain for all women at every visit during pregnancy. [C]
- 4. Pregnant women with inadequate weight gain at 28 weeks who are unresponsive to nutritional treatment need additional surveillance. Consider consultation /referral to advanced prenatal care provider. [C]

DISCUSSION

No systematic reviews or controlled trials of screening for inappropriate weight gain during pregnancy were identified. Recommendations endorsed by the Institute of Medicine (IOM), AAP and ACOG (1995) have been based on the pre-pregnancy BMI. Women with a BMI below 19.8 kg/m² are recommended to gain 12.7 to 18.2 kg (28 to 40 lb), women with a BMI of 19.8 to 26.0 kg/m² are advised to gain between 11.4 and 16.0 kg (25 to 35 lb), and women with a high BMI (26.0 to 29.0 kg/m²) are recommended to gain between 6.8 and 9.1 kg (15 to 20 lb). Women who have a very high BMI (i.e., above 29 kg/m²) are advised to gain at least 6.8 kg (15 lb) (IOM, 1990).

Maternal BMI of less than 20 kg/m² at the start of pregnancy is associated with increased prevalence of preterm delivery and low-birth-weight infants (Sebire et al., 2001). This retrospective analysis did not look at weight gain over the course of pregnancy on these outcomes.

For inadequate weight gain, only balanced protein-energy supplementation may be safe and effective. High-protein and isocaloric protein-energy supplementation may be associated with untoward fetal effects. For excessive weight gain, protein-energy restriction is not significantly effective and may adversely impact birth weight (Kramer, 2000).

Excessive weight gain may be associated with adverse changes in fetal or neonatal weight and minor maternal morbidity, but these data are difficult to separate from data concerning baseline obesity (Kelly et al., 1997). Maternal overweight condition increases the risk of antepartum stillbirth, especially term antepartum stillbirth, whereas weight gain during pregnancy was not associated with risk (Stephansson et al., 2001).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine assessment of BMI at first visit	Sebire et al., 2001	II-2	Fair	В
2	Nutrition counseling for inadequate weight gain or initial BMI <20 kg/m ²	Kramer, 2000 Sebire et al., 2001	II-2	Fair	В
3	Routine screening for inappropriate weight gain at each visit	Kelly et al., 1997	III	Fair	С
4	The practical evaluation of weight gain at 24 to 28 weeks	Kelly et al., 1997	II-2	Fair	С
5	Individualized weight gain based on pre-pregnancy weight	IOM, 1990	III	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 26. Nutritional Supplements: New

Weeks 10-12

BACKGROUND

Women in the United States commonly (expect to) practice multivitamin supplementation throughout pregnancy. This tradition is based on the assumption that women have increased nutritional requirements during pregnancy that cannot be met by diet alone.

RECOMMENDATIONS

Multivitamins

- 1. Multivitamin supplements should be taken one month preconceptually and should be continued through the first trimester. [C]
- 2. Pregnant women taking nutritional supplements for a medical condition should continue that supplementation throughout pregnancy (e.g., B-12 with pernicious anemia and folate with seizure disorders). [I]
- 3. Pregnant women on restrictive diets (vegetarians, bariatric surgery) should have nutrition consultation to customize vitamin supplementation regimen. [I]

Folate

- 4. Folate supplements (400 mcg daily) should be taken one month preconceptually, continued through the first trimester and should be administered as part of the multivitamin supplementation. [A]
- 5. Women who have delivered a child with an open neural tube defect (NTD) should supplement their diets with 4 mg folate daily for at least one month prior to conception and through the first trimester to reduce the risk of recurrence. [A]

Calcium

6. Calcium supplementation may be considered to reduce the risk of preeclampsia in high-risk women and those with low baseline calcium intake. [A]

Omega3

- 7. There is insufficient evidence to support the use of Omega 3 supplements in the prevention of preterm birth, preeclampsia, and low birth weight. [I]
- 8. Other dietary supplements should be used with caution and only after discussion with provider. [I]

Nutrition has long been hypothesized to have a role in the etiology of preeclampsia. It is now well understood that, while preeclampsia is clinically evident late in pregnancy, the casual exposure(s) and many of the pathophysiologic changes are present months earlier. Periconceptional exposures may be particularly relevant, as they may affect implantation and/or decidual vascular remodeling (Bodnar et al., 2006). After adjusting for covariates, Bodnar and colleagues showed that regular use of multivitamins in the periconceptional period was associated with a 45 percent reduction in preeclampsia (n=1835) risk compared with nonuse. The analysis in this study showed a lack of a protective effect from multivitamins among overweight women. This prospective cohort study from 1997-2001 included pregnant women aged 14 to 44 years who were carrying singleton infants. Taking multivitamins or prenatal vitamins regularly was defined as at least once per week, not to include supplements that subjects began using during pregnancy.

Three systematic reviews were identified that addressed supplementation during pregnancy with individual vitamins. Individual folate supplementation in pregnancy (approximately 500 micrograms) resulted in increased or maintained serum folate levels and red cell folate levels, and increased hemoglobin levels late in pregnancy (Mahomed, 2001). Periconceptual folate supplementation has a strong protective effect against NTD (odds ratio=0.28). Preconceptual folate has been shown to decrease the incidence of neural tube defects. It did not, however, have any measurable effect on any other pregnancy outcome. There was no impact on any other maternal or infant outcome. Adequate folate supplementation can be provided through the use of multivitamins containing 400 mcg of folic acid. Individual pyridoxine (vitamin B-6) supplementation was associated with decreased dental decay in pregnant women (Mahomed & Gulmezoglu, 2001a). Supplementation with vitamin D during pregnancy may lead to a small reduction in birth weight and a higher daily mean maternal weight gain (Mahomed & Gulmezoglu, 2001b). These data support the hypothesis that periconceptional vitamin supplementation may extend benefits beyond a reduction in NTD risk.

Multivitamins

Goh and colleagues' meta analysis of seven case control analytic studies states that there is a protective effect of taking prenatal multivitamin supplementation against three of the most prevalent forms of childhood cancers. There is an 18 percent protective decrease risk for pediatric brain tumors, 47 percent for neuroblastomas, and 36 percent protective effect for leukemia (Goh et al., 2007).

Calcium

A Cochrane review (Hofmeyr, et al, 2006) found that calcium supplementation during pregnancy is a safe and relatively inexpensive means of reducing the risk of preeclampsia in women at increased risk, and women from communities with low dietary calcium. Calcium supplementation appears to almost halve the risk of preeclampsia, and to reduce the rare occurrence of the composite outcome 'death or serious morbidity'.

LC-PUFA

The overall meta-analysis on the intake of long-chain polyunsaturated fatty acids found no evidence that supplementation influenced the percentage of preterm deliveries, the rate of low-birth-weight infants, or the rate of preeclampsia or eclampsia.

Dietary ingredients used in dietary supplements are not subject to the pre-market safety evaluations required of new food ingredients, new uses of old food ingredients, or medications. Although the Dietary Supplement Health and Education Act (DSHEA) does give the FDA the right to ban harmful dietary supplements, the burden of proof is on the FDA. No mandatory system exists for reporting the harmful effects of dietary supplements or the production and packaging of products. That means the concentration or dosage of ingredients in different products, and what contaminants are in the product, are unknown.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine vitamin supplementation during pregnancy	Goh et al., 2007 Mahomed, 2001 Mahomed & Gulmezoglu, 2001a, b	I III III	Fair	В
2	Regular periconceptional multivitamin use	Bodnar et al., 2006	II-2	Fair	С
3	Routine calcium supplementation for high-risk and low dietary intake	Hofmeyr et al., 2006	I	Good	A
4	Continuation of preconceptual vitamin supplements until the end of first trimester	Werler et al., 1999	II-3	Good	В
5	Continuation of preconceptual folate until the end of the first trimester	Lumley et al., 2001	I	Good	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 27. Obesity: New Weeks 10-12

BACKGROUND

Obesity is defined as a BMI of 30 kg/m² or greater and affects approximately one-third of adult women. Obese women are at increased risk for several pregnancy complications.

RECOMMENDATIONS

- 1. Recommend the following for obese pregnant women: [I]
 - a. Provision of specific information concerning maternal and fetal risks of obesity
 - b. Consideration of screening for gestational diabetes mellitus (GDM) on presentation or in the first trimester and repeated screening later in pregnancy if results are initially negative
 - c. Assessment and possible supplementation of vitamin B12, folate, iron, and calcium for women who have undergone bariatric surgery
 - d. Anesthesia consultation before labor
 - e. Possible use of graduated compression stockings, hydration, and early mobilization during and after cesarean section
 - f. Continuation of nutrition counseling and exercise program after delivery, and consultation with weight loss specialists before attempting another pregnancy.

DISCUSSION

Obesity was associated with an increased risk of gestational hypertension, preeclampsia, gestational diabetes, and fetal macrosomia as well as increased cesarean delivery rate. Operative and postoperative complications include increased rates of excessive blood loss, operative time greater than two hours, wound infection, endometritis and anesthetic challenges. Potential intrapartum complications include difficulty estimating fetal weight, inability to obtain interpretable external fetal heart rate and uterine contraction patterns, and difficulty performing emergent cesarean delivery (ACOG Committee Opinion #315, 2005).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Recommendations for obese pregnant women	ACOG, 2005	III	Fair	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 28. History of Gastric Bypass/Bariatric Surgery: New

Weeks 10-12

BACKGROUND

The number of obese women of childbearing age undergoing bariatric surgery is increasing, resulting in questions regarding appropriate management of subsequent pregnancies. Pregnancy outcomes after bariatric surgery are consistent with general community outcomes. Nutritional and vitamin deficiencies, specifically iron, vitamin B12, folate and calcium are the most common complications.

RECOMMENDATIONS

- 1. Women with a gastric band should be monitored by their general surgeons during pregnancy because adjustment of the band may be necessary. [C]
- 2. Women who have undergone bariatric surgery should be evaluated for nutritional deficiencies and need for nutritional supplementation where indicated (e.g., Vitamin B12, folate, iron, and calcium). [C]
- 3. Women who experience dumping syndrome should NOT be screened for gestational diabetes with a glucose load but rather with fasting and two-hour postprandial glucose values. [C]

DISCUSSION

Obesity occurs in one in three adult women. A large percentage of bariatric procedures are performed on women of reproductive age (Wax et al., 2007). There are limited data and no randomized studies concerning pregnancy after bariatric surgery. Patients who undergo bariatric surgery are at risk of becoming pregnant unexpectedly after weight loss following surgery. All patients are advised to delay pregnancy for 12 to 18 months after surgery to avoid pregnancy during the rapid weight loss phase.

Pregnancies after bariatric surgery are less likely to be complicated by gestational hypertension, diabetes, macrosomia, and cesarean delivery when compared to pregnancies of obese women (Gurewitsch et al., 1996; Wax et al., 2007). Two prospective studies involving approximately 70 patients after laparoscopic adjustable gastric banding showed it was safe for both mother and newborn (Bar-Zohar et al., 2006) and the outcomes were similar to the general community rather than those of severely obese women (Dixon et al., 2005).

There are three main types of bariatric surgery including malabsorptive procedures (i.e., jejunoileal bypass), restrictive procedures (i.e., gastric banding), and combined procedures. While more common with malabsorptive procedures, nutritional and vitamin deficiencies can occur after bariatric surgery. Bypassing the pyloric portion of the stomach decreases stomach acidity as well as secretion of intrinsic factor. This leads to impaired absorption of vitamin B-12 and iron as well as impaired release of nutrients from food (Gurewitsch et al., 1996).

Dumping syndrome can occur after gastric bypass. These women may not tolerate a glucose load and should be screened for gestational diabetes with fasting and two-hour postprandial glucose values for one week at 24 to 28 weeks gestation (Wax et al., 2007).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Women who have undergone bariatric surgery should be evaluated for nutritional deficiencies and may need vitamin supplementation	Gurewitsch et al., 1996 Wax et al., 2007	II	Poor	С
2	Women with adjustable gastric bands should be monitored by their general surgeons during pregnancy	ACOG, 2005 #315	III	Poor	С
3	Women with dumping syndrome should not undergo diabetes screening with a glucose load	Wax et al., 2007	III	Poor	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 29. Screening for Gonorrhea:

Weeks 10-12

BACKGROUND

The CDC (1998) reports that there are approximately one million new cases of gonorrhea each year, and up to 80 percent of women infected with gonorrhea are asymptomatic. The reported prevalence among pregnant women varies from 0.4 to 7.5 percent. In pregnancy, infection with this organism can be asymptomatic or cause cervicitis, endometritis, or systemic illness. It has also been associated with septic abortion, neonatal ophthalmic infections, and abscesses of Bartholin's or Skene's glands. Maternal infection with gonorrhea has been associated with adverse pregnancy outcomes such as preterm labor, premature rupture of membranes (PROM), and preterm delivery (McGregor et al., 1990).

RECOMMENDATIONS

- 1. Recommend screening for gonorrhea in all pregnant women. [B]
- 2. Pregnant women with positive cultures should be treated with ceftriaxone, per the CDC guidelines. [B]
- 3. Pregnant women with positive screens for gonorrhea should be screened for other sexually transmitted diseases (STDs) and follow local mandatory reporting requirements. [I]
- 4. Recommend performing a test of cure (TOC) during pregnancy after completing antibiotic therapy. TOC in pregnant women, unlike non-pregnant women, is recommended due to risk of complications resulting from persistent or recurrent infections. [I]
- 5. Recommend counseling to decrease rate of reinfection. [C]
- 6. Recommend referring the partner for testing and treatment, as appropriate. [C]
- 7. Infected pregnant women must abstain from intercourse pending TOC. [C]

DISCUSSION

Pelvic inflammatory disease (PID) occurs in 10 to 20 percent of untreated gonococcal infections in women. PID is an important cause of chronic pelvic pain, ectopic pregnancy, and infertility. Early detection and treatment of gonococcal infection in asymptomatic pregnant women offers the potential benefits of preventing future complications of infection. Similarly, early detection and treatment during pregnancy has the potential to reduce morbidity from obstetric complications. Antibiotic treatment effectively reduces the morbidity of untreated gonococcal infections. However, high rates of reinfection emphasize the need for measures to prevent future infection (Vuylsteke et al., 1993).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine gonorrheal screening during pregnancy	CDC, 1998	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ OE = Ouality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 30. Screening for Chlamydia:

Weeks 10-12

BACKGROUND

Chlamydia trachomatis is one of the most common STDs in the United States. It is a leading cause of urethritis, cervicitis, PID, infertility, chronic pelvic pain, and ectopic pregnancy. In pregnancy, it can lead to preterm labor and delivery with resultant complications. Infection rates for neonatal conjunctivitis range between 15 and 25 percent and for neonatal pneumonitis between five and 15 percent. The morbidity and mortality rates for pregnant and nonpregnant women are equal.

RECOMMENDATIONS

- 1. Recommend screening all pregnant women for Chlamydia trachomatis at the initial physical examination. [B]
- 2. Pregnant women with positive cultures should be treated with azithromycin or erythromycin, per the CDC guidelines. [A]
- 3. Pregnant women with positive screens for Chlamydia should be screened for other sexually transmitted diseases (STDs). [I]
- 4. Recommend performing a test of cure (TOC) during pregnancy after completing antibiotic therapy. TOC in pregnant women, unlike nonpregnant women, is recommended due to risk of complications resulting from persistent or recurrent infections. [C]
- 5. Recommend counseling to decrease rate of re-infection. [C]
- 6. Recommend referring partner for testing and treatment, as appropriate. [C]
- 7. Infected pregnant women must abstain from intercourse pending TOC. [C]

DISCUSSION

The CDC reports that there are about four million new cases of Chlamydia each year, and up to 75 percent of women infected with Chlamydia are asymptomatic. The reported prevalence among pregnant women varies from two to 37 percent (Hammerschlag et al., 1979; Leu, 1991).

Chlamydia is the presumed cause of 25 to 50 percent of the 2.5 million pelvic inflammatory disease (PID) cases each year. PID is an important cause of infertility and ectopic pregnancy in American women (Rolfs et al., 1992). Infection during pregnancy increases the risk of postpartum and postabortion endometritis. Each year more than 155,000 infants are born to Chlamydia-infected mothers, with a vertical transmission rate greater than 50 percent (CDC, 1998). Neonatal infection can result in ophthalmic neonatorum and pneumonia (Blackwell et al., 1993). Acute Chlamydia infection has also been implicated as a factor in stillbirth and preterm delivery (Gencay et al., 2000).

Early detection and treatment of Chlamydia infection in asymptomatic pregnant women offers the potential benefits of preventing future complications of infection, as noted above. Early detection and treatment during pregnancy has the potential to reduce morbidity from obstetric complications. Due to ethical considerations about withholding treatment for Chlamydia, the evidence to support such treatment is indirect; antibiotic treatment effectively reduces the morbidity of untreated Chlamydia infections. High rates of reinfection emphasize the need for measures to prevent future infection (Vuylsteke et al., 1993).

High-risk profiles for asymptomatic Chlamydia infection can be devised. A large majority of cases occur in persons under age 25 (CDC, 1998). Demographic and behavioral variables have been associated with higher rates of infection: unmarried, history of STDs, new or multiple sexual partners, early sexual activity, low socio-economic status, and black race. Evidence of cervical ectopy, friability, or erythema as well as mucopurulent discharge on pelvic exam is suggestive of Chlamydia infection (Stergachis et al., 1993).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine screening for Chlamydia trachomatis at initial physical examination	Hammerschlag et al., 1979	II-2	Fair	В
2	Treatment per CDC guidelines for positive cultures	Blackwell et al., 1993	II-2	Fair	A
3	Screening for other STDs, if Chlamydia screen is positive	Vuylsteke et al., 1993	II-2	Fair	В
4	TOC after completion of antibiotic therapy	Working Group Consensus	III	Poor	С
5	Counseling to prevent reinfection	Vuylsteke et al., 1993	II-2	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 31. Screening for and Prevention of Cervical Cancer: Undate Weeks 10-12

BACKGROUND

Pregnant women who are exposed to oncogenic human papilloma virus are at risk for cervical cancer. Screening for cervical cancer usually begins within three years of a woman becoming sexually active or by age 21, whichever comes first. The screening is performed annually with conventional cervical cytology smears or every two years using liquid-based cytology in women with no history of dysplasia. Pregnancy presents an opportunity to detect disease in those women not previously screened, and to initiate preventative measures in those who fit criteria for human papilloma virus (HPV) immunization.

RECOMMENDATIONS

- 1. Women current with routine screening for cervical cancer do not need to undergo additional testing. If the woman will come due for routine screening before the eight week postpartum visit, a screening test should be performed at the first prenatal visit. [B]
- 2. For women who do not receive cervical cancer screening antenatally, screening should be considered at the eight-week postpartum visit to ensure compliance with routine cervical cancer screening guidelines. [B]
- 3. Recommend performing cervical screening in pregnancy with a brush sampler and spatula. [A]
- 4. Recommend women with abnormal cervical cytology during pregnancy be managed based on local algorithms, which may include repeat testing, observation, or colposcopy. [C]

DISCUSSION

Once the number one cancer killer of women, cervical cancer mortality has decreased by over 70 percent since the 1950s, now ranking the 13th most frequently diagnosed cancer among American women (Saslow et al., 2002). This decrease is largely attributed to implementation and widespread use of cervical cytology testing, which can identify dysplasia in the premalignant stage, along with treatment of these early lesions.

The American Cancer Society (ACS) (Saslow, 2002) recommends routine cervical screening for sexually active women between the ages of 21 and 70. Furthermore, ACS recommends cervical screening be performed annually with conventional cervical cytology smears or every two years using liquid-based cytology. Women over age 30 who have had three consecutive, technically satisfactory normal/negative cytology results may be screened every two to three years (unless they have a history of in utero diethylstilbestrol (DES) exposure, are HIV positive, or are immunocompromised by organ transplantation, chemotherapy, or chronic corticosteroid treatment) (Saslow et al., 2002).

The United States Preventative Services Task Force (USPSTF) strongly recommends screening for cervical cancer in women who have been sexually active and have a cervix. Indirect evidence suggests most of the benefit can be obtained by beginning screening within three years of onset of sexual activity or age 21 (whichever comes first) and screening at least every three years (USPSTF, 2003). All pregnant women are included in this population, and recommendations for screening apply during this time in their lives. There is no evidence of an increased incidence of cervical dysplasia during pregnancy that would necessitate more frequent testing (Lurain & Gallop, 1979). This fact, combined with increased rates of false positive cervical cytology in pregnancy, challenges the common practice of uniformly performing cervical smears at the first antenatal visit.

The goal in evaluating abnormal cervical cytology is to rule out the presence of invasive cervical cancer (LaPolla et al., 1988). Colposcopy is safe during pregnancy, but should be performed only by colposcopists experienced in pregnancy exams (Wright et al., 2007).

The use of cytobrush and spatula may cause minimal spotting in pregnancy, but is not associated with any adverse outcomes (Hoffman et al., 1991; Koonings et al., 1992). The endocervical swab is less sensitive than a brush for endocervical sampling and should therefore not be used (Martin-Hirsch et al., 1999).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening cervical smear in pregnancy	Lurain & Galop, 1979	II-2	Good	В
2	Method of cervical smears	Hoffman et al., 1991 Koonings et al., 1992	I	Good	A
3	Management of abnormal cervical smears	Wright et al., 2007	III	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 32. Screening for HSV: New

Weeks 10-12 or onset of symptoms

BACKGROUND

Herpes Simplex Virus (HSV) is one of the most common sexually transmitted infections but it is not a reportable disease so the true incidence is not known. It is estimated that approximately 45 million adolescent and adult Americans are infected with HSV-2 (Fleming et al., 1997). However, HSV-1 can also cause genital disease.

Approximately 10 percent of women who are HSV-2 seronegative have partners who are seropositive and are at risk of transmission during pregnancy (Gardella et al., 2005). Most new infections in pregnancy are asymptomatic (Brown et al., 1997). Approximately 80 percent of infected infants are born to mothers with no reported history of HSV infection (Whitley et al., 1988).

RECOMMENDATIONS

- 1. Routine HSV culture-based screening of pregnant patients is not recommended. [I]
- 2. Symptomatic patients, those who are seropositive, or seronegative patients who have infected partners require further testing and counseling. [B]

Maternal HSV screening has been proposed as a means to decrease neonatal transmission in pregnant patients by identifying asymptomatic patients who are seropositive or seronegative patients who have infected partners. These patients could then be offered suppressive therapy or be counseled regarding ways to decrease transmission during pregnancy.

Several cost effective analyses have been done with variable results. The estimated cost to prevent one case of neonatal herpes ranges from \$200,000 to \$4,000,000 (ACOG, 2007). No evidence of cost effectiveness of screening exists from either clinical trials or cohort studies in pregnancy (ACOG, 2007). Although screening may be beneficial in select couples or populations, ACOG currently does not recommend routine screening for HSV in pregnant women.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine HSV screening of pregnant patients is not recommended	ACOG, 2007	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 33. Counseling for Cystic Fibrosis Screening: Update

Weeks 10-12

BACKGROUND

Cystic fibrosis (CF) is an autosomal recessive genetic condition. More than 1,300 mutations have been identified in the gene for cystic fibrosis, but the severity of disease (the phenotype) resulting from some of these mutations is not well characterized. Screening tests for common mutations are available and can reduce a couple's risk for having a child with cystic fibrosis. The risk of being a carrier depends on an individual's ethnicity and family history.

RECOMMENDATIONS

- 1. Information about cystic fibrosis (CF) should be provided to all couples. [I]
- 2. For couples who desire screening at <18 weeks' gestation, only one partner should initially be screened; if the screening is positive then the other partner should be screened. [I]
- 3. Cystic fibrosis carrier screening should be offered to all couples who desire it. Informed consent should be obtained prior to testing. [I]
- 4. Either sequential (testing one partner first) or concurrent (testing both partners simultaneously) carrier screening for cystic fibrosis is appropriate. The latter option may be preferred if there are time constraints for decisions regarding prenatal diagnostic testing or termination of the affected pregnancy. [I]
- 5. Recommend genetic counseling for individuals with a family history of cystic fibrosis, or for individuals found to be carriers of two cystic fibrosis mutations who have not previously received a diagnosis of cystic fibrosis. [I]

DISCUSSION

The current recommendations regarding counseling and the option of subsequent screening for CF are based on the expert opinions of the American College of Medical Geneticists, ACOG, and the National Institutes of Health (NIH). The sensitivity of the screening test and the carrier risk vary among different ethnic groups. The results often are reported with a table of the residual carrier risk for each ethnic group, and it is the provider's responsibility to interpret the results based on the patient's ethnicity. A negative carrier screening test result can reduce but not eliminate the risk of being a cystic fibrosis carrier. ACOG educational materials explain the relative risks for carrying CF, screening options, and subsequent options, should a couple learn that they carry the CF gene (ACOG, 2005).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Counseling for cystic fibrosis screening	ACOG, 2005	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 34. Management of Depression during Pregnancy: New When diagnosed

BACKGROUND

Untreated maternal depression is associated with various adverse pregnancy outcomes to include premature birth, fetal growth restriction, low-birth-weight infants, increased life stress, decreased social support, poor maternal weight gain, alcohol and drug use, and smoking. Treatment options for pregnant patients with depression may involve pharmacological and/or nonpharmacological options.

RECOMMENDATIONS

- 1. When antenatal depression symptoms are mild to moderate, consider referring patients for non-pharmacological treatment, such as Interpersonal Therapy (IPT). [A]
- 2. When pharmacological treatment of depression is necessary during pregnancy, the potential risks of SSRI exposure during pregnancy should be balanced with the potential risks of untreated depression on the mother and fetus. [B]
- 3. Avoid paroxetine use during pregnancy when possible. Consider fetal echocardiography for women exposed to paroxetine during early pregnancy. [B]
- 4. Choice of medications should be based on the well-characterized reproductive safety profiles of the medication, while also considering the severity of the depressive disorder and the wishes of the pregnant patient. [C]
- 5. Multidisciplinary management of the pregnant patient with depression is recommended to the extent that it is possible. This may involve the patient's obstetrician, behavioral healthcare provider, primary care physician, and pediatrician. [C]

RATIONALE

There are various nonpharmacological treatments for depression during pregnancy, which do not present the same risks as antidepressant medication. Two systematic reviews (Misri & Kendrick, 2007; Bledsoe & Grote 2006) identified several efficacious psychotherapeutic and biologic treatments for major depression. Regarding psychotherapy, Interpersonal Psychotherapy (IPT) has the most empirical support at this time (Adouard et al., 2005; Grote et al., 2004; Spinelli and Endicott, 2003; Spinelli, 1997) and is ideal for patients who are dealing with role transitions into motherhood. Although Cognitive Behavioral Therapy (CBT) has not been researched specifically related to depression during pregnancy, there is a plethora of empirical evidence behind its utility as an efficacious nonpharmacological treatment for Major Depressive Disorder and postpartum depression (Misri et al., 2004). Additional research is needed to further validate CBT as an efficacious treatment for depression during pregnancy. Due to the potential risks associated with pharmacological treatment, and the empirical support behind CBT in general, it may also be considered an appropriate first-line treatment option.

Promising biologic treatments include light therapy (Epperson et al., 2004; Oren et al., 2002), which has been noted as especially useful for women who note depressive symptoms in relationship to seasonal changes. Ryan, Mills & Misri (2005) also cited electroconvulsive therapy (ECT) to be "relatively safe and effective" for treating depression during pregnancy, although research indicates it is most appropriate for treating severe psychosis or suicidality. ECT should not be considered until all other treatment options have been attempted.

The teratogenic effect of SSRI use during pregnancy was most recently examined in two large case-controlled studies, the National Birth Defects Prevention Study and the Slone Epidemiology Center Birth Defects Study. The

National Birth Defects Prevention Study found no significant associations between SSRI use overall and congenital heart defects, but did find an association between SSRI use, particularly paroxetine, during early pregnancy and anencephaly, craniosynostosis, and omphalocele. The absolute risks remained small and associations were found after more than 40 statistical tests were performed. In the Slone Epidemiology Center for Birth Defects Study, SSRI use overall was not associated with craniosynostosis, omphalocele, or heart defects. However, the study found associations between paroxetine and right ventricular outflow defects and between sertraline and omphalocele and atrial and ventricular septum defects. The authors conducted 42 comparisons in their analyses (Louik et al., 2007). In another comparison from the National Birth Defects Prevention Study the authors found no association between the use of SSRIs during early pregnancy and significantly increased risks of congenital heart defects or of most other categories of birth defects (Alwan et al., 2007). GlaxoSmithKline raised concerns about a 1.5 to two-fold increased risk of congenital cardiac malformations, namely atrial and ventricular septal defects, associated with first-trimester paroxetine exposure. This resulted in the manufacturer changing paroxetine's pregnancy FDA category from C to D. Given that the absolute risk of associated malformations remains small, SSRIs in general are not considered to be major teratogens. It is important to note that current literature on the risk of general and specific malformations associated with SSRI exposure during pregnancy is limited and often conflicting. As such, it is strongly recommended that pharmacological treatment of depression during pregnancy be individualized and that providers balance potential risks of SSRI exposure during pregnancy with potential risks of untreated depression on the mother and fetus.

As the only FDA Pregnancy Category D agent with a higher risk of cardiovascular malformation, paroxetine should be avoided in pregnant women. All other SSRIs are FDA Pregnancy Category C agents and generally considered safe in pregnancy. However, SSRIs as a class have been associated with risk of miscarriage, preterm labor, and an increase in persistent pulmonary hypertension in the newborn. The SADHEART (Glassman et al., 2002), ENRICHED, and CREATE (Lespérance et al., 2007) studies indicate that SSRIs are safe medications in cardiac patients.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Interpersonal Psychotherapy (IPT) is an efficacious treatment for depression during pregnancy	Adouard et al., 2005 Bledsoe & Grote, 2006 Grote et al., 2004 Spinelli & Endicott, 2003 Spinelli, 1997	I	Fair	В
2	Light therapy is promising for treating depression during pregnancy, especially when affected by seasonal change	Epperson et al., 2004 Oren et al., 2002	I	Fair	В
3	SSRI use prior to 20 weeks' gestation, with the exception of paroxitine, has not been shown to increase congenital malformations	Einarson & Einarson, 2005	II-2	Fair	В
4	SSRI use is associated with a neonatal withdrawal syndrome	Levinson-Castiel, 2006	II-2	Fair	С
5	SSRI use is associated with an increased rate of persistent pulmonary hypertension	Chambers, 2006	II-2	Fair	В
7	Behavioral therapy has benefit in postpartum depression	AHRQ, 2005	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

BACKGROUND

Prenatal care providers have a significant role in educating women concerning the importance of good oral health during pregnancy. Periodontal disease prevalence among women of reproductive age is estimated at 37 percent to 46 percent and can be as high as 30 percent among pregnant women. In addition, fewer than half of women receive dental care during pregnancy. The prenatal care team can encourage women to maintain a high level of oral hygiene, to visit an oral health professional, and promote the completion of all needed treatment during pregnancy. Instruction on oral health for pregnant women should include expected physiologic changes in the mouth and interventions to prevent threats to their oral health.

Periodontal disease is a bacterial infection characterized by gingivitis (gum inflammation, bleeding, redness, tenderness and sensitivity) and periodontitis. If left untreated, periodontal disease can result in the formation of pockets around teeth caused by the destruction of the attachment of gums to teeth and teeth to the alveolar bone. Eventually it may lead to tooth loss. Periodontal disease is both preventable and curable. Treatment of periodontal disease in pregnant women is safe, and improves periodontal health.

Treatment of periodontal disease during pregnancy and the risk of adverse outcomes to the fetus have been debated in the literature. The most recent research completed does not support a direct relationship between provision of periodontal treatment in pregnancy to reduce adverse outcomes in pregnancy

RECOMMENDATIONS

- 1. Assessment of oral health and instruction on maintaining a high level of oral hygiene should be offered to all pregnant women during their initial prenatal assessment to promote oral health and the general health of the woman. [C]
- 2. Preventative dental treatment is safe and should be provided as early in pregnancy as possible. [B]
- 3. Routine dental care, including x-rays and periodontal therapy, are effective and safe during pregnancy, and should be recommended. [B]
- 4. There is insufficient evidence to recommend the routine treatment of periodontal disease in order to alter the rates of preterm delivery (PTD), low birth weight (LBW) or fetal growth restriction. [I]

DISCUSSION

A systematic review of 29 studies suggests a correlation between periodontal disease and preterm birth (Xiong et al., 2006). The meta-analysis focused on preterm low birth weight, low birth weight, preterm birth, birth weight by gestational age, miscarriage or pregnancy loss, preeclampsia, and gestational diabetes mellitus. Of the chosen studies, 29 suggested an association between periodontal disease and increased risk of adverse pregnancy outcome (odds ratios [ORs] ranging from 1.10 to 20.0) and 15 found no evidence of an association (ORs ranging from 0.78 to 2.54). A meta-analysis of the clinical trials suggested that oral prophylaxis and periodontal treatment may reduce the rate of preterm LBW (pooled risk ratio (RR): 0.53, 95 percent confidence interval [CI]: 0.30-0.95, P < 0.05), but did not significantly reduce the rates of preterm birth (pooled RR: 0.79, 95 percent CI: 0.55-1.11, P > 0.05) or LBW (pooled RR: 0.86, 95 percent CI: 0.58-1.29, P > 0.05).

The New York State Department of Health (2006) published practice guidelines on oral health during pregnancy. This guideline stated that at the first prenatal visit, the prenatal care provider should conduct an assessment to identify women who require immediate oral healthcare and make appropriate referrals. This assessment should include interviewing the patient for problems in the mouth, previous dental visits and access to a dental provider. The American Academy of Periodontology (2004) endorsed preventative oral care services in pregnant women in their policy statement based on scientific literature that has indicated women with periodontal disease may be at risk of delivering preterm, LBW babies.

Periodontal disease is both preventable and curable. Dental services have been found to be safe and effective and improve periodontal disease during pregnancy (Michalowicz et al., 2006). Diagnostic X-rays have been found to be safe during pregnancy when a protective apron with a thyroid collar is used (American Dental Association, 2006).

A large multicenter randomized control trail (Michalowicz et al., 2006) demonstrated that treatment of periodontitis during pregnancy is safe but such treatment does not significantly alter the rates of PTD, LBW or fetal growth restriction. However, birth outcome findings from this study must be interpreted cautiously, in light of the fact that some control subjects who developed severe periodontal disease received periodontal therapy, but were not removed from the control group. Xiong and colleagues (2006) conducted a comparative review of pregnant women and adverse fetal outcomes in pregnant women. They found great variation in periodontal disease definitions, as well as no universally accepted standard for periodontal disease diagnosis among the studies reviewed. They did find a large body of evidence pointing to inconsistent conclusions on the relationship between periodontal disease and pregnancy outcomes, especially in economically disadvantaged women.

Additional multicenter intervention studies are needed to increase the understanding of the relationship between periodontal treatment and pregnancy outcomes.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Provide dental screening and patient teaching on oral health during pregnancy at the first visit	American Academy of Periodontology, 2004 Dasanayake et al., 2008 NY State Dept of Health, 2006	III II-2 III	Fair	С
2	Preventive dental services are safe in pregnant women and should be provided early in pregnancy to prevent oral disease	American Academy of Periodontology, 2004 American Dental Association, 2006 New York State Dept of Health, 2006	II-2	Good	В
3	Routine dental care, including X-rays and periodontal therapy, are effective and safe during pregnancy, and should be recommended	New York State Dept of Health, 2006 American Academy of Periodontology, 2004 American Dental Association, 2006	II-2	Good	В
4	Routine treatment of periodontal disease has not been proven to decrease rates of preterm birth, low birth weight or fetal growth restriction	Michalowicz, et al., 2006 Xiong X, et al., 2006	I II-2	Good	I

 $LE = Level \ of \ Evidence; \ OE = Ouality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 36. Prenatal Screening for Fetal Chromosomal Abnormalities: New Weeks 10-12; 16-20

BACKGROUND

There is a three to five percent chance for a pregnancy to be complicated by a fetal structural or karyotype abnormality. Many of these abnormalities are detectable prior to delivery. Prenatal detection of fetal abnormalities provides an opportunity for preparation and/or intervention that may optimize the desired pregnancy outcome. Normal findings on prenatal tests may also decrease parental anxiety and stress.

Methods of prenatal evaluation broadly fall into screening and diagnostic categories. While screening modalities gather information used to calculate an individualized risk for the pregnancy, the results are not definite. These risks are usually reported both as a ratio of the likelihood that the baby(s) will be abnormal (e.g., 1:300) and more generally as "high risk" or "low risk". High risk is usually defined as being a ratio of more than 1:100 to 1:270

where the cutoff value depends on the specific test selected. Diagnostic testing provides yes or no (i.e., affected or not affected) results.

Screening modalities include measurement of maternal serum analytes, ultrasound evaluation, or a combination of maternal serum analyte and ultrasound evaluation. These modalities can variably be applied in each of the three trimesters of pregnancy but are typically performed in the first and second trimesters. The information obtained from these modalities can be combined to yield a complex array of screening strategies, each with its own inherent strengths and weaknesses including varied accuracy rates.

Multiple screening and testing modalities are now defined and offered but the individual tests/strategies are not uniformly available. Due to the complex nature of the testing strategies, the potential harm of both screening and diagnostic testing, their varied local availability, and their inherent elective nature, it is imperative that detailed counseling be provided to the prospective mother prior to electing or declining a specific testing strategy.

Ultrasound can be diagnostic of certain fetal anomalies but a fetal tissue sample is necessary to diagnose or exclude fetal karyotype abnormalities. Fetal tissue samples are usually obtained by chorionic villus sampling (CVS), amniocentesis, or fetal cord blood sampling (cordocentesis). Each of these methods has limitations and inherent risks of provoking a pregnancy loss. Some large studies have shown amniocentesis to be significantly less likely to cause pregnancy loss than cordocentesis or CVS but the risk of CVS in experienced hands has been reported to be very low in other studies. Amniocentesis is also the most widely available of the diagnostic methods. Chorionic villus sampling provides an earlier result than either amniocentesis or cordocentesis.

RECOMMENDATIONS

- 1. All pregnant women, regardless of age, should be offered a prenatal screening test for the most common clinically significant fetal anomalies as a routine part of prenatal care. [B]
- 2. Women presenting for care at appropriate gestational ages should have aneuploidy screening and diagnostic options available to them that provide first-trimester results as well as strategies that provide second-trimester results. The specific first-trimester screening strategy made available by or in the institution must be decided prior to embarking upon that strategy. [B]
- 3. Initial limited and comprehensive prescreen/pretest counseling methods may include written or multimedia communication, one-on-one, or group counseling formats. Posttest and late entry counseling should be provided in an individualized one-on-one format. [B]
- 4. Screening programs should show respect for the needs and quality of life of the woman and her family. Counseling should be nondirective and should respect a woman's choice to accept or to refuse any or all of the testing or options offered at any point in the process. [I]
- 5. The following modes of prenatal screening/diagnostic testing should be available for women receiving prenatal care in the DoD/VA: [B] (see Appendix E)
 - a. No test at all
 - b. Screening with results in first trimester
 - c. Screening with results in second trimester
 - d. Diagnostic/invasive test in first and second trimester.
- 6. In order to make these screening and diagnostic options available, each institution providing prenatal care should provide locally or arrange for access to: genetic counseling, first- and second-trimester serum marker assessment, first-trimester nuchal translucency (NT) measurement, basic and comprehensive second-trimester ultrasound assessment, first-trimester chorionic villus sampling and second-trimester amniocentesis. [I]
- 7. All women considered high-risk, due to maternal age, personal or family history, or the result of a previous test, should be offered the choice of a first- or second-trimester screening strategy and the choice of first- or second-trimester diagnostic testing including appropriate comprehensive pre- and post-test genetic counseling. [I]
- 8. A comprehensive ultrasound may be offered as a primary or follow-on screening test. [B]

- 9. First-trimester NT should be interpreted for risk assessment only when performed by a trained sonographer who is accredited to provide this service [B] and when offered together with biochemical markers. [A]
- 10. For women who undertake first-trimester screening (FTS), second-trimester serum alpha fetoprotein (AFP) screening and/or ultrasound examination should be offered to screen for open neural tube defects (ONTD). [B]
- 11. Pregnant women with persistent unexplained elevations of maternal serum alphafetoprotein (MSAFP) are at increased risk for adverse perinatal outcome and should receive specialized prenatal care. [B]
- 12. The Quad Marker Screen should be used rather than the Triple Marker Screen when second-trimester serum screening is undertaken. [B]

Common Chromosome Conditions

The most common chromosome conditions associated with advanced maternal age involve the presence of an additional chromosome (21, 18, 13, or X). Of these, trisomy 21, 18, and 13 are associated with congenital anomalies and mental handicap.

Most families who have a child with an open neural tube defect (ONTD), Down syndrome (DS) or trisomy 18 (T18) have no prior family history of the same. The incidence of ONTD varies with racial background and geographical location. While maternal age is the key risk factor for trisomy 21, 18 and 13, more than half of children born with DS are born to women less than 35 years old. Using a maternal age of 35 as a cutoff for offering diagnostic testing will only identify about 40 percent of affected pregnancies (Summers et al., 2003). The incidence of DS approximates one in 700 births regardless of race or geographical location.

Prenatal Screening

Maternal serum analyte screening with multiple serum markers (e.g., alphafetoprotein, human chorionic gonodatropin [HCG], unconjugated estriol and inhibin) has been demonstrated to be a cost-effective means of antenatal screening for several categories of serious fetal structural abnormalities, fetal aneuploidy, and placental abnormalities. Specific structural fetal abnormalities include open neural tube defects (ONTD) (e.g., anencephaly and open spinal defects), ventral wall defects (e.g., omphalocele and gastroschisis), as well as other rare conditions (e.g., skin disorders and congenital nephrosis).

The specific fetal aneuploid conditions commonly detected through maternal serum analyte screening include Down syndrome (trisomy 21) and Edward's Syndrome (trisomy 18). Sex chromosome abnormalities or other aneuploid conditions are less reliably detected.

ONTDs occur in one to two/1,000 live births; 90 to 95 percent of ONTD cases occur in mothers without risk factors such as a positive family history, medical therapy for maternal seizure disorder, or pregestational diabetes mellitus. ONTDs are associated with high rates of perinatal mortality, morbidity, and long-term developmental disability.

Ventral wall defects occur in 0.5 to one infant/1,000 live births and are associated with an increased incidence of associated serious fetal anomalies and aneuploidy, omphalocele, or fetal growth restriction. Both require immediate postnatal surgical treatment for optimal outcome.

The practice of using solely the cut-off of maternal age of 35 or over to identify at-risk pregnancies is inferior to screening tests that consist of maternal serum markers and ultrasound assessment of nuchal translucency (Resta et al., 2005).

Several large, multicenter trials have shown that in the first trimester, a combination of nuchal translucency measurement, serum markers, and maternal age is a very effective screening test for Down syndrome (Malone et al., 2003; Wald et al., 2003; Wapner et al., 2003). First-trimester screening can lead to a diagnosis of fetal aneuploidy much earlier in the pregnancy than second-trimester screening/diagnostic methods. Earlier detection allows the woman and her family to make decisions about continuing the pregnancy in a more private manner (diagnosis can be made before it is evident that the patient is pregnant) (ACOG, 2007; Malone et al., 2005).

Ultrasound has become a valid method to screen for ONTD (Lennon et al., 1999).

The decision whether or not to undergo a screening strategy or diagnostic test should be greatly influenced by whether or not the woman would consider pregnancy termination for an anomalous fetus (ACOG, 2007). Thus, this issue should be addressed when counseling women about screening and diagnostic testing.

Women who would continue a pregnancy regardless of the result of screening or diagnostic testing should be less inclined to undergo screening or diagnostic testing because the results are not likely to provide her with useful information, except the reassurance that comes with a low-risk screening test. Accordingly, the women who would most benefit from a normal/low-risk result are women who started out high-risk e.g. women > 35 years of age (ACOG, 2007; Berkowitz et al., 2006).

Women who would consider pregnancy termination should be more likely to undergo screening testing because they would be more likely to undergo diagnostic testing in the event of an abnormal test (Berkowitz et al., 2006).

Women who want diagnostic testing regardless of the result of screening testing would reasonably skip screening tests and move directly to diagnostic testing. For *a priori* low-risk women, an amniocentesis by an experienced provider would be appropriate (Eddleman et al., 2006). For *a priori* high-risk women, either a CVS or an amniocentesis would be appropriate (Wapner et al., 2003).

Benefit and Harm

To date, there is no clear evidence that data obtained from prenatal aneuploidy screening or testing provides any utility in terms of improving outcome for the fetus. Ultimately, the potential benefit of screening and diagnostic testing is to provide information to the pregnant women and her involved partner/family. Whether or not the test is useful for the pregnant women and her partner/family depends on their perceived benefits of the testing.

Potential benefits of prenatal screening/testing include:

- Peace of mind that comes with a normal test
- The screening test provides more individualized risk numbers that might assist the pregnant woman in deciding whether or not she would choose to undergo diagnostic testing
- A diagnostic test provides a definitive answer regarding the fetal karyotype
- A definitive answer could facilitate decision-making about whether to continue or terminate the pregnancy.

There is potential harm in the screening and diagnostic testing (ACOG, 2007):

- The prevalence in the population for fetal aneuploidy in the second trimester is small, resulting in relatively high false positive screening test results
- The great majority of women who have abnormal screening tests will ultimately deliver normal babies (>95%)
- False positive tests occur in five percent of the overall population and in 20 percent or more of women over 35 years old. False positive tests cause maternal/familial anxiety and unnecessary procedures. The likelihood of having a normal baby when the screening tests are abnormal is approximately 95 percent
- Unnecessary diagnostic tests, in the case of false positive screening testing, can result in complications leading to the delivery of a previable fetus or fetuses resulting in fetal wastage/pregnancy loss (Biggio et al., 2004)
- Ongoing maternal/family anxiety in the case of an abnormal screening test, particularly when the woman declines to undergo diagnostic testing, can have a significant negative impact for the duration of the pregnancy and beyond.

Screening Protocols

Many studies have been published that address screening for fetal chromosomal abnormalities (ACOG, 2007; SOGC, 2007). Studies also suggest that diagnostic testing via karyotype analysis on tissue obtained at the time of chorionic villus sampling (CVS) (Caughey et al., 2006) or amniocentesis is less risky than previously thought when these procedures are performed by experienced providers (Eddleman et al., 2006).

Multiple algorithms have been proposed to standardize screening protocols. These algorithms are exceedingly complex and are not suitable for use by the patient (ACOG, 2007). They include calculations based on variations of first- and second-trimester maternal serum markers and first- and second-trimester fetal ultrasound findings. Each of these screening markers, whether used independently or in combination with other markers, alter the sensitivity and specificity, and hence the overall performance of the tests (see Appendix E: Table E5).

Validity of Tests

Recent data overwhelmingly support the use of the Quad Screen compared to the Triple Screen (ACOG 2007; Wald et al., 1997). The second-trimester Triple Screen should no longer be considered standard of care.

While the Quad Screen is available throughout most of the military and civilian community, newer methods of testing involving the first trimester are less widely available, particularly for those algorithms involving ultrasound (ACOG, 2007). First-trimester screening methods have benefits compared to second-trimester testing, including potentially earlier diagnosis (in those algorithms that disclose to the patient the calculated first-trimester risk), greater sensitivity for the same screen positive rate and greater privacy (diagnosis can be made before it is evident that the patient is pregnant).

A potential increased risk of first-trimester screening is that the diagnostic test (CVS) is less widely available and may pose higher risk of loss than second-trimester testing particularly when performed by less experienced physicians. The attributable risk of CVS overall appears to be controversial but true if comparing standard quoted CVS risk (0.5 to two percent) compared to the recently identified second-trimester amniocentesis risk (0.15 percent) (Alfirevic et al., 2003).

Conclusion

Maternal serum analyte screening should be considered a pure screening modality as there is a relatively high false-positive rate (i.e., five to seven percent of all screened women will have a positive test while more than 95 percent of screen-positive women will have a fetus without a structural abnormality or aneuploidy). However, given the relative low cost and non-invasive nature of maternal serum screening and the serious nature of the fetal abnormalities potentially detected, the current standard of care and respect for patient autonomy results in the recommendation that maternal serum analyte screening should be offered to all pregnant women. Pre-test counseling should emphasize that the decision to undergo screening must be made by the woman after she has considered a number of factors, including personal attitudes and beliefs concerning miscarriage, elective pregnancy termination, birth of a child with a major birth defect or aneuploidy, and the potential anxiety associated with false-positive screening results.

Maternal serum analyte screening should be offered to all pregnant women, but should not be considered a routine, mandatory laboratory test. Pre-test counseling and patient education are required to ensure that women understand the limitations and high false-positive rate, as well as the need for subsequent non-invasive (targeted sonography) and invasive (amniocentesis) testing often used in women with positive screening test results. Routine sonographic examination of low-risk pregnant women improves the accuracy of maternal serum analyte screening as risk estimation is highly dependent upon accurate gestational dating. Women under age 35 at estimated date of confinement (EDC) should be offered invasive testing, generally by amniocentesis, if their screening results yield a risk estimate similar to the mid-gestation risk of a 35-year-old woman (1/270). For women age 35 or older at EDC, maternal serum analyte screening can be chosen instead of direct diagnostic testing by amniocentesis or chorionic villus sampling. Such screening will detect approximately 89 percent of fetuses with Down syndrome in this population with only 25 percent of pregnant women requiring amniocentesis (Haddow et al., 1994).

Elevated MSAFP is predictive for ONTD as well as a variety of other fetal anomalies, including abdominal wall defects and central nervous system malformations. The benefit of detection of ONTD by amniocentesis should be weighed against the risk of fetal loss from the procedure (0.2 to 1.3 percent).

Pregnant women who have persistent serum elevations of alpha-fetoprotein (AFP) in the absence of evidence of fetal abnormalities have been shown to have a two- to three-fold increase in their relative risk for preterm delivery, preterm premature rupture of membranes (PROM), preeclampsia, fetal growth restriction, and intrauterine fetal death. Relative to women with normal AFP levels, unexplained persistent elevations of maternal serum AFP may be indicative of a mild chronic fetomaternal hemorrhage or abnormal decidual-chorionic interface. Thus, women with

at least two values of MSAFP exceeding 2.5 MOM, when corrected for gestational age, should be referred to advanced prenatal care follow-up.

Down syndrome (trisomy 21) occurs in 1/800 births, increasing in risk with advancing maternal age. Eighty percent of babies with Down syndrome are born to women under 35 with no risk factors. Low MSAFP is associated with increased risk for Down syndrome (Haddow et al., 1992). If risk for Down syndrome is calculated solely on age versus AFP, detection increases from 25 to 37 percent. Pregnant women with fetuses affected by trisomy 21 tend to have lower than average levels of MSAFP and unconjugated estriol with elevated levels of serum HCG, when compared to women carrying euploid fetuses. Adding serum HCG and uncongugated estriol ("triple screen") increases detection to 56 to 75 percent without increasing false positivity (Smith-Bindman et al., 2001). Triple screen also increases the antenatal detection rate for a variety of chromosome disorders, particularly sex chromosome abnormalities (Kellner et al., 1995). Ultrasound to assess fetal age is indicated for all women with low MSAFP or abnormal triple screen. It should be followed by amniocentesis for gestational age-adjusted persistent abnormal values. The benefit of increased detection of chromosome abnormalities should be weighed against the risk of fetal loss from amniocentesis.

Edward's Syndrome (trisomy 18) occurs in approximately one in 5,000 live births and is associated with a high rate of fetal death or early neonatal demise. Affected individuals surviving the neonatal period typically have profound neurodevelopmental delay and are unlikely to survive beyond five years of age. Pregnant women with fetuses affected by trisomy 18 tend to have lower than average levels of MSAFP, HCG, and unconjugated estriol. Approximately 50 percent of fetuses with trisomy 18 can be detected with maternal serum analyte screening and follow-up fetal karyotype analysis of screen-positive women.

Customary practice is to offer amniocentesis or chorionic villus sampling to all women age 35 or older at the time of birth, and to women whose risk of Down syndrome by maternal serum analyte screening is equivalent to that of a 35-year-old woman. Data from randomized trials suggest the attributable risk of pregnancy loss due to amniocentesis is less than 1:1500 when performed by experienced clinicians. Accordingly, ACOG has recommended amniocentesis be available to women of all ages regardless of their a priori risk for carrying a fetus with aneuploidy (ACOG, 2007).

For gravidas over 35, maternal serum analyte screening with subsequent confirmatory fetal karyotype analysis of screen-positive women identify up to 89 percent of fetuses with Down syndrome, with a false positive rate of 25 percent. For pregnant women over 35 who are willing to accept a potentially false-negative screen, the quad screen is a cost effective alternative to routine amniocentesis. This alternative practice could make more than 75 percent of amniocenteses unnecessary, thereby also reducing amniocentesis-associated fetal losses (Haddow et al., 1994). The complexity of the pre-screening and pre-testing counseling requires referral of high-risk women to a qualified healthcare provider for counseling. Any pregnant women determined to have a fetus with a serious structural abnormality or fetal aneuploidy should receive advanced prenatal care.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Offer multiple marker maternal serum analyte screening to all pregnant women at gestational ages between 15 and 20 weeks	ACOG, 2007 Haddow et al., 1992 Malone et al., 2005	II-1	Good	В
2	Provide pre-test patient education and counseling	Nadel et al., 1990 Dahl et al., 2006 Davey et al., 2005	II-2	Good	В
3	Women at high-risk for fetal aneuploidy (age =35 at delivery or prior first child or fetus with aneuploidy) require genetic counseling	Haddow et al.,1994	II-1	Good	В
4	Screen-positive women require targeted ultrasound examination for	Smith-Bindman et al., 2001 ACOG, 2007	II-1	Good	В

	risk modification and counseling prior to decision for invasive testing				
5	Women with persistent unexplained elevations of maternal serum AFP are at increased risk for adverse prenatal outcome	ACOG, 2007 SOGC, 2008 Dugoff et al., 2005	I	Good	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

Ultrasound

Ultrasound is commonly used in pregnancy for other indications (see I-37). These ultrasounds are performed for a host of reasons to include earlier detection of severe anomalies, confirmation of dating, general assessment of fetal well-being, and maternal reassurance. It is not possible to completely separate aneuploidy screening from the above when ultrasounds are performed.

Counseling

Multiple factors may influence a woman's decision regarding which, if any, tests to choose. These factors may include: local availability of the testing, cost of the testing, the position of the woman/family regarding whether or not she would continue a pregnancy given an adverse fetal condition and whether or not she would consider the risk of diagnostic testing to be worth gaining this information. In order for a woman to come to an informed decision about which method of testing, if any, to undergo, she must be carefully counseled. Because of the complexity and changing nature of the currently available testing, extensive counseling is required to clarify the nature of the testing and allow appropriate informed consent. Unfortunately, many patients perceive the counseling they were provided as inadequate (Dahl et al., 2005).

Few studies evaluated the relative efficacy of various approaches to genetic counseling. Methods limited to brief counseling alone lead to higher rates of dissatisfaction with care and with testing, and are inadequate for women making decisions about such testing (Dahl et al., 2006; Davey et al., 2005).

Audio-visual counseling was found to be an effective means to educate patients about genetic screening and does not require a trained genetics professional to administer (Fries et al., 2005). In another randomized trial (Hunter et al., 2005) assessing changes in knowledge, decisional conflict, state anxiety, satisfaction, and pregnancy outcomes, all participants showed a significant increase in knowledge and a decrease in decisional conflict post-intervention. While all reported high levels of satisfaction, those in individual counseling were significantly more satisfied than those receiving group counseling or the decision aid. This study has shown unique benefits with each type of intervention such that women and their partners preferred individual genetic counseling, while they learned best in group counseling sessions, and experienced the least decisional conflict regarding genetic testing with a decision aid.

Comprehensive Counseling should include:

- Initial brief counseling/information This counseling/information, ideally provided in the first trimester, seeks to provide summary information and identify women who desire to forgo any screening or diagnostic testing for fetal aneuploidy/anomalies and to provide an opportunity for women to begin to consider screening/testing options.
- Comprehensive prescreen/pretest counseling. This counseling should be comprehensive in nature and should be provided to all women who are considering undertaking a screening strategy or diagnostic testing for fetal aneuploidy/anomalies. Comprehensive counseling should include information regarding the elective nature of the testing, the various available screening strategies, the potential benefits and limitations of screening tests, the potential risks and benefits of diagnostic testing, the locally available diagnostic testing strategies, and the financial and institutional limitations of pregnancy termination in the DoD/VA.
- *Posttest counseling*. This counseling should be provided to all women who have undergone screening or diagnostic testing when the result of the testing is abnormal or "high risk." This posttest counseling should include a discussion of the significance of the result, including its limitations such as the false positive rate and an outline of further options and management strategies for the woman and her family.

Late entry counseling. This counseling should be provided to women presenting for prenatal care when the
gestational age of her pregnancy limits options for screening strategies or diagnostic testing. The
counseling should be based on the individual circumstances including the gestational age and patient
desires.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	All women, regardless of age, should be offered aneuploidy screening	ACOG, 2007	III	Fair	В
2	When discussing options with patients, providers should furnish information on detection and false positive rates, advantages and disadvantages of each testing method	ACOG, 2007	III	Fair	В
3	Unique benefits with each type of intervention: individual counseling, group counseling sessions, and use of decision aids and audiovisual presentation	Hunter et al., 2005 Fries et al., 2005	I	Fair	В
5	First-trimester screening can lead to a diagnosis of fetal aneuploidy much earlier	ACOG, 2007 Malone et al., 2003, 2005 Wapner et al., 2003 Wald et al., 2003	I	Good	A
6	Measurement of nuchal translucency alone is less effective for first-trimester screening than is the combined test (nuchal translucency measurement and biochemical markers)	Nicolaides et al., 2004 Snijders et al., 2002	IIb	Fair	В
7	Patients undergoing first-trimester screening for aneuploidy should be offered maternal serum alpha fetoprotein (MSAFP) in the second trimester to screen for open neural tube defects	Lennon et al., 1999 Nicolaides et al., 1992	II	Fair	В

 $\overline{LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)}$

Visits During Weeks: 16-27

I- 37. Obstetric Ultrasound: Undate Week 16-20

BACKGROUND

Ultrasound is commonly performed for a host of reasons to include earlier detection of severe anomalies, confirmation of dating, general assessment of fetal well-being, and maternal reassurance. It is not possible to completely separate aneuploidy screening from the above when ultrasounds are performed.

Fetal assessment by a comprehensive sonographic survey has been proven to be a useful means of ascertaining fetal health and establishing an accurate gestational age in, pregnant women.

Women with specific risk factors, or who develop high-risk conditions that may complicate the pregnancy, require additional surveillance including ultrasound(s) to assist in decision making.

None-the-less, the routine use of screening ultrasound in low risk women has not been conclusively demonstrated to improve long-term outcome in the offspring of these women. Thus, from a cost effectiveness standpoint, the routine use of screening ultrasound in well-dated pregnancies remains controversial.

A single screening ultrasound examination at 18-20 weeks for all pregnant women who desire the examination after having been counseled regarding the limitations and safety of the exam is supported by ACOG.

ACTION ITEM

Second trimester scanning should be recommended and available to women considering an invasive test on the basis of age, or other risk factors, when the absence of soft markers may lower the estimated risk and assist decision-making.

RECOMMENDATIONS

- 1. Recommend counseling and educating all pregnant women prior to scheduling sonographic studies about the potential benefits, limitations, and safety of prenatal ultrasound. Documentation of education and counseling is recommended; however, written informed consent is not deemed necessary. [C]
- 2. A complete obstetric sonographic examination should be recommended and available to women considering an invasive test on the basis of age, or other risk factors, when a more accurate gestational age is required for decision-making regarding medical or antenatal routine care interventions, or for predicting actual date of delivery [A]
- 3. A complete obstetric sonographic examination should be recommended and available to women or who are at increased risk for a songraphically detectable maternal or fetal abnormality where an intervention may improve the outcome (See table for list of indications) [A].
- 4. There is insufficient evidence to recommend for or against complete obstetric sonographic examination in the second trimester to all low-risk asymptomatic consenting pregnant women [I]
- 5. All complete obstetric sonographic studies should be performed and interpreted by qualified healthcare providers. [A]

(See Standard for Performance of Antepartum Obstetrical Ultrasound Examination at: http://www.aium.org/publications/clinical/obstetric.pdf)

Table 5. Indications for Ultrasonography During Pregnancy

A. Evaluation Of Known Or Suspected Complications Of Pregnancy:

- confirm intrauterine pregnancy
- suspected ectopic pregnancy
- vaginal bleeding
- abdominal and pelvic pain
- maternal pelvic or adnexal masses
- uterine abnormalities
- cervical insufficiency
- suspected amniotic fluid abnormalities
- suspected placental abruption
- premature rupture of membranes
- premature labor
- suspected placenta previa
- suspected hydatidiform mole
- evaluate abdominal / pelvic pain or mass

-

B. Pregnancy Dating:

- uncertain gestational age
- assigned gestational age and clinical size discrepancy
- evaluation of suspected multiples

C. As Component of Screening For Fetal Aneuploidy:

- abnormal biochemical markers
- history of previous congenital anomaly
- to assess findings that may increase or decrease the risk of aneuploidy
- family, environmental or maternal history increasing the risk for fetal anomalies
- to screen for fetal anomalies

D. Evaluation of Fetal Growth and Well Being:

- confirm cardiac activity
- suspected fetal death
- determine fetal presentation
- fetal condition in late registrants for prenatal care
- medical conditions posing high risk of fetal growth abnormalities
- signs of fetal growth abnormality
- follow up of known fetal anomaly

E. As adjunct For Procedures:

- amniocentesis, chorionic villus sampling or fetal surgery
- external cephalic version
- cervical cerclage placement/evaluation
- embryo transfer, or localization and removal of an intrauterine device

RATIONALE

Neither early, late, nor serial ultrasound examination in low risk pregnancy has been proven to improve perinatal morbidity or mortality. Clinical trials show that a single mid-trimester ultrasound examination detects multiple gestations and congenital malformations earlier in pregnancy, but there is currently insufficient evidence that early detection results in improved short term perinatal outcomes.

Routine second-trimester ultrasound can lower the rate of induction for presumed post-term pregnancy, a benefit likely to accrue primarily to women with unreliable dates, among whom ultrasound is more accurate than the unreliable dates for predicting actual date of delivery. It is also unclear whether the likeliest potential benefits of routine second-trimester ultrasound (reduced induction of labor for postterm pregnancy and increased induced abortions for fetal anomalies) would justify widespread testing from a cost effectiveness standpoint.

No benefits of routine ultrasound examination of the fetus in the third trimester have been demonstrated despite multiple randomized controlled trials. Additional trials of third-trimester placental grading are needed to adequately evaluate the potential benefits of screening for placental appearance.

DISCUSSION

One meta-analysis of controlled trials of routine versus selective ultrasound evaluation before 24 weeks' gestation found that routine screening provided better gestational age assessment (with subsequent lower incidence of induction for post-term pregnancy), earlier detection of multiple gestations, and greater detection of unsuspected

fetal abnormalities (with subsequent increased terminations). There were, however, no significant overall differences regarding perinatal morbidity or mortality (LeFevre et al., 1993; Nielson, 2001).

One descriptive systematic review examining women's views about antenatal ultrasound showed that most women were satisfied with ultrasound examinations, but did not include any controlled trials comparing satisfaction in women undergoing routine screening versus no screening (Bricker et al., 2000).

The RADIUS Trial, the largest randomized-controlled trial performed in the United States (Ewigman et al., 1993), showed no benefit to routine ultrasound (a mid-trimester study and a second study in the mid-third trimester) in low-risk pregnant women; however, this trial has been extensively criticized for methodologic problems and the selection of inappropriate outcome variables (Copel et al., 1994). Additionally, there was a high rate of exclusion of eligible participants and a relatively high rate of ultrasound use for "indicated" reasons in the control and excluded patients. Most importantly, the detection rate for serious fetal anomalies in the sonographic studies performed <24 weeks' gestation was only 17 percent, considerably lower than three other large trials which reported detection rates of 51 to 74 percent (ACOG, 1997). Further evaluation of the data (Crane et al., 1994) demonstrated a statistically significant difference in the detection rate of serious anomalies prior to 24 weeks' gestation in women who had their early sonographic study performed in a tertiary care center, compared to those whose studies were performed in a non-tertiary care or private office setting. This suggests that the sensitivity of routine ultrasound to detect fetal anomalies may vary greatly among facilities and providers, but that all efforts should be made to have obstetric sonographic studies performed by experienced and skilled obstetric sonographers and interpreting physicians.

The only large randomized controlled trial (RCT) demonstrating an improvement in perinatal outcome with routine mid-trimester ultrasound was the Helsinki Trial (Saari-Kemppainen et al., 1990), in which the perinatal mortality was 4.2/1,000 live births in the routine ultrasound group compared to 8.4/1,000 in the selective study group (P<.05). This decline in perinatal mortality was largely attributed to the early pregnancy termination of anomalous fetuses.

A Norwegian study demonstrated that routine obstetric sonograms performed between 16 and 20 weeks' gestation reduced the median number of sonographic exams per patient compared to a group of patients receiving only indicated studies (Eik-Nes, 1993).

A follow-up study of children at ages eight to nine delivered to women participating in the Swedish RCT (Waldenstrom et al., 1988) demonstrated no adverse neurologic developmental effects from prenatal ultrasound exposure (Kieler et al., 1998).

There have been no RCTs of routine versus selective mid-trimester ultrasound conducted in a military population. Furthermore, previous RCTs in other populations may not be applicable to current practice patterns in terms of following standardized criteria for the images obtained during routine complete ultrasounds exams, the qualifications of clinicians and physicians interpreting the images, and the use of routine mid-trimester sonography in conjunction with maternal serum analyte screening (Ecker & Frigoletto, 1999).

The American College of Radiology and the American Institute of Ultrasound in Medicine (AIUM), in collaboration with ACOG published a Practice Bulletin on Ultrasound in Pregnancy (ACOG 2009). The following advantages support the ACOG/AIUM statement:

- Evidence that carefully conducted mid-trimester sonograms may decrease the incidence of labor induction and increase the detection of serious fetal anomalies, multiple gestations, and women at risk for placenta previa. The early detection of serious fetal anomalies could potentially improve perinatal outcome in our population, either through patient-based decisions to terminate fetuses with serious or lethal anomalies, or by allowing for appropriate evaluation/counseling/education and possible transfer to appropriate tertiary care of all women choosing to continue their pregnancy who are located in remote areas and receiving care at Level I/II treatment facilities (Bricker & Neilson, 2001).
- Precise gestational dating improves the accuracy of maternal serum analyte screening resulting in fewer false positive tests. Most women who have a positive screening test undergo further counseling and ultrasound assessment. Reducing the false positive risk of maternal serum analyte screening reduces the cost of the additional counseling, associated comprehensive/genetic ultrasound evaluation, and invasive diagnostic testing precipitated by the false positive testing. These false positive tests result in maternal and family member emotional distress. Further, the testing can result in diagnostic testing that can result in the unintended loss of a normal fetus.

- Potential improvement in the emotional/psychological state of the woman and her family.
- Respect for maternal autonomy in the decision-making process for perinatal screening tests.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Counsel and educate prior to scheduling sonographic study	Chervanak & McCullough, 1992 Working Group Consensus ACOG Feb, 2009	III	Fair	С
2	A complete obstetric sonographic examination should be recommended and available to women considering an invasive test on the basis of age, or other risk factors, when a more accurate gestational age is required for decision-making regarding medical or antenatal routine care interventions, or for predicting actual date of delivery	ACOG Feb, 2009 Watson et al., 2007 ACOG, Practice Bulletin #98, 2008 Mongelli et al., 1996 Wilcox et al., 1993	I	Good	A
3	Use ultrasound to evaluate / diagnose women who are at increased risk of sonographically detectable maternal or fetal complications or uncertainty regarding gestational age or fetal health	ACOG 2009	Ш	Good	В
4	Complete obstetric sonographic examination for all consenting low-risk women	Society of Obstetricians and Gynecologists of Canada (SOGC), 1999 ACOG Feb, 2009 Working Group Consensus	III	Poor	I
5	Complete obstetric sonographic studies performed and interpreted by qualified healthcare providers	ACOG Practice Patterns, 1997 Crane et al., 1994 AIUM Guidelines, 2007	I	Good	A

 $LE = Level \ of \ Evidence; \ OE = Ouality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 38. Education about Symptoms of Preterm Labor:

Week-24

BACKGROUND

The majority of women who are admitted for the treatment of preterm labor, often in the advanced stages of labor and delivering within 12 hours of admission, recognized that there was something "different" about their pregnancy for hours or even days prior to seeking medical attention.

True preterm labor is defined as progressive cervical effacement and dilation in the presence of regular uterine contractions at a gestational age of at least 20 weeks, but no more than 37 weeks. A growing body of evidence suggests that progesterone administered to women at high risk for preterm birth significantly prolongs gestation. Additionally, many experts assert that the tocolysis of acute preterm labor allows the administration of antenatal corticosteroids and optimizes neonatal outcome. Thus, in addition to early risk factor assessment for preterm birth (see A-4), comprehensive patient education regarding the symptoms of preterm labor may maximize the opportunity for early evaluation and intervention to prevent delivery.

RECOMMENDATIONS

- 1. Pregnant women should be educated about the most common symptoms of preterm labor:
 - a. Low, dull backache
 - b. Four or more uterine contractions per hour. Uterine contractions may be perceived by the patient as:
 - Menstrual-like cramps
 - Sensation of the "baby rolling up in a ball"
 - Increased uterine activity compared to previous patterns
 - Abdominal cramping (may be associated with diarrhea)
 - c. Increased pelvic pressure (may be associated with thigh cramps)
 - d. Change in vaginal discharge such as change in color of mucus, leaking of clear fluid, spotting or bleeding or discharge associated with itching or fish-like odor immediately after intercourse
 - e. General sensation that "something feels different" (e.g., agitation, flu-like syndrome, and sensation that baby has "dropped").
- 2. A pregnant woman who experiences any of the above symptoms or is unsure about the presence of any of the above, should lie down on her side with one of her hands on her lower abdomen to palpate for uterine contractions for an additional hour. If symptoms persist and/or she palpates four or more uterine contractions in the hour, she should seek immediate medical care. The exception to this is the pregnant woman who notes the presence of vaginal bleeding, leaking of clear fluid from the vagina, or a vaginal discharge with a fish-like odor immediately after intercourse, all of which should prompt immediate medical attention. [I]
- 3. Re-emphasize to the pregnant woman that she is the most important link in the early diagnosis of preterm labor, and that early diagnosis and treatment of preterm labor increases the chances for a healthy infant.
- 4. Educate the pregnant woman that she can safely continue moderate exercise and activity during her pregnancy so long as she does not notice any of the symptoms of preterm labor. The exception to this is that she may notice some increase in uterine cramping with moderate exercise or activity. This is of no consequence so long as the cramping ceases when she stops her activity. She should limit her activity to no more than two hours per session. [B]
- 5. Women with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy. If their work is strenuous or they spend long periods of time on their feet they should limit their work week to 40 hours and workday to eight hours during the last trimester (beginning at 28 weeks) or sooner if they frequently experience symptoms of preterm labor while at work. Pregnant women should attempt to limit periods of time on their feet to three hours. [B]
- 6. There is no evidence that sexual intercourse increases the probability of preterm labor in women with uncomplicated pregnancy. They may experience some uterine contractions following orgasm; however, this is a normal response and she only needs to seek medical attention if they persist at four or more per hour for at least three hours, or if vaginal bleeding or spotting is noted.

DISCUSSION

Providers and their patients should maintain an ongoing dialogue regarding the potential early symptoms of preterm labor as well as the ability of the woman to maintain a normal lifestyle so long as her pregnancy remains uncomplicated.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Educate about the common symptoms of preterm labor	Herron et al., 1982 Katz et al., 1990 Morrison, 1990 Ross et al., 1986	II-2	Good	A
2	Perform intensive self-assessment if unsure about the presence of preterm labors symptoms prior to self-referral	Working Group Consensus	III	Poor	I
3	Educate the pregnant woman that she is a vital link in the early detection and treatment of preterm labor	Herron et al., 1982 Katz et al., 1990	II-2	Good	В
4	A regular, moderate exercise program does not increase the risk for preterm labor	See I-3 "Exercise During Pregnancy"	II-1	Good	В
5	Physically demanding labor/work and prolonged standing increase risk for preterm birth, hypertension, and preeclampsia	AAP/ACOG, 1997 Gabbe & Turner, 1997 Luke et al., 1995 Mozurkewich et al., 2000 Teitelman et al., 1990	II-2	Good	В
6	Coitus is not associated with an increased risk for preterm labor	Read & Klebanoff, 1993	II-2	Good	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 39. Counseling for Trial of Labor: Update

Week 24

BACKGROUND

A trial of labor after previous cesarean delivery has been accepted as a way to reduce the overall cesarean rate. Although vaginal birth after cesarean delivery (VBAC) is appropriate for many women with a prior low-transverse cesarean delivery, several factors increase the likelihood of a failed trial of labor which ultimately leads to increased maternal and perinatal morbidity and mortality. The rate of uterine rupture for women in spontaneous labor after one prior cesarean delivery is approximately 0.5 percent.

Cesarean delivery on maternal request is defined as a cesarean delivery for a singleton pregnancy on maternal request at term in the absence of any medical or obstetric indicators. The overall U.S. cesarean rate rose to 29.1 percent in 2004, and limited evidence suggests that cesarean delivery on maternal request is also increasing for unclear reasons. Cesarean delivery on maternal request should be guided by the best possible information regarding potential health outcomes for both mother and baby.

RECOMMENDATIONS

- 1. Appropriate candidates for a trial of labor include women with one prior low transverse cesarean and no other contraindications to labor or vaginal delivery. Women with two prior low transverse cesareans are candidates provided they have undergone a previous vaginal delivery. [B]
- 2. Women who meet the criteria for a possible trial of labor should be counseled regarding the risks and benefits of VBAC versus repeat low transverse cesarean delivery. Ideally, informed consent should be documented in the antepartum period after 24 weeks, and again at the time of admission for delivery.

3. There is insufficient evidence to recommend for or against cesarean delivery on maternal request. [I]

DISCUSSION

Induction of labor may be necessary for women who desire a trial of labor after cesarean (ACOG, 2006). However, the potentially increased risk of uterine rupture associated with any induction should be discussed with the patient and documented in the medical record (ACOG, 2006). Induction of labor in VBAC candidates should not be considered unless in consultation with an obstetrician/gynecologist (MEDCOM, 40-18). Misoprostol should not be used for induction of labor in women who have had a cesarean delivery or major uterine surgery (ACOG, 2004). There is insufficient data to make recommendations regarding the use or avoidance of misoprostol for pregnancy termination in the first and second trimester (e.g. 19 week intrauterine fetal death). A physician who is independently privileged to monitor and evaluate labor and perform urgent cesarean delivery should be immediately available in the hospital throughout active spontaneous/augmented labor or at the initiation of labor induction (ACOG, 2004). Anesthesia and personnel for urgent cesarean delivery should be available in the hospital throughout active spontaneous/augmented labor or at the initiation (MEDCOM, 40-18). Potential facility constraints and other staffing requirements should be considered before proceeding with trials of labor (MEDCOM, 40-18).

There is currently insufficient evidence to evaluate fully the benefits and risks of cesarean delivery on maternal request as compared to vaginal delivery. Until quality evidence becomes available, any decision to perform a cesarean delivery on maternal request should be carefully individualized and consistent with ethical principles. Given that the risks of abnormal placentation and associated morbidity rise with each cesarean delivery, cesarean delivery on maternal request is not recommended for women desiring several children (NIH Consensus, 2006).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Appropriate candidates for trial of labor	ACOG, 2004	III	Good	В
2	Counseling for trial of labor should be performed twice during pregnancy	ACOG, 2004 Working Group Consensus	III	Poor	I
3	Perform cesarean delivery on maternal request (recommend neither for or against)	AHRQ Evidence Report, 2006 NIH Consensus, 2006	I	Fair Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

Visits during Weeks: 28-37

I- 40. Screening for Gestational Diabetes: Update

Week 28

BACKGROUND

Routine screening of all pregnant women for gestational diabetes mellitus (GDM) should be performed at 24 to 28 weeks' gestation. GDM is defined as marked impairment of glucose metabolism initially identified during pregnancy, and has also been associated with childhood obesity. Pregnant women with GDM are at increased risk for developing fetal macrosomia and requiring operative delivery. Uncontrolled or poorly controlled gestational diabetes may also lead to neonatal morbidity, such as hypoglycemia, polycythemia, and hyperbilirubinemia. Treatment aimed at normalizing glucose metabolism has been shown to reduce these risks. Therefore, any pregnant woman with GDM should have additional surveillance and management beyond the scope outlined in this guideline.

RECOMMENDATIONS

- 1. Recommend screening all pregnant women for GDM at 24 to 28 weeks' gestation. [B]
- 2. Screening for GDM should be performed by randomly administering a 50 gram oral glucose tolerance test (GTT) followed by a blood draw one hour later. Generally accepted threshold values of the 1-hour screen are between 130 mg/dL and 140 mg/dL. Pregnant women who are positive require the diagnostic three-hour GTT. [B]
- 3. In the three-hour GTT a 100-gram glucose load is administered to a woman who has fasted overnight (minimum eight hours). Blood draws are performed fasting and at one, two and three hours after the oral glucose load. No special diet is required before this test. [C]
- 4. Two acceptable sets of threshold values for the three-hour 100-gram GTT can be used to diagnose gestational diabetes: the National Diabetes Data Group (NDDG) criteria and the Carpenter/Coustan conversion criteria. Institutions should adopt one of these two criteria sets based upon their population demographics. There should NOT be variance within the facility itself, though variance may occur between facilities. [B]
- 5. For patients with only one abnormal value, consider one of the following: [C]
 - a. Undergo a repeat three-hour 100-gram glucose challenge test approximately one month following the initial test
 - b. Have dietary management and intermittent postprandial glucose testing performed in a manner similar to women with gestational diabetes.
- 6. Patients with a history of gastric bypass surgery may experience a "dumping" syndrome following ingestion of large quantities of simple sugar. An alternative to the 50-gram glucose tolerance test in these patients includes a fasting and two-hour postprandial finger sticks for one week. Target ranges are 90 mg/dL or lower fasting and 120 mg/dL or lower for postprandial. [C]

DISCUSSION

GDM is defined as marked impairment of glucose metabolism first identified in pregnancy. Incidence is usually quoted as two to three percent, with a range of 0.31 to 37.4 percent noted. There is a higher prevalence in American Indian and Hispanic populations and a very low incidence among Caucasian teens (Garner et al., 1997; Stephenson, 1993). Pregnant women initially presenting for prenatal care with preexisting risk factors may benefit from early screening (at the time of the initial laboratory panel) in addition to the routine 24- to 28-week screen, although the benefit of treating women with GDM identified early in pregnancy has not been scientifically demonstrated. In view of this, there are theoretical benefits to treatment aimed at normalizing glucose metabolism in early pregnancy. Commonly used risk factors prompting screening early in pregnancy are: history of GDM in prior pregnancy, previous delivery of a macrosomic infant (\geq 4,000g), body mass index >28, first degree relative with diabetes, and high-risk ethnic groups (i.e., Native Americans, Hispanics, and Pacific Islanders). Women with an abnormal one-hour screen, but a normal three-hour diagnostic test early in pregnancy, should undergo repeat testing with the three-

hour GTT at 24 to 28 weeks' gestation. Additionally, women with a normal one-hour screen early in pregnancy should also undergo repeat screening with a one-hour 50-gram GTT at 24 to 28 weeks' gestation.

Routine screening should be done with a randomly administered 50-gram oral GTT followed by a blood draw one hour later. Generally accepted threshold values of the one-hour screen used to select the subpopulation of women for the diagnostic three-hour GTT vary between 130 and 140 mg/dL. Using a 130 mg/dL threshold will result in an overall increase in sensitivity for the detection of gestational diabetes, but will result in approximately 25 percent of all screened women requiring a three-hour GTT, while a 140 mg/dL threshold will detect approximately 80 percent of women with GDM with 15 percent of screened women requiring a three-hour GTT. The threshold values for identifying women to undergo the three-hour diagnostic test should be decided after careful review of internal pregnancy outcome information, population demographics and clinic resources. Pregnant women who have a one-hour GTT result \geq 200mg/dL have sufficient glucose impairment to be considered indicative of gestational diabetes without further diagnostic testing by a three-hour GTT and should immediately begin appropriate treatment and monitoring, in lieu of undergoing diagnostic testing with the three-hour GTT.

The growing body of evidence shows that a high-carbohydrate diet before oral GTT is not necessary in normally nourished pregnant women. The preparatory diet has negligible effect on the performance of the GTT, and can potentially delay both the diagnosis and the management of gestational diabetes.

There are two acceptable sets of threshold values for the three-hour 100-gram glucose challenge that can be used to diagnose gestational diabetes. The older criteria defined by the NDDG (1979) defines gestational diabetes if at least two of the four values equal or exceed 105mg/dL for the initial fasting specimen, 190 mg/dL for the specimen obtained at one hour, 165 mg/dL at two hours and 145 mg/dL at three hours for specimens collected after the 100-gram glucose load, respectively. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus has proposed altered values, which are believed to more closely approximate the original Carpenter and Coustan criteria of 95 mg/dL, 180 mg/dL, 155 mg/dL and 140 mg/dL for the fasting, one-, two- and three-hour specimens, respectively (Carpenter & Couston, 1982; NDDG, 1979). There is currently insufficient evidence-based comparison data to recommend one specific criteria set over the other. The lower threshold set is estimated to increase the proportion of a pregnant population diagnosed with gestational diabetes by one to three percent.

Pregnant women with only one abnormal value have been demonstrated to manifest increased risk for macrosomic infants and other morbidities. However, because the relationship between carbohydrate metabolism and fetal macrosomia is a continuum, there is current controversy regarding the optimal management of these women. Reasonable management options include: repeating the three-hour GTT approximately one month later, or initiating dietary modification and glucose monitoring similar to women with established GDM.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Perform a routine screening for GDM at 24 to 28 weeks with a random one-hour 50-gram glucose challenge test	Danilenko-Dixon et al., 1999 Griffin et al., 2000 Williams et al., 1999	II-2	Fair	В
2	Early screening of selected pregnant women with risk factors for GDM	Working Group Consensus	III	Poor	I
3	Method of screening is a random one- hour 50-gram glucose challenge	ACOG, 2001 Naylor et al., 1997	II-1 II-3	Good	В
4	All pregnant women with a one-hour positive test require a three-hour GTT	ACOG, 2001	III	Fair	В
5	Acceptable sets of threshold values for the three-hour 100 gram glucose challenge	ACOG, 2001 ADA, 2002	II-3	Fair	В
6	One abnormal value for a three-hour GTT warrants consideration of dietary management and glucose monitoring, or a repeat three-hour GTT approximately one month after the initial test	ACOG, 2001 Langer et al., 1987 Lindsay et al., 1989	III II-2 II-2	Fair	С
7	A high-carbohydrate diet before oral GTT is not necessary in normally nourished pregnant women	Buhling et al., 2004 Crowe et al., 2000 Entrekin et al., 1998	II-1	Poor	С
8	Patients with history of gastric bypass may not tolerate the 50-gram GTT; alternative is a fasting and two-hour postprandial finger sticks	Burt, 2005	III	Poor	С

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 41. Iron Supplement: Update

Week 28

BACKGROUND

Iron supplementation in pregnancy is commonly practiced and generally expected by women in the United States. This tradition is based on the assumption that women have increased nutritional requirements during pregnancy that cannot be met by diet alone.

RECOMMENDATIONS

- 1. There is insufficient evidence to recommend for or against routinely supplementing iron for all pregnant women. [I]
- 2. Women exhibiting signs or symptoms of anemia at any time during their pregnancy should be evaluated upon presentation. [I]
- 3. Obtain a serum ferritin if iron deficiency anemia is suspected. Recommend supplementing with at least 50 mg elemental iron (325 mg ferrous sulfate) twice a day (bid) in all pregnant women diagnosed with iron deficiency anemia (abnormal ferritin). [B]

DISCUSSION

Published trials confirmed the improvements in hematological status but did not evaluate other clinical outcomes (Milman et al., 1999; O'Brien et al., 1999; Pena-Rosas & Viteri, 2006).

A Cochrane systematic review (Mahomed, 2001) found no evidence to recommend for or against routine iron supplementation. There was a paucity of information related to clinically relevant maternal and infant outcomes (Pena-Rosas & Viteri, 2006).

Another Cochrane systematic review found insufficient data assessing clinical maternal and neonatal effects of iron administration in women with iron deficiency anemia (Reveiz et al., 2007). Again, of concern was a lack of trials with clinically relevant outcomes and paucity of data on adverse effects.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine iron supplementation	Pena-Rosas & Viteri, 2006 Ziaei et al., 2007	II-3 I	Poor	I
2	Selective iron supplementation	Hemminki & Rimpela, 1991 Reveiz et al., 2007	I	Good	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 42. Anti-D Prophylaxis for Rh-Negative Pregnant Women: Update

Week 28

BACKGROUND

The incidence of Rh incompatibility varies by race and ethnicity. Approximately 15 percent of whites are Rh negative, compared with five to eight percent of African Americans, and one to two percent of Asians and Native Americans. Among whites, an Rh negative woman has an approximate 85 percent chance of mating with an Rh positive man, 60 percent of whom are heterozygous and 40 percent of whom are homozygous at the D locus. Pregnant women who have had D antigen isoimmunization in a previous pregnancy have an increased risk for development of fetal anemia and hydrops in future pregnancies. Since the introduction of anti-D (Rhogam) immune globulin injections during and after pregnancy in women who are D-antigen negative, the incidence of isoimmunization has fallen from 10 cases to 1.3 cases/1.000 live births.

RECOMMENDATIONS

- 1. Recommend determination of paternal erythrocyte antigen status for screen-positive women. [I]
- 2. Recommend administering anti-D prophylaxis to all unsensitized D-negative pregnant women. [B]
- 3. Recommend using either 300 mcg of anti-D immunoglobulin at 28 weeks or 100 mcg of anti-D-immunoglobulin at 28 and 34 weeks' gestation. [I]
- 4. Pregnant women who have had isoimmunization in a previous pregnancy or who are screened positive for antibody screen should be referred to a Maternal Fetal Medicine specialist for care. [A]

DISCUSSION

The term "isoimmunization" refers to the detection of maternal antibodies to red blood cell antigens.

All trials of antenatal anti-D prophylaxis included routine postpartum anti-D prophylaxis for women with Rhpositive infants when clinically indicated.

A Cochrane review of two fair-quality RCTs shows a decrease in isoimmunization rates of Rh-negative women after antenatal anti-D prophylaxis, though only at a dose of 100 mcg at 28 and 34 weeks' gestational age (Crowther, 2001).

A qualitative systematic review of randomized and non-randomized studies supports antenatal anti-D prophylaxis with either single dose (300 mcg at 28 weeks) or two-dose (100 mcg at 28 and 34 weeks) regimens of antenatal anti-D prophylaxis to reduce isoimmunization rates (Urbaniak, 1998).

Only two dose regimens have been evaluated by RCTs, and the evidence supporting the two 100-mcg dose regimen is of similar magnitude to the non-randomized evidence supporting the single dose regimens (250 mcg to 300 mcg) (Crowther, 2001).

Administration of anti-D immunoglobulin is recommended for all Rh-negative mothers regardless of paternal blood type, due to the inaccuracy of genotyping individuals.

Recent advances in Doppler technology have led to the development of noninvasive methods to assess the degree of fetal anemia. Studies have reported a good correlation between the peak systolic velocity in the fetal middle cerebral artery and hemoglobin in fetuses that have undergone two previous transfusions, expanding the clinical use of this Doppler test. The recommendation for middle cerebral artery Doppler ultrasonography does have some limitations. There is a higher false-positive rate after 34-35 weeks' gestation. In addition, the measurements must be done by a practitioner specifically trained to perform Doppler for measurement of peak systolic velocity in the fetal middle cerebral artery.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Anti-D prophylaxis for unsensitized D-negative pregnant women	Crowther, 2001 Urbaniak, 1998	I	Fair	В
2	Middle cerebral artery Doppler ultrasonograph for women who demonstrate evidence of isoimmunization or with a history of a prior hydropic infant	ACOG Practice Bulletin #75, 2006	I	Good	A

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 43. Assess for Preterm Labor: Update

Weeks 28, 32

BACKGROUND

The assessment of risk for various adverse perinatal outcomes has become a routine component of prenatal care. One of the principal adverse outcomes that has been subjected to such risk assessment and profiling is preterm labor and subsequent preterm delivery. Preterm delivery, defined as delivery prior to 37 weeks' gestation, occurs in approximately 11 percent of all pregnancies in the United States. Efforts to identify and prevent preterm delivery have been hampered by the lack of an effective preventive method and treatment modalities that are only effective in delaying preterm births for a few days. Early efforts at lowering the preterm delivery rate focused on the use of risk factor profiling. Unfortunately, subsequent analysis of such risk profiles demonstrated that only approximately 50 percent of women who delivered prematurely were identified by the risk profile system. Thus, all pregnant women must be considered at risk for preterm labor until they reach 37 weeks' gestation. This risk spans a wide spectrum and the approach of the practice guideline will be as follows:

- Screen each pregnant woman for clinically substantive risk factors (see A-4)
- Provide patient education regarding early clinical signs and symptoms of preterm labor and appropriate responses (see I-38)
- Inquire about the presence of clinical signs or symptoms of preterm labor at each visit between 24 and 36 weeks' gestation.

RECOMMENDATIONS

- 1. Pregnant women should be educated about the most common symptoms of preterm labor:
 - a. Low, dull backache
 - b. Four or more uterine contractions per hour. Uterine contractions may be perceived by the patient as:
 - Menstrual-like cramps
 - Sensation of the "baby rolling up in a ball"
 - Increased uterine activity compared to previous patterns
 - Abdominal cramping (may be associated with diarrhea)
 - c. Increased pelvic pressure (may be associated with thigh cramps)
 - d. Change in vaginal discharge such as change in color of mucus, leaking of clear fluid, spotting or bleeding or discharge associated with itching or fish-like odor immediately after intercourse.
 - e. Sensation that "something feels different" (e.g., agitation, flu-like syndrome, and sensation that baby has "dropped").
- 2. A pregnant woman who experiences any of the above symptoms or is unsure about the presence of any of the above, should lie down on her side with one of her hands on her lower abdomen to palpate for uterine contractions for an additional hour. If symptoms persist or she palpates four or more uterine contractions in the hour, she should seek immediate medical care. The exception to this is the pregnant woman who notes the presence of vaginal bleeding, leaking of clear fluid from the vagina or a vaginal discharge with a fish-like odor immediately after intercourse, all of which should prompt immediate medical attention.
- 3. If no diagnosis of preterm labor is established, continuation in the guideline is appropriate.

DISCUSSION

While multicomponent efforts aimed at reducing prematurity have had heterogeneous results in prospective trials, there are no obvious harmful effects and such efforts are anticipated to foster a provider-patient relationship and empower the pregnant woman with a positive sense of active promotion of her baby's health.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Educate the pregnant woman that she is a vital link in the early detection and treatment of preterm labor	Herron et al., 1982 Katz et al., 1990	II-2	Good	В
2	Perform intensive self-assessment if unsure about the presence of preterm labor symptoms prior to self-referral	Working Group Consensus	III	Poor	I

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 44. Daily Fetal Movements Counts:

Weeks 28; All following visits

BACKGROUND

Nearly one-half of all fetal deaths occur in pregnancies of low-risk women. Since fetal movement is a sign of fetal well-being, it may be beneficial for all women to learn to assess fetal movement during the third trimester. One hundred percent of fetuses between 30 to 39 weeks' gestation and 98 percent of fetuses 24 to 27 weeks' gestation, move by the 75th minute of observation, so maternal perception of movement should occur within 1½ hours (Patrick

et al., 1982). A decrease in fetal movement may indicate fetal jeopardy and should immediately prompt the pregnant woman to seek further evaluation of fetal well-being.

RECOMMENDATIONS

- 1. Recommend instructing all pregnant women about the importance of assessing fetal movement on a daily basis beginning in the third trimester. [B]
- 2. Recommend instructing all pregnant women as to the course of action they should take if they do not perceive the minimum fetal movement counts within the time frame specific to their healthcare facility. [B]

DISCUSSION

Fetal movement counting is by far the oldest and simplest of all fetal assessment techniques. In Moore and Piacquadio's (1989) study of 2,519 pregnant women, the fetal mortality rate was 8.7/1,000 among women who had no instruction in formal daily fetal movement assessment, and fell to 2.1/1,000 when women: 1) kept a record of how long it took to feel 10 fetal movements, and 2) took prompt action to seek further evaluation of fetal well-being when they did not perceive 10 movements within a two-hour time frame. In contrast, Grant and Hepburn (1984) did not observe significant differences in unexplained fetal death between counting and non-counting groups of women, but did note that there seemed to be a time period of decreased fetal movement prior to actual fetal death. Most data suggest an improvement in perinatal outcomes with the early identification of decreased fetal activity (Moore & Piacquadio, 1989; Neldam, 1980; Pearson & Weaver, 1976; Sadofsky & Yaffe, 1973).

Many methods of counting fetal movements have been proposed. Most research supports the idea that compliance among low-risk pregnant women is highest when the monitoring method is minimally time-consuming and relatively simple (Davis, 1987). The number of fetal movements perceived is arbitrary, though some studies suggest that the perceived lack of fetal movement for two hours or more requires further evaluation (Connors et al., 1988; Moore & Piacquadio, 1989; Wilailak et al., 1992).

Most authorities agree that once a decrease in fetal movement is reported, further and prompt investigation is warranted, usually via external fetal monitoring. It is imperative then, that women are given relevant information to assist them in recognizing warning signs of potential fetal compromise.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Instruct all pregnant women to assess fetal movement on a daily basis beginning in the third trimester	Moore & Piacquadio, 1989 Neldam, 1980	II-2	Good	В
2	Instruct all pregnant women as to the course of action they should take if they do not perceive the minimum fetal movement counts within the time frame specific to their healthcare facility	Moore & Piacquadio, 1989 Neldam, 1980 Pearson & Weaver, 1976 Sadofsky & Yaffe, 1973	II-2	Good	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 45. Counseling for Family Planning:

Week 32

BACKGROUND

Antepartum counseling for family planning allows the pregnant woman and provider ample time for discussion and informed decision-making. The different options for birth control discussed during pregnancy, including permanent sterilization, may enable the woman to consider the pros and cons of each method and choose the one that best fits her lifestyle.

RECOMMENDATIONS

1. Recommend antepartum counseling and educating all pregnant women regarding family planning, to include various temporary contraceptive means and/or permanent sterilization. [C]

DISCUSSION

Family planning counseling and education provided early in pregnancy may allow the couple to discuss the various methods of birth control and make an informed decision. This is opposed to waiting until later in pregnancy when the discomforts of pregnancy may cloud judgment. Involving husbands in antenatal family planning counseling sessions has been shown to lead to joint decision-making and encourage women's use of contraception during the postpartum period (Soliman, 2000). Counseling that accesses a woman's expectations regarding birth control, followed by a careful explanation of the side effects of a contraception choice, may reduce the rate of unplanned pregnancy (Rosenfeld & Everett, 1996). There are many factors that influence the choice of contraception, some of which include maternal age, parity, and medical history.

Women desiring sterilization as their preferred form of birth control should be thoroughly counseled as to the intended permanent nature of this procedure. While sterilization reversal is possible in some cases, it is both a difficult and costly procedure that most insurance companies will not cover (Pati et al., 2000).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Antepartum counseling for family planning	Pati & Cullins, 2000	III	Poor	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 46. Screening for Group B Streptococcus (GBS): Update

Week 36

BACKGROUND

Group B streptococcus (GBS) infections are the leading cause of serious neonatal infections (i.e., sepsis, meningitis, and pneumonia) within the first seven days of life (early-onset infection). A preventive strategy using intrapartum antibiotics for prophylaxis (IAP) in women who have been identified as GBS carriers has been proven to decrease the incidence of early-onset GBS infections of the newborn.

RECOMMENDATIONS

- 1. Recommend screening all pregnant women for Group B streptococcus (GBS) at 35 to 37 weeks' gestation, using a rectovaginal culture and selective broth media to identify colonized women. [B]
- 2. Screening should be repeated every four weeks until delivery. [C]
- 3. Pregnant women with positive rectovaginal cultures should be treated with intrapartum IV chemoprophylaxis with either Penicillin or Ampicillin (if no contraindications) (a). [A]
- 4. Pregnant women who have had a previous child with early-onset GBS infection or have GBS bacteruria in the current pregnancy should receive intrapartum antibiotics, without screening cultures. [A]
- ^(a) Management of the GBS-colonized parturient with a history of an allergic reaction to penicillin agents: due to emerging resistance to previous second-line antimicrobial agents, clindamycin and erythromycin (10 to 15 percent resistant strains in most centers), alternative second-line agents for women with a history of allergic reactions to penicillin or ampicillin are listed below:
 - a. Administer cefazolin 2gm IV load, followed by 1 gm IV every eight hours, for allergic reaction other than immediate hypersensitivity

b. Administer vancomycin 1 gm IV load, followed by 1 gm IV every 12 hours, for immediate hypersensitivity reaction (anaphylaxis, dyspnea, rapid onset of urticarial rash).

DISCUSSION

Based on evidence from a large retrospective cohort study, the CDC released national prevention guidelines in 2002. The guidelines, developed in collaboration with ACOG and AAP, resulted from data showing that routine screening and prophylaxis for GBS carriers prevented more cases of early-onset disease than the obstetrical risk factor-based method.

The guidelines for treatment are listed below, but there is a significant degree of confusion among providers of obstetric care as to how to treat GBS bacteruria and clarification of the literature in this area may prove helpful. Any amount of GBS that shows up in a urine culture during pregnancy should alert the provider to the likelihood of heavy GBS colonization in the woman and warrant IAP without the need for an additional screening culture during the 35-37 week time frame. However, GBS in the urine should be evaluated for treatment at the time of discovery based on the same criteria used to evaluate and treat other cases of ASB or UTI in pregnancy (i.e., antibiotic therapy generally initiated only in the presence of > 100K colonies of a single offending organism or with fewer than 100k colonies in women symptomatic of UTI).

Additionally, there has been intense interest in tests for rapid identification of GBS. These include real-time polymerase chain reaction (PCR), optical immunoassay (OIA), DNA hybridization, colorimetric assay using starch serum media, latex agglutination and enzyme immunoassay. In a large, systematic review published in April 2006, "many of the GBS tests, with the exception of real-time PCR and OIA, took either too long or were not of sufficient accuracy to be feasible for maternal intrapartum testing to aid decision-making concerning antibiotic prophylaxis to prevent neonatal GBS disease" (Honest et al., 2006). They further concluded that "in light of the poor methodologic quality of the existing studies and the imprecision of the evidence for PCR, a robust technology assessment comparing the most promising tests (PCR and OIA) is needed before reaching recommendations for practice." In the event that rapid test technology is eventually implemented, systems will need to be in place for women at high risk of penicillin anaphylaxis to continue to receive late antenatal testing, to allow for sufficient time for GBS susceptibility testing.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Pregnant women should be screened for GBS at 35 to 37 weeks' gestation using a rectovaginal culture and selective broth media to identify colonized women	ACOG, 2002 CDC, 2002 Main, 2000 Main & Slagle, 2000	II-1	Good	В
2	Treat positive rectovaginal cultures with intrapartum IV chemoprophylaxis with either Penicillin or Ampicillin	ACOG, 2002 CDC, 2002 Main, 2000 Main & Slagle, 2000 Smail, 2001	I	Good	A
3	Women who have had a previous child with early-onset GBS infection or GBS bacteruria in the current pregnancy should receive intrapartum antibiotics, without screening cultures	ACOG, 2002 CDC, 2002	II-1	Good	A
4	Pregnant women presenting in labor <37 weeks' gestation should receive intrapartum IV chemoprophylaxis	ACOG, 2002 Boyer, 1986 CDC, 2002	II-1	Good	A
5	For women in labor at term with unknown culture status, administer IAP if the duration of membrane rupture ≥18 hours or maternal temperature ≥100.4°F (38°C)	ACOG, 2002 CDC, 2002	II-1	Fair	В
6	Prophylactic antibiotics should be administered at least two hours prior to delivery, when possible ^(a)	De Cueto et al., 1998 Lin et al., 2001	II-2	Good	В
7	Women undergoing scheduled cesarean delivery prior to the onset of labor with intact membranes do not require prophylactic antibiotics, unless they have had a previous child with early-onset GBS infection	Hagar et al., 2000	III	Fair	С

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

^(a) Management of the parturient anticipated to deliver imminently following admission: as it is difficult to anticipate accurately when a woman will deliver, women identified as candidates for IAP should receive prophylactic antibiotics regardless of the interval between admission and delivery as vertical transmission rates have been shown to have a clinically and statistically significant decrease within two hours of maternal administration. Thus, withholding of IAP from women solely on the basis of anticipated admission-delivery interval should be discouraged.

BACKGROUND

Fetal non-cephalic presentation at term can result in cesarean section delivery. Examination at 36 weeks can identify non-cephalic presentation. External version of the fetus to the vertex position can allow a trial of labor for vaginal delivery. Vaginal delivery is associated with less morbidity and mortality than cesarean section delivery.

RECOMMENDATIONS

- 1. Recommend screening for non-cephalic presentation for all patients at 36 weeks' gestation. [B]
- 2. There is insufficient evidence to recommend for or against Leopolds versus cervical exam as the best screening method to determine fetal presentation. [I]
- 3. Recommend ultrasound for confirmation, if non-cephalic presentation is suspected. [B]
- 4. If non-cephalic presentation is confirmed and there are no contraindications, recommend external cephalic version at 37 weeks or beyond and referral to an advanced prenatal care provider. [B]

DISCUSSION

No systematic reviews or RCTs comparing Leopold's maneuvers to other manipulations were found. Two nonrandomized trials were found that evaluated Leopold's maneuvers as a screening test for fetal malpresentation, but did not assess the effect on maternal morbidity/mortality or infant mortality. The studies were of fair quality and suggest that the specificity for Leopold's to predict fetal malposition is high, but its sensitivity is only modest (Lydon-Rochelle et al., 1993; Thorp et al., 1991).

External cephalic version for breech presentation at term is associated with a significant reduction in non-cephalic births and cesarean sections, without significant effects on perinatal mortality (Hofmeyr & Kulier, 2001b). External cephalic version for breech presentation prior to term does not reduce the number of non-cephalic births nor does it improve pregnancy outcomes (Hofmeyr, 2001). There is no evidence to support the use of postural management for breech presentation (Hofmeyr & Kulier, 2001c). If external cephalic version for breech presentation cannot be accomplished, planned cesarean delivery for term breech decreases perinatal and neonatal death and neonatal morbidity. There is a modest increase in maternal morbidity but no effect on maternal mortality (Hannah et al., 2000; Hofmeyer & Hannah, 2001).

EVIDENCE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Screening for non-cephalic presentation at 36 weeks' gestation	Hofmeyr, 2001a	II-2	Fair	В
2	Leopolds versus cervical exam for determining fetal presentation	Lydon-Rochelle et al., 1993 Thorp et al., 1991	II-2	Fair	I
3	Ultrasound for presentation confirmation	Thorp et al., 1991	II-2	Good	В
4	External cephalic version at 37 weeks or beyond, if there are no contraindications	Hofmeyr & Kulier, 2001a & 2001b	I	Good	В

 $\overline{LE = Level \ of \ Evidence; \ QE = Quality} \ \overline{of \ Evidence; \ SR = Strength} \ of \ Recommendation (See Appendix A)$

Visits During Weeks: 38-41

I- 48. Consider Weekly Cervical Check/stripping (sweeping): Update Weeks 38-41

BACKGROUND

Post-dates pregnancies (over 42 weeks) occur in 10 percent of uncomplicated pregnant women. Post-dates pregnancies have a higher incidence of induction of labor, operative delivery, post-partum hemorrhage and shoulder dystocia. Routine membrane stripping, in low-risk pregnant women with accurate dating criteria, has been proposed as a method of encouraging earlier delivery to prevent post-dates pregnancy.

RECOMMENDATIONS

- 1. Consider offering routine membrane sweeping to all pregnant women every visit beginning at 38 weeks. [C]
- 2. There is insufficient data to encourage or discourage this practice in women known to be GBS-colonized. [I]

DISCUSSION

Membrane sweeping lessens the incidence of post-dates pregnancies and the need for medical inductions (NNT = 8) (Boulvain et al., 2005). A well-done meta-analysis of randomized trials found no harm regarding neonatal morbidity/mortality if women undergo routine weekly "membrane stripping" beginning at 38 weeks' gestation (Boulvain et al., 1999 & 2001, 2005). No "serious maternal morbidity/mortality," increased cesarean-sections, instrumental delivery rates, or maternal infection was found. ACOG (2002) states that the risks of membrane stripping in women colonized with GBS "have not been investigated in well-designed prospective studies. Therefore data are insufficient to encourage or discourage this practice in women known to be GBS-colonized." Membrane sweeping in women who are positive GBS carriers may increase susceptibility to litigation in the event of a GBS-related adverse fetal/neonatal outcome despite the fact that randomized trials found no harm regarding increased neonatal or maternal morbidity/mortality (Cohen & Goldberg, 2006).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Membrane stripping at each visit beginning at 38 weeks	Boulvain et al., 2005	I	Fair	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 49. Term Management: New

Weeks 38-41

BACKGROUND

Intrapartum fetal distress, meconium staining, postmaturity syndrome and primary cesarean section rates all increase after the 40th week of gestation (Devoe, 1983). Pregnancies continuing past the 41st week carry additional risk of oligohydramnios, perinatal morbidity and mortality (Sims & Walther, 1989). The goal of antepartum fetal testing is to prevent adverse fetal and maternal outcomes, to include fetal death. The success of antenatal fetal testing at predicting these outcomes, as well as the appropriate time to initiate antenatal fetal testing, have both been topics of debate in the medical community.

RECOMMENDATIONS

1. In the absence of contraindications, labor induction should be offered to women who reach 41 and 0/7 weeks undelivered. [A]

- 2. In those patients with a favorable cervix (Bishop score > 6), induction after 39 weeks may be considered. [B]
- 3. When labor induction is offered or planned, women should be educated on the risks of induction, including length of induction, discomfort involved, and the process in determining appropriate timing of induction. [B]
- 4. Antepartum fetal testing should begin as soon as possible after 41 and 0/7 weeks if not scheduled for induction at this time. [C]
- 5. Testing should consist of weekly amniotic fluid assessment and twice weekly non-stress testing (NST). [C]
- 6. Inadequate amniotic fluid index should prompt further evaluation to determine the need for delivery. [B]

DISCUSSION

Much debate has arisen concerning the appropriate timing and appropriate use of induction at term. Induction at 41 weeks completed compared with expectant management showed no difference in neonatal outcome. The major studies showed an equal or lower rate of cesarean in those randomized to induction (Heimstad et al., 2008; Sanchez-Ramos et al., 2003).

Induction after 39 weeks in patients with documented favorable cervices has been shown to have increased length of time in Labor and Delivery, but neonatal outcome and mode of delivery showed no difference (Nielsen et al., 2005). In institutions where facilities are limited, the increased length of labor may make that prohibitive. Generally, women are less satisfied with induction over spontaneous labor, more so when inductions take longer than expected or are more uncomfortable than expected (Shetty et al., 2005). Given that inductions of women with favorable cervices take longer to deliver on average than spontaneous labor (Nielsen et al., 2005), involvement of the patient's expectations and education on the process and risks is very important for patient satisfaction.

Additionally, the appropriate timing and usefulness of antenatal testing has been debated. No significant differences in perinatal outcomes or C-section rates were observed between a group who had testing initiated at 40 weeks and a control group with testing initiated at 41 weeks (Rosen et al., 1995). On the other hand, adverse perinatal outcomes have been observed among patients between 41 and 42 weeks' gestation, similar to those seen in patients that are post-term (>42 weeks' gestation) (Guidetti et al., 1989). Based on these data, initiation of antenatal testing is recommended at the beginning of the 41st week.

The majority of studies reviewed used a twice-weekly NST and once weekly amniotic fluid index (AFI) for antenatal surveillance, the regimen recommended by ACOG (1999). There is general agreement that an AFI >5 cm (Rutherford et al., 1987) or a single pocket measuring >2 cm (Chamberlain, 1984) represents adequate amniotic fluid volume. Placental dysfunction with resultant decreased renal perfusion may lead to oligohydramnios (Seeds, 1980), or low amniotic fluid volume. A correlation between fetal acidosis and a non-reactive NST has been observed (Manning et al., 1993), leading to the NSTs use in screening for fetal well-being.

	Recommendations	Sources of Evidence	LE	QE	SR
1	Inducing at 41 weeks reduced C-section	Heimstad et al., 2007 Sanchez-Ramos et al., 2003	I	Good	A
2	Induction after 39 weeks with favorable cervix	Nielsen et al., 2005	I	Fair	В
3	Unrealistic expectations regarding induction length and pain leads to decreased patient satisfaction	Shetty et al., 2005	II-2	Fair	В
4	Antepartum fetal testing beginning at 41 weeks	Guidetti et al., 1989 Rosen et al., 1995	I	Good	A
5	Antepartum testing should consist of weekly AFI and biweekly NST	ACOG, 1999	III	Fair	С
6	Abnormal testing may indicate fetal compromise and should prompt further surveillance or delivery	Chamberlain, 1984 Manning et al., 1993 Rutherford et al., 1987	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 50. Immunization HPV Vaccine: New

Prior to discharge; Postpartum visit

BACKGROUND

Cervical cancer is currently the 13th most frequently diagnosed cancer among American women (Saslow et al, 2002). Over 70 percent of cervical cancers result from infection with high-risk human papilloma virus (HPV) types 16 and 18 (Wright et al., 2007). The U.S. Food and Drug Administration has approved a quadrivalent HPV vaccine for use in women between nine and 26 years of age. This vaccine is given in a series of three injections: an initial injection followed by subsequent injections at two and six months from date of initial injection. Pregnant women are members of the population at risk for cervical cancer due to exposure to oncogenic human papilloma virus. Pregnancy presents an opportunity to initiate preventative measures in those who fit criteria for HPV immunization. For women who do not receive cervical cancer screening antenatally, screening should be considered at the eightweek postpartum visit to ensure compliance with routine cervical cancer screening guidelines.

RECOMMENDATIONS

- 1. Offer vaccination before postpartum discharge to all women ≤ 26 years of age who have not previously completed HPV vaccination series. [B]
- 2. Women who begin their HPV vaccination series in the immediate postpartum period should complete the series with subsequent vaccinations at two months and six months following the first injection in the series. The eight-week postpartum visit provides an opportunity for the second injection. [C]
- 3. Vaccination to protect against HPV in individuals with a history of dysplasia is controversial and the decision to proceed in this situation should be made between a patient and her provider. [I]
- 4. Women who have initiated the HPV vaccine series before becoming pregnant should halt the series during pregnancy, and resume after delivery. [I]
- 5. HPV vaccination may be given to lactating women. [I]

	Recommendations	Sources of Evidence	LE	QE	SR
1	HPV vaccine reduces the incidence of cervical intraepithelial neoplasia and cervical cancer	Brison et al., 2007	II-2	Good	В
2	Report to Congress: Prevention of Genital Human Papillomavirus Infection	Julie Louise Gerberding, M.D., M.P.H. Director Centers for Disease Control and Prevention, January 2004	III	Poor	I

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 51. Education - Shaken Baby Syndrome (SBS): New At discharge; Postpartum visit

BACKGROUND

Shaken Baby Syndrome (SBS) is a preventable cause of injury and death. Thousands of cases occur each year in the United States. Unfortunately, evidenced-based documentation does not exist regarding prevention strategies.

The SBS toolkits are derived from educational components of the National Center on SBS but are customized to military families. The kits were developed in consultation with a steering committee and were tested with several focus groups.

RECOMMENDATIONS

1. All pregnant women and fathers should receive education about Shaken Baby Syndrome prior to discharge from the hospital. [I]

DISCUSSION

Each year in the United States, an estimated 1,200 to 1,400 children are injured or killed by shaking. Approximately 25 percent of victims of shaking die from their injuries while 80 percent of those who survive are left with life-long brain injury. Medical costs for the care of these infants can surpass \$1 million.

The Military Services' reports of child abuse fatalities have demonstrated that of the small number of total fatalities, a majority were under the age of two and a substantial number involved SBS or inflicted traumatic brain injury. In most of the fatalities, the child's father, stepfather, or father surrogate committed the abuse.

Caregivers may resort to shaking a baby out of frustration with the infant's behavior (i.e., inconsolable crying); lack of parenting knowledge or skills and unrealistic expectations about infants' behavior. A comprehensive regional program of parent education was instituted in an eight-county region of western New York and monitored for 5.5 years. The program was administered to parents prior to discharge from the hospital and included information on the dangers of violent shaking and alternative responses. Patients were also asked to sign a commitment statement. The incidence of abusive head injury decreased by 47 percent (Dias et al., 2005).

In April 2007, the DoD in conjunction with the National Center on Shaken Baby Syndrome, launched a Department-wide initiative to prevent SBS. This campaign consisted of three key components: (1) A service provider toolkit containing parenting education curriculum for military fathers, and brochures and other educational resources listing the toll-free Military OneSource phone number for 24-hour support; (2) DVDs with educational messages designed for use with new parents in a variety of settings; and (3) A public service announcements that aired DoD-wide.

A Child Development Educational Approach, "The Period of PURPLE Crying®" program, approaches SBS prevention by helping parents and caregivers understand the frustrating features of crying in normal infants that can lead to shaking or abuse. The program was developed by the National Center on Shaken Baby Syndrome, the Harborview Injury Prevention and Research Center of the University of Washington, and the University of British Columbia. With a grant received from the Doris Duke Charitable Foundation and the George S. and Delores Dore

Eccles Foundation, empirical tests have been completed on a new SBS prevention program. The program was tested through four different types of delivery systems: maternity services, pediatric offices, prenatal classes and nurse home visitor programs. More than 4,800 parents participated in the research and 75 parents participated in focus groups to develop the 10-minute DVD and 11-page booklet. Testing spanned three years of randomized controlled trials and results are expected to be submitted for publication in the coming year.

Available Resources

- Education may be guided using the Shaken Baby Syndrome toolkits from the DoD Family Advocacy Program accessible at: www.militaryhomefront.dod.mil/service/fap/sbs.
- The SBS toolkit materials from the DoD Family Advocacy Program website may be printed and given to new parents (www.militaryhomefront.dod.mil/service/fap/sbs), or the SBS Toolkits can be purchased from the National Center on Shaken Baby Syndrome (www.dontshake.com).
- Consider showing one of the educational DVDs to new parents prior to discharge from the hospital, e.g. "Portrait of Promise," available from Children's Hospital of Minnesota (http://xpedio02.childrensmn.org/stellent/groups/public/@xcp/@web/@forparents/documents/policyre ferenceprocedure/web008431.asp) or "The Period of Purple Crying" from the National Center on Shaken Baby Syndrome (www.dontshake.com).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Use of comprehensive parent education program decreases incidence of abusive head injury	Dias et al., 2005	II	Fair	В
2	SBS prevention kits are customized and validated as tools for military families	DoD SBS Prevention Program National Center on Shaken Baby Syndrome	III	Poor	С

 $LE = Level\ of\ Evidence;\ QE = Quality\ of\ Evidence;\ SR = Strength\ of\ Recommendation\ (See\ Appendix\ A)$

Interventions Not Recommended in Prenatal Care (All Weeks)

I- 52. Routine Screening with Fetal Fibronectin: Update

Not Recommended

BACKGROUND

Fetal fibronectin levels can identify pregnant women at risk for preterm delivery. Routine fetal fibronectin screening of cervical vaginal fluid has been suggested by some experts as a means of reducing preterm delivery among low-risk/asymptomatic pregnancies. However, there is insufficient data to support fetal fibronectin screening in all pregnant women.

RECOMMENDATIONS

- 1. Recommend against routine screening for preterm birth with fetal fibronectin (fFN) test. [D]
- 2. Utilization of fFN testing in symptomatic women between 24 and 34 6/7 weeks' gestation may be useful in guiding management of women with signs and symptoms of preterm labor. [B]

DISCUSSION

In a large meta-analysis, the accuracy for predicting spontaneous preterm birth using the fFN test varied considerably with no significant differences in estimates of accuracy in studies with high/low quality (Honest et al, 2002). Several prospective cohort studies have shown no improvement in outcomes for either mother or baby (Leitech et al., 1999; Ramsey & Andrews, 2003). The routine use of this expensive technology is not justified in light of the low predictive value of either a positive or negative test, along with absence of an effective intervention.

The potential value of fFN testing in the setting of questionable preterm labor is to more precisely discriminate between the subset of women who have true preterm labor versus false labor. A negative test in women with preterm contractions may provide information sufficient to avoid the use of tocolytics and corticosteroids in an individual at low risk for preterm birth (Ramsey & Andrews, 2003).

The following was noted in a memorandum reporting the findings and recommendations of a multidisciplinary and multi-service national Department of Defense (DoD) committee regarding the use of fFN testing as an adjunct to the assessment of suspected preterm labor: the primary benefit [of using the fFN test] is in patients presenting with preterm contractions where [one is] clinically uncertain if the patient will be delivering within one to two weeks. The fFN specimen should only be sent if the result would potentially change the patient's management. It should not be used if it will not alter care (DoD Committee Consensus on Fetal Fibronectin Testing in Pregnancy (2007).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine fetal fibronectin screening at 24 weeks' estimated gestational age (EGA) for prevention of preterm labor (not recommended)	Ramsey & Andrews, 2003 Goldenberg et al., 1996 Honest, 2002 Leitech et al., 1999 Revah et al., 1998 Tekeskin, 2005	I	Good	D
2	Utilization of the fFN test in symptomatic women between 24 and 34 weeks' gestation may be useful in guiding management of women with preterm contractions	ACOG, 2003 Honest, 2002 Tekeskin, 2005	II-2	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 53. Routine Cervical Examination:

Not Recommended

BACKGROUND

Digital cervical examination can identify pregnant women at risk for preterm delivery. Universal screening of cervical dilation and effacement has been suggested as a means of reducing preterm delivery among low-risk/asymptomatic pregnancies. However, there is insufficient data to justify routine digital cervical examination in all pregnant women.

RECOMMENDATIONS

1. Recommend against performing cervical examination to screen for preterm birth prevention in low-risk asymptomatic pregnant women. [D]

DISCUSSION

A large RCT of routine cervical examinations during pregnancy failed to show a statistically or clinically significant difference in rates of low birth weight, delivery at less than 37 weeks' EGA, and preterm premature rupture of membranes between pregnant women randomized to routine cervical examinations versus avoidance of cervical examination (unless clinically indicated) (Buekens et al., 1994). The median number of cervical examinations in the control group was one versus six in the experimental arm of the study.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine cervical examination at 28 weeks' gestation for prevention of preterm labor (not recommended)	Buekens et al., 1994	I	Good	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 54. Routine Antenatal Pelvimetry:

Not Recommended

BACKGROUND

Traditionally, all pregnant women underwent clinical pelvimetry during the course of their pregnancy to detect pelvic diameters that would preclude a trial of labor or place a woman at increased risk of dystocia.

RECOMMENDATIONS

- 1. Recommend against the use of antenatal pelvimetry (clinical or radiographic) in routine prenatal care. [D]
- 2. There is fair evidence that clinical pelvimetry is not effective in predicting the actual occurrence of cephalopelvic disproportion (CPD), and its performance is associated with significant increase in cesarean section rates. [D]

DISCUSSION

Only two randomized trials have evaluated pelvimetry for pregnant women experiencing normal pregnancy. Two additional trials have involved pregnant women with a previous cesarean section. These four trials are summarized in a Cochrane review (Pattinson, 2001). The performance of X-ray pelvimetry may be harmful and is associated with a significant increase in cesarean section rate (odds ratio=2.17) and radiographic exposure to the fetus (Parsons & Spellacy, 1985).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine clinical pelvimetry for estimation of adequacy for trial of labor (not recommended)	Pattinson, 2001	I	Fair	D
2	X-ray pelvimetry may be harmful (not recommended)	Pattinson, 2001	I	Fair	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 55. Routine Urine Dipstick Test:

Not Recommended

BACKGROUND

Random urine dipstick testing for protein and glucose has been traditionally done at each prenatal visit. Concerns have been raised about the efficacy of the urine dipstick in detecting protein elevation that may indicate preeclampsia.

RECOMMENDATIONS

- 1. Recommend against the use of urine dipstick testing for protein and glucose during prenatal visits (the appropriate screening test for gestational diabetes is the one-hour glucola). [D]
- 2. Recommend the use of selective laboratory urinalysis for pregnant women with signs or symptoms of preeclampsia. [B]

DISCUSSION

Glycosuria screening by urine dipstick has poor sensitivity for the detection of gestational diabetes mellitus. In the presence of a routine program of third-trimester one-hour post 50 gm glucose plasma screening for gestational diabetes, urine screening for glycosuria offers no additional benefit. Urine screening could be useful in a setting of no routine plasma screening, but this has not been evaluated (Gribble et al., 1995; Watson, 1990; Hooper, 1996).

Dipstick proteinuria screening is not useful for detecting preeclampsia. The accuracy of dipstick proteinuria assessment compared to 24-hour protein determination is generally poor (Bell et al., 1999; Hooper, 1996). Urine dipstick testing is unreliable in detecting protein elevations that may occur early in the course of preeclampsia (Kuo et al., 1992).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine urine dipstick testing (not recommended)	Kuo et al., 1992	II-2	Fair	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 56. Routine Edema Evaluation:

Not Recommended

BACKGROUND

Routine clinical evaluation of edema has been performed to screen for preeclampsia. Dependent edema (DE) is a common occurrence in normal pregnancies, thus limiting its usefulness as a screening tool for preeclampsia.

According to the NIH consensus, "Edema occurs in too many normal pregnant women to be discriminant and has been abandoned as a marker in this and other classification schemes (for preeclampsia)" (NIH, 2000).

RECOMMENDATIONS

1. Recommend against routine evaluation for edema in pregnancy. [D]

DISCUSSION

No articles were found detailing an RCT of evaluation for edema in pregnancy. Data from the collaborative perinatal project found no significant association between edema and preeclampsia (Friedman & Neff, 1977). No data were found on the effect of screening or treating edema on maternal or neonatal morbidity or mortality or patient satisfaction. There is no evidence that edema is linked to identification of preeclampsia. Edema is not mentioned as a diagnostic criterion for preeclampsia in ACOG Technical Bulletin 219 (1996).

A systematic review (Young & Jewell, 2000) of several interventions for edema showed that rutoside (a flavonoid) improves symptoms associated with edema, but the lack of safety data for this therapy prohibits its recommendation. In addition, intermittent compression and immersion in water both improve some surrogate markers for edema control, but there is no data on their effect in controlling symptoms. One additional RCT (Kent et al., 1999) showed that both static immersion and water aerobics led to a similar diuresis and did not result in as much leg swelling as standing on land. There were two low-quality studies of diuretic therapy for edema, both of which had sufficient methodological flaws as to render their conclusions unusable (Prema et al., 1982; Walker, 1966).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine evaluation for edema in pregnancy (not recommended)	ACOG Technical Bulletin 219, 1996 Kent et al., 1999 Young & Jewell, 2000	II-1	Fair	D

 $LE = Level \ of \ Evidence; \ OE = Ouality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 57. Routine Screening for Cytomegalovirus (CMV):

Not Recommended

BACKGROUND

Cytomegalovirus (CMV) is the most common congenitally acquired infection (0.2 to two percent of all infants) and may result in significant poor perinatal outcome. Some have suggested routine screening for CMV antibody status to identify women at risk for primary CMV infection during pregnancy.

RECOMMENDATIONS

- 1. The evidence is insufficient to recommend for or against routine screening for cytomegalovirus (CMV). [I]
- 2. Recommend counseling pregnant women about methods to prevent acquisition of CMV during pregnancy. [C]

DISCUSSION

Primary CMV infections during pregnancy comprise significant risks for developing fetuses. The principle means of contracting primary CMV is from exposure to young children with CMV infection. Routine serologic screening of pregnant women for CMV has not proven effective in reducing the acquisition of CMV or adverse outcomes. Primary preventive measures should include counseling of pregnant women regarding risk reduction and avoidance of exposure to individuals with active CMV infection. Preconceptual serologic screening for CMV is recommended for day care workers, healthcare providers, and women with multiple sexual partners. Good hand washing and wearing gloves when handling soiled diapers or undergarments would significantly reduce risk for this virus. The appropriate time for counseling and screening for CMV is in the pre-conception period. For background

information refer to the reviews by Henderson and Weiner (1995), Schoub and colleagues (1993), and Trincado and Rawlinson (2001).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine testing of pregnant women for CMV (not recommended)	Working Group Consensus	III	Poor	I
2	Counseling of day care workers on good hand washing	Working Group Consensus	III	Poor	С

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 58. Routine Screening for Parvovirus:

Not Recommended

BACKGROUND

Acute parvovirus B19 infection in pregnancy has been rarely associated with the development of fetal anemia and hydrops. It has been suggested that early detection of this infection may improve fetal outcomes. There is no immunization or treatment for parvovirus B19.

RECOMMENDATIONS

1. Recommend against routine testing for parvovirus in pregnancy. [D]

DISCUSSION

The detection of acute parvovirus infection is based on history, examination, and serologic or DNA-based testing. Women who are identified as having acute parvovirus infection in pregnancy should be referred to a Maternal Fetal Medicine specialist for counseling and follow-up. Routine serologic screening has no role in the prevention of parvovirus and the associated adverse outcomes (Guidozzi et al., 1994).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine testing for parvovirus (not recommended)	Guidozzi et al., 1994	II-3	Fair	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 59. Routine Screening for Toxoplasmosis:

Not Recommended

BACKGROUND

Toxoplasmosis infection has been rarely associated with fetal morbidity and mortality. Common sources for infection include the handling of contaminated meats and cat feces. It has been suggested that early detection and subsequent treatment of this infection may improve fetal outcomes.

RECOMMENDATIONS

1. Recommend against routine testing for toxoplasmosis in pregnancy. [D]

2. Recommend counseling pregnant women about methods to prevent acquisition of toxoplasmosis during pregnancy. [C]

DISCUSSION

Based on the low prevalence of the disease during pregnancy, the uncertain and costly screening, and the possible teratogenicity of treatment, routine serologic screening for toxoplasmosis is not recommended (Frenkel, 1995; Wallon et al., 1999; Wong & Remington, 1994).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine screening for toxoplasmosis (not recommended)	Frenkel, 1995 Wallon et al., 1999 Wong & Remington, 1994	II-3 I II-3	Fair	D
2	Educate about prevention	Working Group Consensus	III	Poor	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 60. Routine Screening for Bacterial Vaginosis: Update

Not Recommended

BACKGROUND

Bacterial vaginosis is found in approximately 10 to 20 percent of normal pregnancies and is a common condition in pregnancy that has been associated with an increased risk for preterm delivery. It has been suggested that screening for bacterial vaginosis may improve fetal outcomes through reduction of preterm labor.

RECOMMENDATIONS

1. Recommend against routine screening for bacterial vaginosis in asymptomatic pregnant women. [D]

DISCUSSION

Three meta-analyses were among the articles reviewed. The meta-analysis by Varma and Gupta tried to obviate the effects of the statistical heterogeneity of prior meta-analyses by separating out low- and high-risk women (Varma & Gupta, 2006). Interestingly, they found that screening and treating bacterial vaginosis in low-risk pregnancies produced a statistically significant reduction in preterm deliveries. However, evidence from numerous other studies showed no improved pregnancy outcomes in asymptomatic, low-risk women screened for bacterial vaginosis. There is a growing amount of data to suggest that pregnant women who are symptomatic or who have a history of prior preterm birth should undergo testing for bacterial vaginosis, and those who test positive for bacterial vaginosis, regardless of gestational age, should be treated. The CDC continues to recommend against treating with clindamycin cream during pregnancy and instead recommends a seven-day course of oral metronidazole or oral clindamycin (CDC 2002). The treatment of asymptomatic bacterial vaginosis in pregnant women does not reduce the occurrence of preterm delivery or other adverse perinatal outcomes (McDonald et al., 2007).

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine screening for bacterial vaginosis (not recommended)	Leitich et al., 2003 McDonald et al., 2007 Riggs et al., 2004 Varma & Gupta, 2006 USPSTF, 2008	I	Good	D

 $\overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 61. Immunization – MMR: (measles/mumps/rubella)

Not Recommended

BACKGROUND

Rubella in the first 16 weeks of pregnancy causes miscarriage, abortion, stillbirth, and Congenital Rubella Syndrome (CRS). The most common manifestations of CRS are hearing loss, developmental delay, growth retardation, and cardiac and ocular defects. Since 1969, when the vaccine was made available in the United States and childhood immunization was initiated, no major periodic rubella epidemics have occurred. Adults accounted for 25 percent of the measles cases reported in 1994 (Baughman et al., 1994). Complications of measles, including pneumonia and encephalitis, are more common among adults than among school-aged children. In 1994, measles was reported in 232 American adults, age 20 or older (Centers for Disease Control, 1994).

RECOMMENDATIONS

1. Recommend against routine measles/mumps/rubella (MMR) immunization during pregnancy. [D]

DISCUSSION

Due to theoretical concerns about possible teratogenicity from administration of an attenuated, live virus vaccine, MMR or measles vaccination is not recommended during pregnancy. Inadvertent administration during pregnancy has never been shown to cause CRS (Krogh et al., 1989). There are no known adverse consequences to vaccination postpartum while breastfeeding.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine administration of MMR during pregnancy (not recommended)	Krogh et al., 1989	II-2	Poor	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 62. Routine Immunization - Varicella:

Not Recommended

BACKGROUND

The CDC recommends that all adults be immunized for varicella, if seronegative. Immunization prevents over 90 percent of varicella infections. Congenital varicella syndrome, while rare, can cause significant neonatal morbidity and mortality. There are theoretical concerns regarding administration of an attenuated virus during pregnancy. These include potential alterations in fetal immunity and inducement of a congenital varicella-like syndrome in the fetus.

RECOMMENDATIONS

- 1. Recommend against routine varicella vaccination in pregnancy. [D]
- 2. Recommend serological testing early in pregnancy for all pregnant women with a negative or uncertain history. [B]
- 3. Recommend offering vaccination postpartum to pregnant women who are non-immune. [B]

DISCUSSION

Four cohort studies were identified. Among U.S. women of childbearing age, the mean incidence of varicella is 2.16/1,000/year. After household exposure, approximately 90 percent of susceptible contacts will develop varicella. Varicella is an uncommon infection during pregnancy; its incidence is estimated at 1/7,500 based on eight cases occurring in 60,000 pregnancies prospectively studied. Maternal infection in the first half of the pregnancy has been associated with congenital varicella syndrome. Varicella infections at any time during pregnancy may result in maternal pneumonia and, rarely, death (Enders et al., 1994; Jones et al., 1994; Pastuszak et al., 1994; Smith et al., 1998).

Among adults with a negative or uncertain history of varicella, approximately 85 to 90 percent will be immune. Generally it is felt that if a woman has a positive history of varicella infection, she should be considered immune. Women with a negative or uncertain history of varicella infection should have their titers checked before receiving the immunization because of the high rate of seropositivity in those individuals. One study demonstrates that this approach is cost-effective (Smith et al., 1998).

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine varicella vaccination in pregnancy (not recommended)	Smith et al., 1998	II-2	Poor	D
2	Serological testing early in pregnancy for pregnant women with a negative or uncertain history	Smith et al., 1998	II-2	Poor	В
3	Postpartum varicella immunization	ACOG Guideline for Perinatal Care, 1998	III	Fair	В

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 63. Routine Ultrasound Evaluation of Cervical Length: Undate Not Recommended

BACKGROUND

Preterm delivery remains one of the principal causes of adverse perinatal outcomes. Multiple interventions to identify pregnant women at risk for preterm delivery have been studied in the recent past. It has been determined that cervical length, as measured by transvaginal sonography, correlates with the incidence of preterm delivery. Observational studies have found a linear relationship between cervical length and the rate of preterm delivery as well as the gestational age of delivery. This finding has prompted questions regarding the usefulness of routine screening of cervical length in pregnant women.

RECOMMENDATIONS

1. Recommend against *routine* cervical length screening at 24 weeks' gestation. [D]

DISCUSSION

Several studies have shown that pregnant women with short cervices detected via routine second-trimester transvaginal ultrasound screening have a greater risk of preterm delivery than do pregnant women without short cervices. The predictive value varies depending on the study population and cervical length cut-off, but in general, short cervical lengths are quite specific, but not sensitive, at predicting preterm delivery. Therefore, a negative finding does not substantially decrease a pregnant woman's risk of preterm delivery, whereas a positive finding does increase the risk. In a routine, low-risk population, one-half of pregnant women with the shortest cervical lengths (<15mm) may deliver preterm. Less than two percent of pregnant women in a low-risk population will have cervical lengths of this size (Heath et al., 2000; Heath et al., 1998; Hibbard et al., 2000; Iams et al., 1996). At the time these studies were conducted, there was no established therapy to prevent preterm delivery in low- or high-risk women. (See prescription of progesterone A-4.)

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine cervical length screening at 24 weeks' gestation (not recommended)	Doyle & Monga, 2004 Grimes-Dennis & Berghella, 2007 Heath et al., 2000 Hibbard et al., 1998 & 2000 Honest et al., 2003 Iams, 2001 Iams et al., 1996 Taipale & Hiilesmaa, 1998 Williams & Iams, 2004	II-2	Fair	D

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 64. Repeat Screening for Anemia, Syphilis, and Isoimmunization: Not Recommended

BACKGROUND

Traditional maternal care often requires repeat testing of all women for anemia, syphilis, and anti-D and non-anti-D antigen antibody development in the mother at 24 to 28 weeks' gestation. This testing was done to identify correctable causes of potential morbidity and mortality in the mother and fetus. Pregnant women with anemia may respond to vitamin and iron supplementation and those with syphilis can be treated with antibiotics. The unborn fetus with D isoimmunization may be helped by in utero transfusion or early delivery.

RECOMMENDATIONS

- 1. Recommend against routine repeat screening for blood group antibodies. [D]
- 2. Recommend against routine repeat screening for anemia and syphilis. [D]
- 3. Recommend providers consider repeat testing for anemia or syphilis at 24 to 28 weeks for women who are at higher risk for these conditions. [C]

DISCUSSION

Repeat screening for anemia, syphilis, and antibody development has been commonly practiced. Little evidence was found to support the routine use of these tests in low-risk pregnant women. One cohort study determined repeat testing of Rh-positive women for anti-D antibody was not necessary (Davis & Abbott, 1986).

Pregnant women who may be at risk for development of anemia secondary to restrictive diets (e.g., vegan diet) or those who had anemia (hematocrit less than 30) at their initial visit warrant retesting during their pregnancy. The

optimal timing or interval of this testing is not known, though this has traditionally been performed at 24 to 28 weeks.

Pregnant women at risk for sexually transmitted disease through high-risk sexual behavior may benefit from repeat testing. However, no data exists to support improved outcomes for mothers or infants in those who are screened.

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Repeat antibody screening (not recommended)	Davis & Abbott, 1986	II-2	Fair	D
2	Repeat anemia and syphilis screening (not recommended)	Working Group Consensus	III	Poor	D
3	Repeat anemia and syphilis screening for high-risk pregnant women	Working Group Consensus	III	Poor	С

 $LE = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

I- 65. Routine Screening for Hypothyroidism:

Not Recommended

BACKGROUND

Recent publications have drawn attention to the role of thyroid hormone status of the mother on the future neuropsychological development of the child. Screening all pregnant women for thyroid hormone status has been suggested. To date, however, there are no evidence-based studies to provide meaningful and clinically relevant data to guide the practitioner.

RECOMMENDATIONS

- 1. Recommend against routine screening for thyroid hormone status of the mother. [D]
- 2. Recommend ensuring adequate iodine intake during pregnancy for pregnant women in areas of the country with questionable levels of dietary iodine. [C]

DISCUSSION

First-trimester hypothyroxinemia (a low for gestational age circulating maternal free T4, whether or not thyroid stimulating hormone [TSH] is increased) may pose an increased risk for poor neuropsychological development of the fetus. This would be a consequence of decreased availability of maternal T4 to the developing brain, its only source of thyroid hormone during the first trimester. The mother is the sole source of thyroid hormones until about 12 weeks' gestation, when the fetal gland becomes active. Also, in pregnancy normal TSH may occur when free T4 levels are low (normal maternal T3 concentrations may prevent an increase in TSH). Hypothyroidism or subclinical hypothyroidism during pregnancy often stems from autoimmune disease (Hashimoto's) but may result from mild iodine deficiency. The presence of thyroid antibodies with a normal TSH may predict those pregnant women who are likely to progress to frank hypothyroidism, which may necessitate closer monitoring of the mother.

The question of relevance is whether low maternal free T4 levels, which are still within the range generally accepted as having no adverse effects for the mother, might interfere with normal neurodevelopment of the offspring. Additionally, when subclinical hypothyroidism or evidence of possible autoimmune thyroid disease (i.e., high anti – thyroid peroxidase antibodies) is present, the clinical relevance of this on maternal pregnancy and outcome is currently unclear.

There is insufficient evidence that screening and early treatment of pregnant women with subclinical hypothyroidism or maternal hypothyroxinemia improves subsequent neonatal outcome. Routine screening, therefore, cannot be recommended at this time.

Interventions Page - 108

EVIDENCE TABLE

	Recommendations	Sources of Evidence	LE	QE	SR
1	Routine Screening for thyroid deficiency (not recommended)	Escobar et al., 2000 Haddow et al., 1999 Pop et al., 1995	III	Poor	D
2	Adequacy of nutritional iodine	Utiger, 1999	III	Poor	С

 $[\]overline{LE} = Level \ of \ Evidence; \ QE = Quality \ of \ Evidence; \ SR = Strength \ of \ Recommendation \ (See \ Appendix \ A)$

Interventions Page - 109

APPENDICES

Appendix A: Guideline Development Process

Appendix B: Screening Items for Self-Administered Questionnaire – First Visit

Appendix C: Hemoglobinopathies

Appendix D: Risk Factors - Preterm Birth

Appendix E: Prenatal Screening for Fetal Chromosomal Abnormalities

Appendix F: Questions for Literature Search

Appendix G: Acronym List

Appendix H: Participant List

Appendix F: Bibliography

APPENDIX A Guideline Development Process

The development update of the VA/DoD Clinical Practice Guideline for Pregnancy Management followed the steps described in "Guideline for Guidelines," an internal working document of the VA/DoD Evidence-Based Practice Working Group that requires an ongoing review of the work in progress. The Working Group of the VA/DoD was charged with updating the evidence-based action recommendations whenever possible.

The Offices of Quality and Performance and Patient Care Services, in collaboration with the network Clinical Managers, the Deputy Assistant Under Secretary for Health, and the Medical Command of the DoD identified clinical leaders to champion the guideline development process. During a preplanning conference call, the clinical leaders defined the scope of the guideline and identified a group of clinical experts from the VA and DoD that formed the Pregnancy Management Working Group. Working Group members included representatives of the following specialties: family practice, OB/GYN (Prenatal Care), nursing, midwifery, genetic counseling, psychology/psychiatry (mental health), maternal fetal medicine specialist, and pharmacy.

The Working Group defined a set of clinical questions within the area of the guideline. This ensured that the guideline development work outside the meeting focused on issues that practitioners considered important and produced criteria for the search and the protocol for systematic review and, where appropriate, meta-analysis.

The Working Group participated in an initial face-to-face meeting to reach consensus about the guideline algorithm and recommendations, and to prepare a draft update document. The draft continued to be revised by the Working Group at-large through numerous conference calls and individual contributions to the document. Following the initial effort, an editorial panel of the Working Group convened to further edit the draft document. Recommendations for the performance or inclusion of specific procedures or services were derived through a rigorous methodological approach that included the following:

- Determining appropriate criteria, such as effectiveness, efficacy, population benefit, or patient satisfaction
- Reviewing literature to determine the strength of the evidence in relation to these criteria
- Formulating the recommendations and grading the level of evidence supporting the recommendation
- Integrating the feedback of the experts from the VA and DoD following their review of the final draft document.

This update of the UCP Guideline is the product of many months of diligent effort and consensus building among knowledgeable individuals from the VA, DoD, academia, as well as guideline facilitators from the private sector. An experienced moderator facilitated the multidisciplinary Working Group. The list of participants is included in Appendix H.

Formulation of Questions

The Working Group developed researchable questions and associated key terms after orientation to the scope of the guideline and to goals that had been identified by the Working Group. The questions specified (adapted from the Evidence-Based Medicine toolbox, Center for Evidence-Based Medicine, [http://www.cebm.net]):

- Population Characteristics of the target patient population
- Intervention Exposure, diagnostic, or prognosis
- Comparison Intervention, exposure, or control used for comparison
- Outcome Outcomes of interest.

These specifications served as the preliminary criteria for selecting studies. Literature searches were conducted on all topics identified in the algorithm or recommendations of the original guidelines. After reviewing the initial search for systematic reviews and meta-analyses, the Working Group decided to focus the search for individual randomized controlled trials (RCTs) on specific interventions specified in a list of questions. (for list of the questions see Appendix F).

Selection of Evidence

The evidence selection was designed to identify the best available evidence to address each key question and ensure maximum coverage of studies at the top of the hierarchy of study types. Published, peer-reviewed RCTs, as well as meta-analyses and systematic reviews that included randomized controlled studies were considered to constitute the strongest level of evidence in support of guideline recommendations. This decision was based on the judgment that RCTs provide the clearest, scientifically sound basis for judging comparative efficacy. The Working Group made this decision recognizing the limitations of RCTs, particularly considerations of generalizability with respect to patient selection and treatment quality. When available, the search sought out critical appraisals already performed by others that described explicit criteria for deciding what evidence was selected and how it was determined to be valid. The sources that have already undergone rigorous critical appraisal include Cochrane Reviews, Best Evidence, Technology Assessment, and AHRQ systematic evidence reports.

In addition to Medline/PubMed, the following databases were searched: Database of Abstracts of Reviews of Effectiveness (DARE) and Cochrane Central Register of Controlled Trials. For Medline/PubMed searches, limits were set for language (English), and type of research (RCT, systematic reviews and meta-analysis).

As a result of the literature reviews, articles were identified for possible inclusion. These articles formed the basis for formulating the guideline recommendations. The following inclusion criteria were used for studies:

- English language only of studies performed in United States, United Kingdom, Europe, Australia, Japan, New Zealand
- Full articles only
- Study populations limited to adults age 17 years or above; all races, ethnicities, cultural groups
- Randomized controlled trials or prospective studies
- Published from 2002 to December 2007.

Seed Guidelines

- VA/DoD Clinical Practice Guideline for the Management of Uncomplicated Pregnancy (2001).
- Institute for Clinical Systems Improvement (ICSI) Health Care Guideline: Routine Prenatal Care, July 2000.
- Guide to Clinical Preventive Services (CPS) Second Edition, Report of the U.S. Preventive Services Task Force, 1996.
- National Institute for Health and Clinical Excellence Clinical Guidelines (UK), 2003. American College of Obstetricians and Gynecologists (ACOG) technical bulletins and guidelines as a respected source for expert opinion.

Admissible evidence (study design and other criteria):

- Original research studies that provide sufficient detail regarding methods and results to enable
 use and adjustment of the data and results.
- Randomized controlled trials (RCTs); systematic reviews (including EPC and HTA reviews); and meta-analyses.
- Relevant outcomes must be able to be abstracted from data presented in the articles.
- Sample sizes must be appropriate for the study question addressed in the paper. RCTs were
 included if they were initiated with 30 or more participants.

Preparation of Evidence Tables (Reports) and Evidence Rating

The results of the search were organized and evidence reports as well as copies of the original studies were provided to the Working Group for further analysis. Each study was appraised by a group of research analysts for scientific merit, clinical relevance, and applicability to the populations served by the Federal healthcare system. The body of evidence was rated for quality and level of evidence.

Recommendation and Overall Quality Rating

Evidence-based practice involves integrating clinical expertise with the best available clinical evidence derived from systematic research. The Working Group received an orientation and tutorial on the evidence United States Preventative Services Task Force (USPSTF) 2001 rating process, reviewed the evidence and independently formulated Quality of Evidence ratings (see Table A-1), a rating of Overall Quality (see Table A-2), and a Strength of Recommendation (see Table A-3).

	Table A-1: Quality of Evidence (QE)			
I	At least one properly done RCT			
II-1	Well-designed controlled trial without randomization			
II-2	Well-designed cohort or case-control analytic study, preferably from more than one source			
II-3	Multiple time series evidence with/without intervention, dramatic results of uncontrolled experiment			
III	Opinion of respected authorities, descriptive studies, case reports, and expert committees			

	Table A-2: Overall Quality		
Good High-grade evidence (I or II-1) directly linked to health outcome			
Fair	High-grade evidence (I or II-1) linked to intermediate outcome; or Moderate-grade evidence (II-2 or II-3) directly linked to health outcome		
Poor	Level III evidence or no linkage of evidence to health outcome		

	Table A-3: Net Effect of the Intervention				
Substantial	More than a small relative impact on a frequent condition with a substantial burden of suffering; or A large impact on an infrequent condition with a significant impact on the individual patient level.				
Moderate	A small relative impact on a frequent condition with a substantial burden of suffering; or A moderate impact on an infrequent condition with a significant impact on the individual patient level.				
Small	A negligible relative impact on a frequent condition with a substantial burden of suffering; or A small impact on an infrequent condition with a significant impact on the individual patient level.				
Zero or Negative	Negative impact on patients; or No relative impact on either a frequent condition with a substantial burden of suffering; or an infrequent condition with a significant impact on the individual patient level.				

Table A-4: Final Grade of Recommendation					
	The net benefit of the intervention				
Quality of Evidence	Substantial	Moderate	Small	Zero or Negative	
Good	A	В	С	D	
Fair	В	В	С	D	
Poor	I	I	I	I	

Strength of Recommendations Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients.
	Good evidence was found that the intervention improves important health outcomes and
	concludes that benefits substantially outweigh harm.
В	A recommendation that clinicians provide (the service) to eligible patients.
	At least fair evidence was found that the intervention improves health outcomes and
	concludes that benefits outweigh harm.
С	No recommendation for or against the routine provision of the intervention is made.
	At least fair evidence was found that the intervention can improve health outcomes, but
	concludes that the balance of benefits and harms is too close to justify a general
	recommendation.
D	Recommendation is made against routinely providing the intervention to asymptomatic
	patients.
	At least fair evidence was found that the intervention is ineffective or that harms outweigh
	benefits.
I	The conclusion is that the evidence is insufficient to recommend for or against routinely
	providing the intervention.
	Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the
	balance of benefits and harms cannot be determined.

Lack of Evidence - Consensus of Experts

Where existing literature was ambiguous or conflicting, or where scientific data were lacking on an issue, recommendations were based on the clinical experience of the Working Group.

Algorithm Format

The goal in developing the guideline for management of UCP was to incorporate the information into a format which would maximally facilitate clinical decision-making. The use of the algorithm format was chosen in light of the evidence that such a format improves data collection, diagnostic and therapeutic decision-making and changes patterns of resource use. However, few guidelines are published in such a format.

The algorithmic format allows the provider to follow a linear approach to critical information needed at the major decision points in the clinical process, and includes:

- An ordered sequence of steps of care
- Recommended observations
- Decisions to be considered
- Actions to be taken

A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm (Society for Medical Decision-Making Committee, 1992). Arrows connect the numbered boxes indicating the order in which the steps should be followed.

Rounded rectangles represent a clinical state or condition.
Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No. A horizontal arrow points to the next step if the answer is YES. A vertical arrow continues to the next step for a negative answer.
Rectangles represent an action in the process of care.
Ovals represent a link to another section within the guideline.

A letter within a box of an algorithm refers the reader to the corresponding annotation. The annotations elaborate on the recommendations and statements that are found within each box of the algorithm. Included in the annotations are brief discussions that provide the underlying rationale and specific evidence tables. Annotations indicate whether each recommendation is based on scientific data or expert opinion. A complete bibliography is included in the guideline.

REFERENCES

Agency for Health Care Policy and Research (AHCPR). Manual for conducting systematic review. Draft. August 1996. Prepared by Steven H. Woolf.

Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D; Methods Work Group, Third US Preventive Services Task Force Current methods of the U.S. Preventive Services Task Force: a review of the process. Am J Prev Med 2001 Apr;20(3 Suppl):21-35.

- Society for Medical Decision-Making Committee (SMDMC). Proposal for clinical algorithm standards, SMDMC on Standardization of Clinical Algorithms. Med Decis Making 1992 Apr-Jun;12(2):149-54.
- United States Preventive Service Task Force (USPSTF). Guide to clinical preventive services. 2nd edition. Washington, DC: US Department of Health and Human Services, Office of Disease Prevention and Health Promotion, 1996.
- Woolf SH. Practice guidelines, a new reality in medicine II. Methods of developing guidelines. Arch Intern Med 1992 May;152(5):946-52.

APPENDIX B

Screening Items for Self-Administered Questionnaire – First Visit

The following questions may help in constructing the self-administered questionnaire for the first visit risk-assessment. Facilities may modify these questions. Please refer to the risk indicators listed in the **Prenatal Risk Assessment Checklist** – (See A-2, Table 1)

Imr	nediate Concerns
1	Are you currently having any vaginal bleeding?
2	Are you currently experiencing any significant abdominal pain/cramping ?
3	Do you have a history of ectopic pregnancy ?
4	Do you have a history of any severe pelvic infections requiring hospitalization?
5	Do you have a history of pelvic surgery for either infertility or infection?
6	Do you have diabetes that requires medication?
7	Do you have any other chronic medical condition that requires medication?
Infe	ections
8	Do you currently have, have you ever had or been exposed to tuberculosis, or have you lived with anyone who had tuberculosis?
9	Were you ever stationed overseas?
10	Were you born outside of the United States?
11	Do you currently have, have you ever had or been exposed to hepatitis ?
12	Do you currently have, have you ever had or been exposed to any sexually transmitted diseases including Chlamydia, herpes, gonorrhea, syphilis, venereal warts, HPV or HIV?
13	Have you had a rash or viral illness since your last menstrual period?
14	Do you live in a house with cats ?
Med	lical History
15	Do you currently have or have you ever had kidney or bladder problems, urinary tract infection, or cystitis ?
16	Do you currently have or have you ever had ulcers, stomach problems, or colitis?
17	Do you currently have or have you ever had an abnormal Pap smear or female or gynecological problems ?
18	Have you ever had infertility problems ?
19	Do you currently have or have you ever had heart disease ?
20	Do you currently have or have you ever had rheumatic fever ?
21	Do you currently have or have you ever had high blood pressure ?
22	Do you currently have or have you ever had pneumonia or asthma ?
23	Do you currently have or have you ever had epilepsy or seizures ?

24	Do you currently have or have you over had emotional problems?	
24	Do you currently have or have you ever had emotional problems ?	
25	Do you currently have or have you ever had thyroid problems ?	
26	Do you currently have or have you ever had diabetes?	
27	Do you currently have or have you ever had varicose veins or blood clots in your legs?	
28	Do you currently have or have you ever had bleeding tendencies ?	
29	Are you currently in need of or have you ever had an operation ?	
30	Do you currently have or have you ever had broken bones or concussions ?	
31	Are you currently having or have you ever had blood transfusions ?	
32	Do you currently have or have you ever had lupus or other autoimmune diseases ?	
33	Are you allergic to any medications?	
Gen	netic Screening	
34	Will you be 35 years old or older when the baby is due?	
35	Have you, the baby's father, or anyone in either of your families ever had Down's syndrome (mongolism)?	
36	Have you, the baby's father, or anyone in either of your families ever had any other chromosomal abnormality ?	
37	Have you, the baby's father, or anyone in either of your families ever had neural tube defect (e.g., Spina Bifida or Meningomyelocele)	
38	Have you, the baby's father, or anyone in either of your families ever had anencephaly?	
39	Have you, the baby's father, or anyone in either of your families ever had hemophilia or other bleeding disorders ?	
40	Have you, the baby's father, or anyone in either of your families ever had muscular dystrophy?	
41	Is there a family history of multiple births ?	
Mis	cellaneous	
42	Do you wear seat belts ?	
43	Do you live with anyone who hits you or hurts you in any way?	
44	Have you, the baby's father, or anyone in either of your families ever had cystic fibrosis ?	
45	Have you, the baby's father, or anyone in either of your families ever had sickle cell disease?	
46	Do you or the baby's father have a birth defect ?	
47	Do you or the baby's father have any close relatives with mental retardation?	
48	Do you, the baby's father, or a close relative in either of your families have a birth defect, family disorder, or a chromosomal abnormality not listed above ?	
	ial & Lifestyle History	
49	Do you smoke?	
50	Do you drink alcohol?	
51	Have you used marijuana, LSD, speed, heroin, crystal, crack, or cocaine?	
52	What medicines or recreational drugs have you taken since becoming pregnant (include all prescription and nonprescription drugs)?	

53	What is your occupation ?	
54	Is this a planned pregnancy?	
55	What is the highest level of education you have completed?	
56	Are you a vegetarian?	
57	Since becoming pregnant, have you been exposed to any X-rays or toxic chemicals?	
Mei	nstrual History	
58	What was the first day of your last normal menstrual period?	
59	Was your last menstrual period on time?	
60	Have you taken birth control pills or Depo Provera in the last year?	
61	How many days from the first day of your period to the first day of your next period?	
62	How many days does your period last?	
Pre	gnancy History	
63	How many previous pregnancies have you had (include miscarriages and abortions)?	
64	For each pregnancy what was the date , hospital , number of weeks pregnant , type of delivery (vaginal/C-section), birth weight, sex, and what were the complications (if any)?	

APPENDIX CHemoglobinopathies

Sickle Cell Disease

Sickle cell disease refers to a group of autosomal recessive disorders involving abnormal hemoglobin (hemoglobin S). Asymptomatic individuals with heterozygous Hb S genotypes (carriers) are said to have sickle cell trait. The most severe form of the disease, Hb SS (homozygous Hb S), is called sickle cell anemia.

Sickle cell disorders are found not only in patients who have the hemoglobin genotype SS, but also in those who have Hb S and one other abnormality of β -globin structure or β -globin production. The most common of these are Hb SC disease and Hb S β -thalassemia. When inherited with Hb S, these may cause clinically significant hemolytic anemia similar to Hb SS.

Sickle cell disease occurs most commonly in people of African origin. Approximately one in 12 African Americans has sickle cell trait. One in every 300 African-American newborns has some form of sickle cell disease, and approximately one in 600 has sickle cell anemia. Hemoglobin S is also found in high frequency in other populations such as Greeks, Italians (particularly Sicilians), Turks, Arabs, Southern Iranians, and Asian Indians.

The diagnosis of hemoglobinopathies, including sickle cell disorders, is made by hemoglobin electrophoresis. In the homozygous form, nearly all the hemoglobin is Hb S with small amounts of Hb A_2 and Hb F. Heterozygous sickle cell trait (Hb AS) is identified by a larger percentage of Hb A and an asymptomatic course. Solubility tests (Sickledex) alone are inadequate for diagnosis of sickle cell disorders because they cannot distinguish between the heterozygous AS and homozygous SS genotypes. In addition, they fail to detect other pathologic variants such as Hb C trait, β -thalassemia trait, Hb E trait, Hb B trait, and Hb D trait.

The Thalassemias

The thalassemias represent a wide spectrum of hematologic disorders that are characterized by a reduced synthesis of globin chains, resulting in microcytic anemia. Thalassemias are classified according to the globin chain affected, with the most common types being α -thalassemia and β -thalassemia.

Alpha-Thalassemia

Alpha-thalassemia usually results from a gene deletion of two or more copies of the four α -globin genes. Deletion of one α -globin gene (α -/ $\alpha\alpha$) is clinically unrecognizable, and laboratory testing yields normal results. Deletion of two α -globin genes causes α -thalassemia trait, a mild asymptomatic microcytic anemia. The deletions can be on the same chromosome or in cis ($\alpha\alpha$ /--), or on each chromosome or in trans (α -/ α -). Individuals with these chromosomal abnormalities are referred to as carriers and are at an increased risk for having a child with a more severe form of thalassemia caused by deletions of three or four copies of the α -globin gene (α -thalassemia major).

Alpha-thalassemia trait (α -thalassemia minor) is common among individuals of Southeast Asian, African, and West Indian descent. It also is common in individuals with Mediterranean ancestry. Individuals with Southeast Asian ancestry are more likely to carry two gene deletions in cis or on the same chromosome (--/ α) and are at an increased risk for offspring with Hb Bart's or Hb H disease. Hemoglobin H disease, which is caused by the deletion of three α -globin genes, usually is associated with mild to moderate hemolytic anemia. Alpha-thalassemia major (Hb Bart's) results in the absence of α -globin (--/--); this is associated with hydrops fetalis, intrauterine death, and preeclampsia.

Beta-Thalassemia

Beta-thalassemia is caused by a mutation in the β -globin gene that causes deficient or absent β -chain production, which results in absence of Hb A. Classification of β -thalassemias is based on a description of the molecular mutation or by clinical manifestations. Individuals who are heterozygous for this mutation have β -thalassemia minor. Those who are homozygous have β -thalassemia major (Cooley's Anemia) or a milder form called thalassemia intermedia. Beta-thalassemia major is characterized by severe anemia with resultant extramedullary erythropoesis , delayed sexual development, and poor growth. Elevated levels of Hb F in individuals with β -thalassemia major partially compensate for the absence of Hb A; however, death usually occurs by age 10 years

unless treatment is begun early with periodic blood transfusions. With transfusion, the severe anemia is reversed and extramedullary erythropoesis is suppressed. In homozygotes with the less severe β^+ -thalassemia mutations, often referred to as β -thalassemia intermedia, variable but decreased amounts of β -chains are produced and, as a result, variable amounts of Hb A are produced. The genes for Hb S and β -thalassemia usually behave as alleles, with only one gene inherited from each parent. The expression of the resulting Hb S/ β -thalassemia is determined by the type of β -thalassemia mutation (6).

Beta-thalassemia minor, common in individuals of Mediterranean, Asian, Middle Eastern, Hispanic, and West Indian descent, varies in severity of disease. Depending on the amount of β -chain production, it usually is associated with asymptomatic mild anemia. Beta-thalassemia minor often occurs in association with Hb S. In the most severe form, no normal β -globin chains are produced. This results in a clinically severe syndrome called sickle cell- β 0-thalassemia, in which no Hb A is produced.

APPENDIX D Risk Factors - Preterm Birth

Table D1. Risk Factors for Preterm Delivery

	Risk Factor	Surveillance	Reference
1	African American race	Normal	Wen et al., 1990
2	Age <17 or >35	Normal	Wen et al., 1990
4	Single parent	Normal	Lettieri et al., 1993
4	Smoking	Normal	Kramer, 1987 Cnattingius et al., 1999
5	Multiple first- trimester abortions	Normal	Lettieri et al., 1993
7	Poor nutrition or low pre-pregnancy weight (BMI < 18)	Normal	Buescher et al., 1993 Higgins et al., 1989
8	Stressful job or more than 3 hours working on feet per 8-hour work day	Normal	Mozurkewich et al., 2000 Luke et al., 1995 Teitelman et al., 1990
8	Lower genital tract infection at 24 weeks' gestation (gonoccus, Chlamydia, bacterial vaginosis) **	Normal	Andrews et al., 2000 Goldenberg et al., 2000 Hauth et al., 1995
9	Periodontal disease	Normal	Goepfer et al., 2004 Jeffcoat et al., 2001
10	Anemia	Normal	Meis et al., 1995 Mercer et al., 1996
11	Abdominal surgery between 20 and 36 weeks' gestation	HIGH	Dudley & Cruikshank, 1990 Coleman et al., 1997
12	Multiple gestation (the risk rises in direct proportion to the number of fetuses)	HIGH	CDC, 2002c
13	Cervical surgery (Cone, Loop Electrosurgical Excisional Procedure [LEEP])	HIGH	Kramer, 1987 Meis et al., 1995 Mercer et al., 1996
14	Prior spontaneous preterm delivery (risk rises with number of PTBs, African American ethnicity and decrease of gestational age in prior PTB)	HIGH	Iams et al., 1998 Adams et al.,2000 Mercer et al.,1999
15	Vaginal bleeding in more than one trimester * Unexplained vaginal bleeding	HIGH	Strobino & Pantel-Silverman, 1989 Meis et al., 1995 Yang, 2004
16	Cervical dilation >2cm at 24 - 28 weeks' gestation **	HIGH	Papernik et al., 1986 Stubbs et al.,1986 Copper et al., 1995
17	Placenta previa persisting after 24 weeks	HIGH	Lettieri et al., 1993
18	Soft cervical consistency at 24-28 weeks **	HIGH	Copper et al., 1995
19	Cocaine or methamphetamine use	HIGH	St. Pierre et al., 1996
20	Use of assisted reproductive technology	HIGH	Jackson et al., 2004 Schieve et al., 2004 Van Voorhis, 2006
21	Mullerian Anomaly	HIGH	Lettieri et al., 1993

Adapted from Preterm Birth: Causes, Consequences, and Prevention at http://www.nap.edu/catalog/11622.html

- * While vaginal bleeding in more than one trimester increases the risk for preterm delivery by a RR of approximately 2.5, removal of the pregnant woman from the Uncomplicated Pregnancy Guideline is recommended based on additive risks for fetal growth restriction, fetal demise, nonreassuring fetal testing, and intrapartum/postpartum problems.
- ** Cervical examination (digital or sonographic) and testing for gonorrhea, Chlamydia, or bacterial vaginosis in the midtrimester are not recommended as routine interventions in the antenatal care of a woman with an uncomplicated pregnancy; however, a digital or sonographic cervical examination and evaluation for lower genital tract infection may be performed during the evaluation of a woman presenting with signs or symptoms of preterm labor.

REFERENCES

- ACOG (American College of Obstetricians and Gynecologists). Assessment of risk factors for preterm birth. ACOG Practice Bulletin No. 31. Obstetrics and Gynecology 2001; 98:709-716.
- Adams MM, Elam-Evans LD, Wilson HG, Gilbertz DA. Rates of and factors associated with recurrence of preterm delivery. JAMA 2000; 283:1591-1596.
- Andrews WW, Goldenberg RL, Mercer B, Iams J, Meis P, Moawad A, Das A, Vandorsten JP, Caritis SN, Thurnau G, Miodovnik M, Roberts J, McNellis D. The Preterm Prediction Study: association of second-trimester genitourinary Chlamydia infection with subsequent spontaneous preterm birth. Am J Obstet Gynecol 2000; 183 (3):662-8.
- Buescher PA, Larson LC, Nelson MD, Jr., Lenihan AJ. Prenatal WIC participation can reduce low birth weight and newborn medical costs: a cost-benefit analysis of WIC participation in North Carolina. J Am Diet Assoc 1993; 93 (2):163-6.
- CDC. 2002c. Births: Final Data for 2002. [Online]. Available: http://www.cdc.gov/nchs/data/nvsr/nvsr50/nvsr50_05.pdf [accessed October 17, 2005].
- Cnattingius S, Granath F, Petersson G, Harlow BL. The influence of gestational age and smoking habits on the risk of subsequent preterm deliveries. N Engl J Med 1999; 341 (13):943-8.
- Coleman MT, Trianfo VA, Rund DA. Non-obstetric emergencies in pregnancy: trauma and surgical conditions. Am J Obstet Gynecol 1997; 177:497-504.
- Copper RL, Goldenberg RL, Dubbard MB, Hauth JC, Cutter GR. Cervical examination and tocodynamometry at 28 weeks' gestation: Prediction of spontaneous preterm birth. Am J Obstet Gynecol 1995; 172:666-71.
- Dudley DJ, Cruikshank DP. Trauma and acute surgical emergencies in pregnancy. Semin Perinatol 1990; 14 (1):42-51.
- Goepfert AR, Jeffcoat MK, Andrews WW, Faye-Petersen O, Cliver SP, Goldenberg RL, Hauth JC. 2004. Periodontal disease and upper genital tract inflammation in early spontaneous preterm birth. Obstetrics and Gynecology 104(4):777-783.
- Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. N Engl J Med 2000; 342 (20):1500-7.
- Goldenberg RL, Iams JD, Das A, Mercer BM, Meis PJ, Moawad AH, Miodovnik M, VanDorsten JP, Caritis SN, Thurnau GR, Dombrowski MP, Roberts JM, McNellis D. The Preterm Prediction Study: sequential cervical length and fetal fibronectin testing for the prediction of spontaneous preterm birth. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 2000; 182 (3):636-43.
- Hauth JC, Goldenber RL, Andrews WW, Dubbard MB, Copper RL. Reduced incidence of preterm delivery with metronidazole and erytromycin in women with bacterial vaginosis. N Engl J Med 1995; 333:1732-6.
- Higgins AC, Moxley JE, Pencharz PB, Mikolainis D, Dubois S. Impact of the Higgins Nutrition Intervention Program on birth weight: a within-mother analysis. J Am Diet Assoc 1989; 89 (8):1097-103.

- Iams JD, Goldenberg RL, Mercer BM, Moawad A, Thom E, Meis PJ, McNellis D, Caritis SN, Miodovnik M, Menard MK, Thurnau GR, Bottoms SE, Roberts JM. The Preterm Prediction Study: recurrence risk of spontaneous preterm birth. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 1998; 178 (5):1035-40.
- Jackson RA, Gibson KA, Wu YW, Croughan MS. 2004. Perinatal outcomes in singletons following in vitro fertilization: A meta-analysis. Obstetrics and Gynecology 103(3): 551-563.
- Jeffcoat MK, Geurs NC, Reddy MS, Goldenberg RL, Hauth JC. Current evidence regarding periodontal disease as a risk factor in preterm birth. Annals of Periodontology/ The American Academy of Periodontology 2001 6(1): 183-188.
- Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. Bull World Health Organ 1987; 65 (5):663-737.
- Lettieri L, Vintzileos AM, Rodis JF, Albini SM, Salafia CM. Does "idiopathic" preterm labor resulting in preterm birth exist? Am J Obstet Gynecol 1993; 168 (5):1480-5.
- Luke B, Mamelle N, Keith L, Munoz F, Minogue J, Papiernik E, Johnson TR. The association between occupational factors and preterm birth: a United States nurses' study. Research Committee of the Association of Women's Health, Obstetric, and Neonatal Nurses. Am J Obstet Gynecol 1995; 173 (3 Pt 1):849-62.
- Meis PJ, Goldenberg RL, Mercer BM. The preterm prediction study: Significance of vaginal infections. Am J Obstet Gynecol 1995; 173:1231.
- Mercer BM, Goldenberg RL, Das A, Moawad AH, Iams JD, Meis PJ, Copper RL, Johnson F, Thom E, McNellis D, Miodovnik M, Menard MK, Caritis S, Thumau GR, Bottoms SF, Roberts J. The preterm prediction study: A clinical risk assessment system. Am J Obstet Gynecol 1996; 174(6):1885-1893.
- Mercer BM, Goldenberg RL, Moawad AH, Meis PJ, Ianis JD, Das AF, Caritis SN, Miodovnik M, Menard MK, Thurnau GR, Dombrowski MP, Roberts JM, McNellis D. The Preterm Prediction Study: Effect of gestational age and cause of preterm birth on subsequent obstetric outcome. Am J Obstet Gynecol 1999; 181(5 I):1216-1221.
- Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: a meta-analysis. Obstet Gynecol 2000; 95 (4):623-35.
- Papiernik E, Bouyer J, Collin D, Winisdoerffer G, Dreyfus J. Precocious cervical ripening and preterm labor. Obstet Gynecol 1986; 67 (2):238-42.
- Schieve LA, Rasmussen SA, Buck GM, Schendel DE, Reynolds MA, Wright VC. Are children born after assisted reproductive technology at increased risk for adverse health outcomes? Obstet Gynecol 2004; 103(6):1154-1163.
- St Pierre A, Mark PM, Michelson R, Condon LM, Nelson AF, Rolnick SJ. Alcohol and other drugs of abuse in pregnancy. HMO Pract 1996; 10 (3):114-8.
- Strobino B, Pantel-Silverman J. Gestational vaginal bleeding and pregnancy outcome. Am J Epidemiol 1989; 129 (4):806-15.
- Stubbs TM, Van Dorsten JP, Miller MC, 3rd. The preterm cervix and preterm labor: relative risks, predictive values, and change over time. Am J Obstet Gynecol 1986; 155 (4):829-34.
- Teitelman AM, Welch LS, Hellenbrand KG, Bracken MB. Effect of maternal work activity on preterm birth and low birth weight. Am J Epidemiol 1990; 131 (1):104-13.
- Van Voorhis BJ. Outcomes from assisted reproductive technology. Obstetrics and Gynecology 2006; 107:183-200.
- Wen SW, Goldenberg RL, Cutter GR, Hoffman HJ, Cliver SP. Intrauterine growth retardation and preterm delivery: prenatal risk factors in an indigent population. Am J Obstet Gynecol 1990; 162 (1):213-8.
- Yang J, Hartmann KE, Savitz DA, Herring AH, Dole N, Olshan AF, Thorp JM Jr. Vaginal bleeding during pregnancy and preterm birth. Am J Epidemiol. 2004 Jul 15;160(2):118-25.

APPENDIX E Prenatal Screening for Fetal Chromosomal Abnormalities

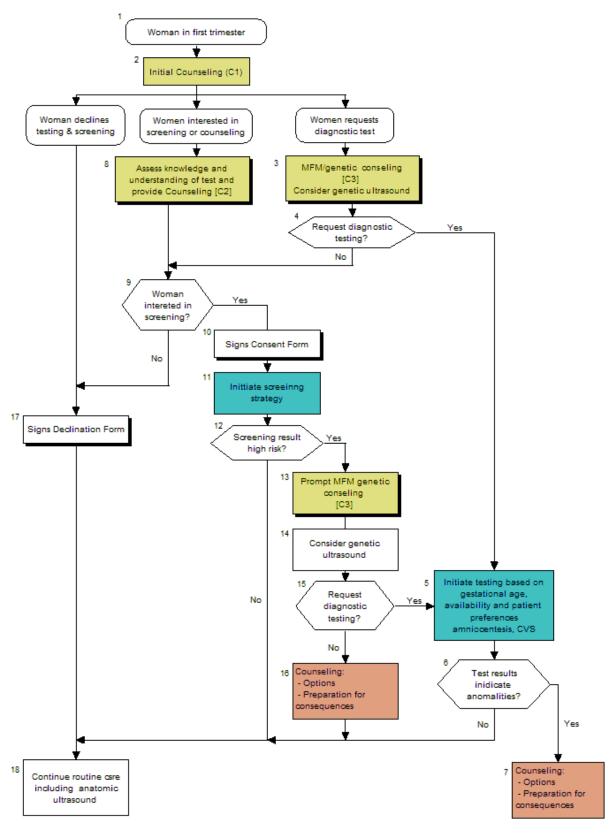


Table E- 1. Available Screening Options **

	First Trimester		First and Second Trimesters Combined			Second Trimester		Ultrasound	
	Age Only	First Trimester Screen	Sequential Screen	Integrated Screen	Serum Integrated Screen	Quad Screen	Triple Screen	Basic Ultrasound	Genetic Ultrasound
Benefits	No cost for this screening	Highest detection rate in the first trimester	Early answers and high detection rate	The highest detection rate overall	The highest detection rate without ultrasound (NT) measurements	Best second trimester test Screens for ONTD		Widely available screen for most common anomalies	Detailed genetic screening ultrasound also looks for structural, non- genetic problems
Problems	80% of babies with Down syndrome born to mothers <35	No screening for ONTD	Requires NT ultrasound measurement, not widely available	No answer given in the first trimester	No answer given in the first trimester	No answer given in the first trimester	Outdated	No answer given in the first trimester	No answer given in the first trimester. Not widely available
Timing	N/A	10 3/7 to 13 6/7	10 3/7 - 13 6/7 and 15 0/7 - 21 6/7	10 3/7 - 13 6/7 and 15 0/7 - 21 6/7	10 3/7 - 13 6/7 and 15 0/7 - 21 6/7	15 0/7 - 21 6/7	15 0/7 - 21 6/7	18-22 weeks	16-22 weeks
Down Syndrome Detection Rate	15-30%	83%	90.40%	92%	87%	81%	69%	50-60%	80-98%
Test Positive Rate	Varies with Age	5%	1.2% and 3.7%	5%	5%	5%	5%		
Odds of Being Affected with Positive Screen	Age Dependant	1 in 23	1 in 7 and 1 in 16	1 in 21	1 in 22	1 in 23	1 in 22	<1 in 100	Varies by each US
False Positive Rate		96%	86% and 94%	95%	95%	96%	95%		
Trisomy 18 Detection Rate		80%	90%	90%	90%	80%			
Open Neural Tube (ONT)Detection Rate	N/A	Not Screened	80%	80%	80%	80%	80%	95%	98%
Markers	>34 yrs	NT + PAPP-A + hCG	NT + PAPP-A +hCG AFP + hCG +uE3 + inhibin	NT + PAPP-A, AFP + hCG + uE3 + inhibin	PAPP-A, AFP + hCG + uE3 + inhibin	AFP + hCG +u E3 + inhibin	AFP + hCG + uE3		

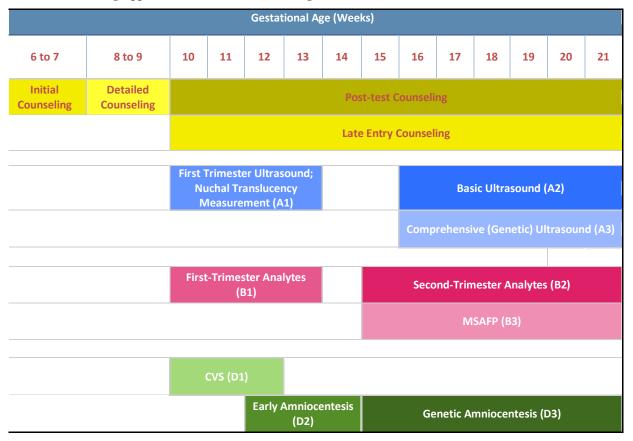
^{**}Data based on ACOG, 2007; SOPG, 2007; SURUSS; FASTER

Table E- 2. Prenatal Screening Tests – Indications and Purpose

	Test	Recommended for	Purpose		
	Prenatal Screening - Ultrasound Tests				
A1	First trimester screen NT measurement (With B1)	Offer to high-risk women. Order this screening test during the first trimester (between 11 weeks, 0 days and 13 weeks, 6 days). Crown-rump length (CRL) must be between 42-79 mm).	Use when mother wants to know the aneuploidy risk prior to 14 weeks. Use with B1. See below.		
A2	Second- trimester routine or basic ultrasound	For routine screening of low-risk women or screening for women who decline aneuploidy screening.	Widely available screen for most common major anomalies. For abnormal result offer follow-up with A3 +/- B2.		
A3	Comprehensive or genetic ultrasound	Offer to high-risk women as a primary or follow-on test.	Comprehensive screening ultrasound looks for markers of genetic abnormalities and other structural, non-genetic problems. For abnormal result offer B2 and/or amniocentesis.		
	Prenatal Screening	g - Serum Marker Tests			
B1	First trimester screen (with NT measurement [A1])	Offer to high-risk women. Order this screening test during the first trimester (between 11 weeks, 0 days and 13 weeks, 6 days). Crown-rump length (CRL) must be between 42-79 mm).	Use when mother wants to know the DS risk prior to 14 weeks. Does not detect ONTD. For abnormal result offer choice of CVS, A3 or amniocentesis.		
В3	Single screen maternal serum screen, alpha fetoprotein only	Offer to high-risk women who have previously undergone first-trimester testing (e.g., mothers who undergo early amniocentesis, chorionic villous samplings or first-trimester screening). Ideal time period is 16-18 weeks gestation; however, reference medians are available for 14-25 weeks in some labs.	Screen for fetal risk of Open Neural Tube Defect (i.e., spina bifida, anencephaly). For abnormal result offer A3 and/or amniocentesis.		
B1 B2	Serum integrated screen (first- and second- trimester serum only) OR integrated screen (first trimester NT (A1) and first- and second- trimester serum screening	First specimen drawn between 10 weeks, 3 days and 13 weeks, 6 days' gestation. Crown rump length (CRL) must be between 36-79mm. Result not provided in first trimester.	First-trimester serum specimen measures PAPP-A. Specimen 2 measures hCG, AFP, uE3 and DIA. When combined with a first-trimester certified ultrasound for nuchal translucency (NT), yields the best detection rate and lowest false-positive rate of all prenatal screens. Result given in second trimester. For abnormal result offer A3 or amniocentesis.		
B2	Quad screen maternal serum	The quad test is the most economical prenatal screening test.	Quad screen for fetal risk of Down syndrome (trisomy 21), trisomy 18,		

	Test	Recommended for	Purpose		
	screen, alpha fetoprotein, hCG, Estriol, & Inhibin A	Quad test - best second-trimester serum screen available. Ideal time period is 16-18 weeks' gestation; however, reference medians are available for 14-25 weeks.	and open neural tube defect (ONTD), spina bifida. Better detection rate and a lower false-positive rate than the triple screen. For abnormal result offer A3 or amniocentesis.		
B1 B2	Sequential screen first-trimester NT measurement and first- and sometimes second-trimester serum marker measurements	First specimen drawn between 10 weeks, 3 days and 13 weeks, 6 days' gestation. Crown rump length (CRL) must be between 36-79 mm and a nuchal translucency measurement must be obtained. Initial result provided in first trimester. Final result provided in second trimester for women having follow-on second-trimester serum measurements.	Specimen 1 measures PAPP-A. Specimen 2 measures hCG, AFP, uE3 and DIA. An interpretation is provided after the first draw so that pregnancies at very high risk for DS can be identified in the first trimester. For abnormal first-trimester result offer choice of CVS, A3 or amniocentesis. For intermediate first-trimester result follow on second-trimester serum maker measurement. For abnormal second-trimester result offer A3 and amniocentesis. For low-risk first-or second-trimester result offer A2.		
	Prenatal Diagnosis - Amniotic Fluid and Chromosome Analyses				
D1	Chorionic villus sampling	Offered in the first trimester to high-risk women. Indications may include: - Women older than 34 years of age - Abnormal first-trimester screen result - Fetal structural abnormalities - Family history of chromosomal abnormality or metabolic or genetic disorder.	First-trimester diagnostic testing (10-14 weeks gestation). Follow up with genetic counseling for abnormal result.		
D2	Early amniocentesis	Not recommended: -Higher rates of failure, pregnancy loss and fetal injury than CVS or routine amniocentesis (D1, D3).	Prenatal diagnosis 10-15 weeks' gestation. Follow up with genetic counseling for abnormal result.		
D3	Chromosome analysis, amniotic fluid	Indications include: - Abnormal first- or second-trimester screening test(s) - Fetal ultrasound abnormalities - Family history of chromosome abnormality or genetic disorder -Elevated risk for open neural tube defect risk (do amniotic fluid AFP with Reflex to Acetylcholinesterase).	Prenatal diagnosis in pregnant patient after 14 weeks' gestation. Follow up with genetic counseling for abnormal result.		

Table E- 3. Timing Opportunities for Prenatal Screening



Institutional Considerations

The process of reviewing scientific evidence and addressing implementation and ethical issues is as important as the specific findings and recommendations of this guideline. With a wide array of new testing technologies and candidate disorders for screening it is more important than ever to establish an objective process of accumulating scientific evidence for forming policy decisions. Accordingly, each institution needs to establish testing strategies they will make available to their beneficiaries. These strategies should take into account the principles and recommendations from above. Accordingly, each institution should have available one or more tests/testing strategies from each of the groups below.

Given the complexity of the varied testing strategies, it is not feasible for every institution to offer the spectrum of potential testing strategies. Institutions need to provide one or more screening strategies giving a first-trimester result and one or more strategies giving a second-trimester result. Each institution must also provide or arrange for access to routine and comprehensive ultrasound, CVS, amniocentesis, and basic and comprehensive counseling.

Table E- 4. Institutional Considerations

	Options	Name / Type of Test	Advantages	Disadvantages	
1 st ter Result	1T US + 1T Serum	First Trimester Combined	1T < 15 weeks	1T < 15 weeks and 2T > 15 weeks	
1 st Trimester Result	1T US + 1T and 2T Serum	Contingency			
Result	1T US + 1T and 2T Serum	Integrated Screen	2T > 15 weeks		
2 nd Trimester Re	1T Serum + 2T Serum	Serum Integrated Screen	2T > 15 weeks		
	2T Serum	Quad Screen	2T > 15 weeks		
Key: 1T – First Trimester; 2T – Second Trimester					

APPENDIX F Questions for Literature Search

- 1. In women experiencing a normal pregnancy does use of the "Centering Pregnancy" model vs. routine care affect neonatal morbidity, rate of preterm delivery, birth weight, patient satisfaction, length of breastfeeding, healthcare cost or utilization, APGAR scores, length of gestation, or method of delivery?
- 2. Does testing a pregnant woman with maternal serum analyte testing in the first trimester and/or performing ultrasound measurement of nuchal translucency in the second trimester, either individually or in combination use, improve fetal or maternal outcomes?
- 3. In women who are candidates for genetic testing, do the credentials of the provider performing the counseling affect maternal or fetal outcomes, or patient satisfaction?
- 4. In women with a history of preterm birth, does treatment with progesterone decrease the rate of preterm delivery?
- 5. In pregnant women with a history of LEEP, what is the effect on preterm delivery of increased surveillance for preterm labor, either by cervical length via US or fetal fibronectin when compared with routine care? Are these patients uncomplicated?
- 6. In women with a history of preterm birth, does screening for cervix incompetence decrease the rate of preterm delivery?
- 7. In pregnant women with a history of GDM, what is the effect of 1st trimester screening on timing of GDM diagnosis, macrosomia, mode of delivery, and fetal morbidity and mortality?
- 8. In pregnant women undergoing 3H GTT testing for GDM, what is the effect of up to three days of a high-carbohydrate diet prior to the testing versus no special diet prior to the testing on the specificity and sensitivity of the test?
- 9. In pregnant women with a history of gastric bypass, when should screening for GDM start and what is the optimal screening method to maximize accurate diagnosis of GDM?
- 10. In pregnant women with a history of gastric bypass, what is the effect of conducting goal-oriented visits, versus standard care, on maternal/fetal morbidity, preterm birth, birth weight, and patient satisfaction?
- 11. In pregnant women with PCOS what is the optimal timing and frequency for screening for GDM? Are these patients still uncomplicated?
- 12. What is the effect on infant and maternal morbidity/mortality, specifically neonatal GBS sepsis and timing of delivery, of treating women with ANY amount of GBS isolated in their urine versus treating only those with >100K CFU isolated?
- 13. In pregnant women at term with positive GBS screening, does stripping or sweeping of membranes compared to not stripping or sweeping of membranes increase GBS sepsis of neonate or chorioamnionitis?
- 14. In women with a history of ectopic pregnancy, what is the effect of early US on the timing and incidence of detection of ectopic pregnancy, method of resolution of ectopic pregnancy, hospitalization rates, and maternal morbidity?
- 15. In pregnant women with partners with a history of HSV disease, what is the effect of serum HSV testing of the partner, as well as transmission prevention education on the incidence of maternal primary HSV in pregnancy, and the incidence of neonatal HSV?
- 16. In pregnant women with a history of HSV, what is the effect of suppressive theory at term versus no suppression on incidence of maternal HSV, neonatal HSV, and C-section rates with HSV presence as an indication?

- 17. In women experiencing a normal pregnancy, what is the effect of elective induction at term versus no elective induction on mode of delivery, APGAR scores, fetal outcomes, and patient satisfaction?
- 18. In pregnant women who test positive for HbSAg what is the effect of maternal hepatitis B vaccination before delivery on the incidence of vertical Hepatitis B transmission to the infant?
- 19. In women experiencing a normal pregnancy that are asymptomatic, does screening for bacterial vaginosis, and subsequently treating, decrease the rate of preterm delivery?

APPENDIX G Acronym List

AAP	American Academy of Pediatrics		
	•		
ACS	American Cancer Society		
ACOG	American College of Obstetricians and Gynecologists		
AFI	Amniotic Fluid Index		
AFP	Alphafetoprotein		
AIUM	American Institute of Ultrasound in Medicine		
ASB	Asymptomatic Bacteriuria		
bid	Twice a Day		
BMI	Body Mass Index		
BPD	BiParielal Dianeter		
CAGE	Alcohol Abuse/Dependency Screening Instrument		
CBC	Complete Blood Count		
CBT	Cognitive Behavioral Therapy		
CDC	Centers for Disease Control		
CF	Cystic Fibrosis		
CI	Confidence Interval		
CMV	Cytomegalovirus		
CNM	Certified Nurse Midwife		
CPD	Cephalopelvic Disproportion		
CPG	Clinical Practice Guideline		
CPS	Clinical Preventive Services		
CRS	Congenital Rubella Syndrome		
DE	Dependent Edema		
DM	Diabetes Mellitus		
ECT	Electroconvulsive Therapy		
EDC	Estimated Date of Confinement		
EDD	Estimated Date of Delivery		
EDPS	Edinburgh Postnatal Depression Scale		
EGA	Estimated Gestational Age		
fFN	Fetal Fibronectin		
FL	Femur Length		
GBS	Group B Streptococcus		
GDM	Gestational Diabetes Mellitus		
L			

GTT	Glucose Tolerance Test	
HBIG	Hepatitis B Immune Globulin	
HC/AC	Head/Abdominal circumference	
HCG	Human Chorionic Gonodatropin	
HIV	Human Immunodeficiency Virus	
HPV	Human Papillomavirus	
HSV	Herpes Simplex Virus	
IAP	Intrapartum Antibiotics for Prophylaxis	
IOM	Institute of Medicine	
IPT	Interpersonal Therapy	
IV	Intravenous	
LBW	Low Birth Weight	
LEEP	Loop Electrosurgical Excisional Procedure	
LMP	Last Menstrual Period	
MDD	Major Depressive Disorder	
MFM	Maternal-Fetal Medicine Physician	
MMR	Measles/Mumps/Rubella	
MOM	Multiples of the Median	
MSAFP	Maternal Serum Alphafetoprotein	
NDDG	National Diabetes Data Group	
HBV	Hepatitis B Virus	
HC/AC	Head/Abdominal Circumference	
NIH	National Institute of Health	
NNT	Number-Needed-To-Treat	
NRT	Nicotine Replacement Therapy	
NST	Non-Stress Testing	
NT	Nuchal Translucency	
NTD	Neural Tube Defect	
OB/GYN	Obstetrician/Gynecologist or Obstetrical/Gynecological	
OIA	Optical Immunoassay	
ONTD	Open Neural Tube Defects	
OR	Odds Ratio	
Pap	Papanicolaou	
PCR	Polymerase Chain Reaction	
PID	Pelvic Inflammatory Disease	

PPD	Purified Protein Derivative
PROM	Premature Rupture of Membranes
PTB	Preterm Birth
PTD	Preterm Delivery
RCT	Randomized Controlled Trials
RPR	Rapid Plasma Reagin
RR	Relative Risks
SBS	Shaken Baby Syndrome
SIDS	Sudden Infant Death Syndrome
SOGC	Society of Obstetricians and Gynaecologists of Canada
SSRI	Selective Serotonin Reuptake Inhibitors
STD	Sexually Transmitted Disease
Td	Tetanus-diphtheria
Tdap	, diphtheria, and acellular pertussis
TOC	Test of Cure
TORCH	Toxoplasmosis, Other infections, Rubella, Cytomegalovirus, Herpes simplex virus
TSH	Thyroid Stimulating Hormone
US	Ultrasound
USPSTF	United States Preventive Services Task Force
VBAC	Vaginal Birth After Cesarean Delivery
VDRL	Venereal Disease Research Laboratory

APPENDIX H Participant List

Susan C. Altenburg, RN, BSN, MS LTC(R)

Certified Nurse Midwife **Evans Army Community Hospital** 1650 Cochrane Circle Fort Carson, CO 80913

Phone: (719) 526-7441

Email: susan.altenburg@amedd.army.mil

Carla Cassidy, RN, MSN, NP

Director, Evidence Based Practice Program Department of Veterans Affairs 810 Vermont Avenue Washington, DC 20420

Phone: (202) 266-4502 Email: Carla.cassidy@va.gov

Martha D'Erasmo MPH

Independent Consultant 4550 North Park Ave, Apt. 505 Chevy Chase, MD 20815 Phone: (301) 654-3152

Email: Marty@hqiinc.com

Ernest Degenhardt, MSN, Adult and Family NP COL, USA

Chief, Evidence Based Practice U.S. Army Medical Command 2050 Worth Road, Suite 26 Fort Sam Houston TX 78234

Phone: (210) 221-8297

Email: ernest.degenhardt@amedd.army.mil

Susan C. Farrar, MD, MPH LCDR MC, USN

Obstetrics and Gynecology Naval Medical Center Portsmouth 620 John Paul Jones Circle Portsmouth, Virginia 23322 Phone: (757) 953-4339/0399

Email: susan.farrar@med.navy.mil; Susanfarrar1@yahoo.com

Trisha L. Farrell, MS, CNM, WHNP CDR, NC, USN

Naval Hospital Bremerton 1 Boone Road

OB/GYN Dept Code 043 Bremerton, WA 98312

Phone: (360) 475-4277

Email: Trisha. Farrell@med.navy.mil

Merlin B. Fausett, MD Lt Col, MC, USAF

Chief of Obstetrics and Maternal Fetal Medicine Consultant to the Surgeon General Wilford Hall Medical Center, 59th Maternal Child Sq. 24601 Fairway Springs San Antonio, TX 78260

San Antonio, TX 78260 Phone: (210) 292-6100

Email: bfausett@mac.com; Merlin.fausett@us.af.mil

Rosalie Fishman, RN, MSN, CPHQ

President

Healthcare Quality Informatics, Inc. 15200 Shady Grove Rd, Suite 350

Rockville, MD 20850 Phone: (301) 296-4542 Email Rosalie@hqiinc.com

Gwenn Garmon, MD, MS

Director of Women's Health JBVAMC Jesse Brown VA Medical Center 820 Damen 11F Chicago, IL 60612

Phone: (312) 569-7354

Email: gwenn.garmon@va.gov

Nancy J. Hughes, CNM COL, USA

Deputy Commander Nursing Consultant, TSG Women's Health Winn Army Community Hospital 1061 Harmon Ave Bldg 302 Ft. Stewart, GA 31314-5674

Phone: (912) 435-6853

Email: nancy.hughes@us.army.mil

Mary Kreuger, MAJ, DO, MPH, USA FAAFO

Family Medicine

Womack Family Medicine Residency

Ft. Bragg, NC

Phone: 910-907-8251

Email: mary.kreuger@us.army.mil

Leonard J. Kuskowski, MD, FACOG CDR, MC, USN

Obstetrics and Gynecology National Naval Medical Center 8901 Wisconsin Ave, Bldg 9 Bethesda, MD 20889

Phone: (301) 295-4394/0367

Email: Leonard.kuskowski@med.navy.mil

Constance H. LaRosa, RN, BSN, MSA

Deputy Field Director, Women's health Strategic Healthcare Group Department of Veterans Affairs-field based at Ann Arbor VAMC

2215 Fuller Road

Ann Arbor, MI 48105-2300 Phone: (734) 845-5050

Email: Connie.Larosa@va.gov

Joanne Marko, MS, SLP

Independent Consultant 17816 Whimsey Court Olney, MD 20832 Phone: (301) 774-5812

Email: nitojo@comcast.net

Jason A. Pates, MD MAJ, MC, USA

Staff, Division of Maternal and Fetal medicine Madigan Army Medical Center 9040 A Fitzsimmons Drive

Tacoma, WA 98431 Phone: (253) 968-3920

Email: jason.pates@amedd.army.mil

Evelyn Patterson, RN, MSN, MBA CPG Coordinator, DoD

U.S. Army Medical Command 2050 Worth Road, Suite 26 Fort Sam Houston TX 78234

Phone: (210) 221-8658

Email: evelyn.patterson@amedd.army.mil

Oded Susskind, MPH

Medical Education Consultant

PO Box 112

Brookline MA 02446 Phone: (617) 232-3558 Email: Oded@tiac.net

Mary C. Wahl, CNM, MSN Lt Col, NC, USAF

Landstuhl Regional Medical Center Obstetrics and Gynecology CMR 402 Box 316 APO AE 09180

Phone: DSN 486-8124

Email: mary.wahl@lnd.amedd.army.mil

APPENDIX IBibliography

- ACOG Committee Opinion No.246: Primary and Preventive Care: Periodic assessments. Compendium of Selected Publications 2001:210.
- ACOG Committee Opinion No. 279: Prevention of early-onset group B streptococcal disease in newborns. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002 Dec;100(6):1405-12.
- ACOG Committee Opinion No. 305: Influenza vaccination and treatment during pregnancy. ACOG Committee on Obstetric Practice. Obstet Gynecol 2004 Nov;104(5 Pt 1):1125-6.
- ACOG Committee Opinion No. 315: Obesity in pregnancy. American College of Obstetricians and Gynecologists. Obstet Gynecol 2005 Sep;106:671–5.
- ACOG Committee Opinion No. 325: Update on carrier screening for cystic fibrosis. Committee on genetics, American College of Obstetricians and Gynecologists. Obstet Gynecol 2005 Dec;106(6):1465-8.
- ACOG Committee Opinion No. 342: Induction of labor for vaginal birth after cesarean delivery.

 American College of Obstetricians and Gynecologists Committee on Obstetric Practice. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006 Aug;108(2):465-8.
- ACOG Committee Opinion No. 357: Primary and preventive care: periodic assessments. ACOG Committee on Gynecologic Practice. Obstet Gynecol 2006 Dec;108(6):1615-22.
- ACOG Committee Opinion No. 419: Use of progesterone to reduce preterm birth. Society for Maternal Fetal Medicine Publications Committee. Obstet Gynecol 2008;112:963-5.
- ACOG Practice Bulletin No. 10: Induction of labor. ACOG Practice Bulletin No. 10. American College of Obstetricians and Gynecologists. Obstet Gynecol 1999.
- ACOG Practice Bulletin No. 31: Assessment of risk factors for preterm birth. Clinical management guidelines for obstetrician-gynecologists. American College of Obstetricians and Gynecologists. Obstet Gynecol 2001;98(4):709–16.
- ACOG Practice Bulletin No. 43: Management of preterm labor. ACOG Committee on Practice Bulletins-Obstetrics. Int J Gynaecol Obstet 2003 Jul;82(1):127-35.
- ACOG Practice Bulletin No. 54: Vaginal birth after previous cesarean . American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;104(1):203-12.
- ACOG Practice Bulletin No. 75: Management of alloimmunization during pregnancy. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:457–64.
- ACOG Practice Bulletin No. 77: Screening for fetal chromosomal abnormalities. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007 Jan;109(1):217-27.
- ACOG Practice Bulletin No. 86: Viral hepatitis in pregnancy. ACOG Practice Bulletin No. 86. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;110:941–55.
- ACOG Practice Bulletin No. 95: Anemia in pregnancy. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:201–7.
- ACOG Practice Bulletin No. 98: Ultrasonography in pregnancy. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:717–26.
- ACOG Practice Bulletin No. 99: Management of abnormal cervical cytology and histology. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008 Dec;112(6):1419-44.
- ACOG Technical Bulletin No. 160: Immunization during pregnancy. Int J Gynaecol Obstet 1993 Jan;40(1):69-79.

- ACOG Technical Bulletin No. 189-February 1994: Exercise during pregnancy and the postpartum period. Int J Gynaecol Obstet. 1994 Apr;45(1):65-70.
- ACOG Technical Bulletin No. 219: Hypertension in pregnancy. Number 219-January 1996 (replaces no. 91, February 1986). Committee on Technical Bulletins of the American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet 1996 May;53(2):175-83.
- ACOG Practice Bulletin. Chronic hypertension in pregnancy. ACOG Committee on Practice Bulletins. Obstet Gynecol 2001 Jul;98(1):suppl 177-85.
- Adebisi OY, Strayhorn G. Anemia in pregnancy and race in the United States: blacks at risk. Fam Med 2005 Oct;37: 655–62.
- Adouard F, Glangeaud-Freudenthal NM, Golse B. Validation of the Edinburgh postnatal depression scale (EPDS) in a sample of women with high-risk pregnancies in France. Arch Womens Ment Health 2005 Jun;8(2):89-95.
- Alderman BW, Zamudio S, Baron AE, Joshua SC, Fernbach SK, Greene C, Mangione EJ. Increased risk of craniosynostosis with higher antenatal maternal altitude. Int J Epidemiol 1995;24 (2):420-6.
- Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database Syst Rev 2003;(3):CD003252.
- Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM; National Birth Defects Prevention Study. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. N Engl J Med 2007 Jun 28;356(26):2684-92.
- American Academy of Pediatrics. Guidelines for Perinatal Care. American Academy of Pediatrics and the American College of Obstetricians and Gynecologists:6th ed. 1998.
- American Academy of Pediatrics and the American College of Obstetricians and Gynecologist. Joint statement on HIV testing. August 1995.
- American Academy of Pediatrics Working Group on Breastfeeding. Breastfeeding and the use of human milk. J Ped 1997;100 (6):1035-9.
- American Academy of Peridontology AAP statement regarding periodontal management of the pregnant patient. J Periodontol;2004 Mar;75(3):495.
- American College of Obstetrics and Gynecologists and the American College of Medical Geneticists. Preconception and prenatal carrier screening for Cystic Fibrosis. Clinical and Laboratory Guidelines. Washington DC:ACOG; October 2001.
- American Dental Association Council on Scientific Affairs. The use of dental radiographs: update and recommendations. J Am Dent Assoc 2006 Sep;137(9):1304-12.
- American Diabetes Association. Report of the Expert Committee on the diagnosis and classification of Diabetes Mellitus. Diabetes Care 2002; 25:S5-S20.
- American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). Targeted tuberculin testing and treatment of latent tuberculosis infection. This statement was endorsed by the Council of the Infectious Diseases Society of America. (ISDA), September 1999. Am J Respir Crit Care Med 2000 Apr;16(4 Pt 2):S221–47.
- Andrews WW, Goldenberg RL, Mercer B, Iams J, Meis P, Moawad A, Das A, Vandorsten JP, Caritis SN, Thurnau G, Miodovnik M, Roberts J, McNellis D. The Preterm Prediction Study: association of second-trimester genitourinary chlamydia infection with subsequent spontaneous preterm birth. Am J Obstet Gynecol 2000 Sep;183(3):662-8.
- Angastiniotis M, Modell B. Global epidemiology of hemoglobin disorders. Ann N Y Acad Sci 1998 Jun 30;850:251-69.
- Askie LM, Duley L, Henderson-Smart D, Stewart L. Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. Lancet 2007;369:1791-8.

- Austin MP, Lumley J. Antenatal screening for postnatal depression: a systematic review. Acta Psychiatr Scand 2003 Jan;107(1):10-7.
- Bailey V, Sherriff J. Reasons for the early cessation of breastfeeding in women from lower socio-economic groups in Perth, Western Australia. Aust J Nutr Dietetics 1992;49(2):40-3.
- Baldwin K. Comparison of selected outcomes of Centering Pregnancy versus traditional prenatal care. J Midwifery Womens Health 2006 Jul-Aug;51(4):266-72.
- Bar-Zohar D, Azem F. Pregnancy after laparoscopic adjustable gastric banding: perinatal outcome is favorable also for women with relatively high gestational weight gain. Surg Endosc 2006;20(10):1580-3.
- Baughman AL, Williams WW, Atkinson WL, Cook LG, Collins M. The impact of college prematriculation immunization requirements on risk for measles outbreaks. JAMA 1994 Dec 21;272 (14):1127-32.
- Beck CT, Gable RK. <u>Further validation of the Postpartum Depression Screening Scale.</u> Nurs Res 2001 May-Jun;50(3):155-64.
- Bell SC, Halligan AW, Martin A, Ashmore J, Shennan AH, Lambert PC, Taylor DJ. The role of observer error in antenatal dipstick proteinuria analysis. Br J Obstet Gynaecol 1999 Nov;106(11):1177-80.
- Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR. Depression during Pregnancy: Overview of clinical factors. Clin Drug Investig 2004;24(3):157-79.
- Benowitz NL, Dempsey DA, Goldenberg RL, Hughes JR, Dolan-Mullen P, Ogburn PL, Oncken C, Orleans CT, Slotkin TA, Whiteside HP Jr, Yaffe S. The use of pharmacotherapies for smoking cessation during pregnancy. Tob Control 2000;9 Suppl 3:III91-4.
- Berens P. Prenatal, intrapartum, and postpartum support of the lactating mother. Pediatr Clin North Am 2001 Apr;48 (2):365-75.
- Berkowitz RL, Cuckle HS, Wapner R, D'Alton ME. Aneuploidy screening: what test should I use? Obstet Gynecol 2006 Mar;107(3):715-8.
- Bhandal N, Russell R. Intravenous versus oral iron therapy for postpartum anaemia. BJOG 2006 Nov;113(11):1248–52.
- Biggio JR Jr, Morris TC, Owen J, Stringer JS. An outcomes analysis of five prenatal screening strategies for trisomy 21 in women younger than 35 years. Am J Obstet Gynecol 2004 Mar;190(3):721-9.
- Blackwell AL, Thomas PD, Wareham K, Emery SJ. Health gains from screening for infection of the lower genital tract in women attending for termination of pregnancy. Lancet 1993Jul 24;342(8865):206-10.
- Bledsoe SE, Grote NK. Treating Depression During Pregnancy and the Postpartum: a preliminary meta-analysis. Res Social Work Pract 2006;16(2):109-20.
- Bodnar LM, Tang G, Ness RB, Harger G, Roberts JM. Periconceptional multivitamin use reduces the risk of preeclampsia. Am J Epidemiol 2006 Sep 1;164(5):470-7.
- Boulvain M, Irion O, Marcoux S, Fraser W. Sweeping of the membranes to prevent post-term pregnancy and to induce labour: a systematic review. Br J Obstet Gynaecol 1999;106(5):481-5.
- Boulvain M, Stan C, Irion O. Membrane sweeping for induction of labor. Cochrane Database Syst Rev 2005 Jan 25;(1): CDC000451.
- Bowell PJ, Allen DL, Entwistle CC. Blood group antibody screening tests during pregnancy. Br J Obstet Gynaecol 1986;93(10):1038-43.
- Boyd RC, Le HN, Somberg R. Review of screening instruments for postpartum depression. Arch Womens Ment Health 2005 Sep;8(3):141-53.
- Boyer KM, Gotoff SP. Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. N Engl J Med 1986 June 26;314 (26):1665-9.

- Bradley KA, Boyd-Wickizer J, Powell SH, Burman ML. Alcohol screening questionnaires in women: a critical review. JAMA 1998 Jul 8;280(2):166-71.
- Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts J, Martin MA.: Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol Assess 2000;4 (16):41-62.
- Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, Martin MA. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol Assess 2000;4(16):i-vi, 1-193.
- Bricker L, Neilson JP. Routine ultrasound in late pregnancy (after 24 weeks gestation). Cochrane Database Syst Rev 2008 Oct 8;(4):CD001451.
- Brison M, Van De Veld N, De Wals M, Claude Boily M. Estimating the number needed to vaccinate to prevent diseases and death related to human papillomavirus infection. CMAJ;2007 Aug 28;177(5):464-8.
- Brown ZA, Selke S, Zeh J, Kopelman J, Maslow A, Ashley RI, Watts DH, Berry S, Herd M, Cory L. The acquisition of herpes simplex virus during pregnancy. N Engl J Med 1997 Aug 21;337:509-15.
- Bryant C, Roy M. Best Start Training Program. Section C. Tampa, FL: Best Start Inc.; 1990.
- Budd KW, Ross-Alaolmolki K, Zeller RA. Two prenatal alcohol use screening instruments compared with a physiologic measure. J Obstet Gynecol Neonatal Nurs 2000 mar-Apr;29(2):129-36.
- Buekens P, Alexander S, Boutsen M, Blondel B, Kaminski M, Reid M. Randomised controlled trial of routine cervical examinations in pregnancy. European Community Collaborative Study Group on Prenatal Screening. Lancet 1994 Sep 24;344(8926):841-4.
- Buescher PA, Larson LC, Nelson MD, Jr., Lenihan AJ. Prenatal WIC participation can reduce low birth weight and newborn medical costs: a cost-benefit analysis of WIC participation in North Carolina. J Am Diet Assoc 1993 Feb;93(2):163-6.
- Buhling KJ, Elsner E, Wolf C, Harder T, Engel B, Wascher C, Siebert G, Dudenhausen JW. No influence of high- and low-carbohydrate diet on the oral glucose tolerance test in pregnancy. Clin Biochem 2004 Apr;37(4):323-7.
- Burt J. Worth the weight: pregnancy after gastric bypass surgery. Adv Nurse Pract 2005 Nov;13(11):45-7.
- Calvert JP, Crean EE, Newcombe RG, Pearson JF. Antenatal screening by measurement of symphysis-fundus height. Br Med J (Clin Res Ed) 1982 Sep 25;285(6345):846-9.
- Campbell MK, Mottola MF. Recreational exercise and occupational activity during pregnancy and birth weight: A case-control study. Am J Obstet Gynecol 2001 Feb;184 (3):403-8.
- Camporesi EM. Diving in pregnancy. Semin Perinatol 1996;Jul 20(4):292-32.
- Carles G, Tobal N, Raynal P, Herault S, Beucher G, Marret H, Arbeille P. Doppler assessment of the fetal cerebral hemodynamic response to moderate or severe maternal anemia. Am J Obstet Gynecol 2003Mar;188:794–9.
- Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol 1982 Dec 1; 44(7):768-73.
- Caughey AB, Hopkins LM, Norton ME. Chorionic villus sampling compared with amniocentesis and the difference in the rate of pregnancy loss. Obstet Gynecol 2006 Sep;108(3 Pt 1):612-6.
- Centers for Disease Control and Prevention, Guideline for Hepatitis B immunization. Available at: http://www.cdc.gov/nip/vaccine/vac-chart-hcp.htm
- Centers for Disease Control and Prevention Questions and Answers Concerning the Safety and Efficacy of Gardasil® June 4, 2007.

- Centers for Disease Control and Prevention Recommendations to prevent and control iron deficiency in the United States. Centers for Disease Control and Prevention. MMWR Recomm Rep 1998;47(RR-3):1–29. (Level III)
- Centers for Disease Control and Prevention. 1998 guidelines for treatment of sexually transmitted diseases MMWR Recomm Rep 1998 Jan 23;47 (RR-1):1-111.
- Centers for Disease Control and Prevention. Current trends CDC criteria for anemia in children and childbearing-aged women. MMWR 1989 June 9;38:400–4.
- Centers for Disease Control and Prevention. Prevention of Varicella. Recommendations of the Advisory Committee on immunization practices (ACIP). MMWR 2007 June 22;56(RR04):1-40.
- Centers for Disease Control and Prevention. Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on immunization practices (ACIP).MMWR 2007 March 12;56(RR02);1-24.
- Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines. May 2002. Center for Disease Control.
- Chamberlain PF, Manning FA, Morrison I, Harman CR, Lange IR. Ultrasound evaluation of amniotic fluid volume I. The relationship of marginal and decreased amniotic fluid volume to perinatal outcome. Am J Obstet Gynecol 1984 Oct;150(3):245-9.
- Chamberlain PF, Manning FA, Morrison I, Harman CR, Lange IR. Ultrasound evaluation of amniotic fluid volume II. The relationship of increased amniotic fluid volume to perinatal outcome. Am J Obstet Gynecol 1984 Oct 1;150(3):250-4.
- Chambers CD, Hernandez-Diaz S, Van Marter LJ, Werler MM, Louik C, Jones KL, Mitchell AA. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. N Engl J Med. 2006 Feb 9;354(6):579-87.
- Chang G, Wilkins-Haug L, Berman S, Goetz MA, Behr H, Hiley A. Alcohol use and pregnancy: improving identification. Obstet Gynecol 1998 Jun;91(6):892-8.
- Chang G, Wilkins-Haug L, Berman S, Goetz MA. Brief intervention for alcohol use in pregnancy: a randomized trial. Addiction 1999 Oct;94(10):1499-508.
- Chang TW, DesRosiers S, Weinstein L. Clinical and serologic studies of an outbreak of rubella in a vaccinated population. N Engl J Med 1970 Jul 30;283(5):246-8.
- Chervenak FA, McCullough LB. Ethical issues in obstetric sonography. Clin Obstet Gynecol 1992 Dec;35(4):758-62.
- Chesley LC. History and epidemiology of preeclampsia-eclampsia. Clin Obstet Gynecol 1984 Dec;27(4):801-20.
- Clapp JF 3rd. Recommending exercise during pregnancy. Contemporary Ob Gyn 2001 January;46 (1):30-49.
- Clapp JF, 3rd, Lopez B, Harcar-Sevcik R. Neonatal behavioral profile of the offspring of women who continued to exercise regularly throughout pregnancy. Am J Obstet Gynecol 1999 Jan;180(1Pt1):91-4.
- Clapp JF, Kim H, Burciu B, Lopez B. Beginning regular exercise in early pregnancy: effect on fetoplacental growth. Am J Obstet Gynecol 2000 Dec;183(6):1484-8.
- Cnattingius S, Granath F, Petersson G, Harlow BL. The influence of gestational age and smoking habits on the risk of subsequent preterm deliveries. N Engl J Med 1999 Sep;341(13):943-8.
- Cohen AW, Goldberg J. Membrane sweeping and GBS: a litigious combination? 2006 Sep;OBG Management:74-81.
- Coleman MT, Trianfo VA, Rund DA. Nonobstetric emergencies in pregnancy: trauma and surgical conditions. Am J Obstet Gynecol 1997 Sep;177:497-504.

- Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, VanDyke R, Bey M, Shearer W, Jacobson RL, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med 1994;33(18):1173-80.
- Connors G, Natale R, Nasello-Paterson C. Maternally perceived fetal activity from twenty-four weeks' gestation to term in normal and at risk pregnancies. Amer J Obstetr Gynecol 1988;158(2):294-9.
- Conway, DL, Langer O. Effects of the new criteria for type 2 diabetes on the rate of postpartum glucose intolerance in women with gestational diabetes. Am J Obstet Gynecol 1999:181:610-14: Level II-2.
- Copel JA, Platt LD, Campbell S. Prenatal ultrasound screening and perinatal outcome. N J Med 1994;330 (8):571-2.
- Copper RL, Goldenberg RL, Dubbard MB, Hauth JC, Cutter GR. Cervical examination and tocodynamometry at 28 weeks' gestation: Prediction of spontaneous preterm birth. Am J Obstet Gynecol 1995;172:666-71.
- Corwin EJ, Murray-Kolb LE, Beard JL. Low hemoglobin level is a risk factor for postpartum depression. J Nutr 2003 Dec;133:4139–42.
- Covington DL, Diehl SJ, Wright BD, Piner M. Assessing for violence during pregnancy using a systematic approach. Matern Child Health J 1997;1(2):129-33.
- Crane JP, LeFevre ML, Winborn RC, Evans JK, Ewigman BG, Bain RP, Frigoletto FD, McNellis D. A randomized trial of prenatal ultrasonographic screening: impact on the detection, management, and outcome of anomalous fetuses. Am J Obstet Gynecol 1994;171 (2):392-9.
- Crowe SM, Mastrobattista JM, Monga M. Oral glucose tolerance test and the preparatory diet. Am J Obstet Gynecol 2000 May;182(5):1052-4.
- Crowther CA, Keirse MJ. Anti-D administration in pregnancy for preventing rhesus alloimmunisation. Cochrane Database Syst Rev 2000;(2):CD000020.
- Cunningham FG, Lindheimer MD. Hypertension in pregnancy. N Engl J Med 1992;32 (14):927-32.
- da Fonseca EB, Bittar RE, Carvalho MH, Zugaib M. Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study. Am J Obstet Gynecol 2003;188:419–24
- Dahl K, Kesmodel U, Hvidman L, Olesen F. Informed consent: providing information about prenatal examinations. Acta Obstet Gynecol Scand 85(12):1420-5.
- Dahl K, Kesmodel U, Hvidman L, Olesen F. Informed consent: attitudes, knowledge and information concerning prenatal examinations. Acta Obstet Gynecol Scand 2006;85(12):1414-9.
- Danilenko-Dixon DR, Van Winter JT, Nelson RL, Ogburn PL, Jr. Universal versus selective gestational diabetes screening: application of 1997 American Diabetes Association recommendations. Am J Obstet Gynecol 1999;181(4):798-802.
- Davey A, Rostant K, Harrop K, Goldblatt J, O'Leary P. Evaluating genetic counseling: client expectations, psychological adjustment and satisfaction with service. J Genet Couns 2005;4(3):197-206.
- Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C. Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research. Health Technol Assess 2000;4(3):i-v, 1-99.
- Davis KG, Abbott RL. Immunohaematological testing of the antenatal patient. Is the Rh(D) positive woman as important as the Rh(D) negative woman? Aust N Z J Obstet Gynaecol 1986;26 (4):253-6.
- Davis L. Daily fetal movement counting. A valuable assessment tool. J Nurse Midwifery 1987;32(1):11-9.

- de Cueto M, Sanchez MJ, Sampedro A, Miranda JA, Herruzo AJ, Rosa-Fraile M. Timing of intrapartum ampicillin and prevention of vertical transmission of group B streptococcus. Obstet Gynecol 1998;91 (1):112-4.
- Dempsey DA, Benowitz NL. Risks and benefits of nicotine to aid smoking cessation in pregnancy. Drug Saf 200;24(4):277-322.
- Department of Defense (DoD) Committee Consensus on Fetal Fibronectin Testing in Pregnancy, Fausett MB. October 2007.
- Department of Defense (DoD). Shaken Baby Syndrome Prevention Program is available at: www.militaryhomefront.dod.mil/service/fap/sbs
- Devoe LD, Sholl JS. Postdates pregnancy. Assessment of fetal risk and obstetric management. J Reprod Med 1983 Sep;28(9):576-80.
- Dewey KG, Heinig MJ, Nommsen LA. Maternal weight loss patterns during prolonged lactation. Am J Clin Nutr 1993;58 (2):162-6.
- Dias MS, Smith K, DeGuehery K, Mazur P, Li V, Shaffer ML. Preventing abusive head trauma among infants and young children: a hospital-based, parent education program. Pediatrics 2005 Apr;115:470-7.
- Dix DN. Why women decide not to breastfeed. Birth 199;18(4):222-5.
- Dixon JB, Dixon ME, O'Brien PE. Birth outcomes in obese women after laparoscopic adjustable gastric banding. Obstet Gynecol 2005 Nov;106 (Pt 1):965-72
- Dolan-Mullen P, Carbonari JP, Tabak ER, Glenday MC. Improving disclosure of smoking by pregnant women. Am J Obstet Gynecol 1991;165(2):409-13.
- Dolan-Mullen P, Ramirez G, Groff JY. A meta-analysis of randomized trials of prenatal smoking cessation interventions. Am J Obstet Gynecol 1994;17(5):1328-34.
- Donders GG, Desmyter J, De Wet DH, Van Assche FA. The association of gonorrhoea and syphilis with premature birth and low birthweight. Genitourin Med 1993 Apr;69(2):98-101.
- Dorfman DH, Glaser JH. Congenital syphilis presenting in infants after the newborn period. N Engl J Med 1990; 323(19):1299-302.
- Doyle NM, Monga M. Role of ultrasound in screening patients at risk for preterm delivery. Obstet Gynecol Clin North Am 2004 Mar;31(1):125-39.
- Dudley DJ, Cruikshank DP. Trauma and acute surgical emergencies in pregnancy. Semin Perinatol 1990;14(1):42-51.
- Duff P. Hepatitis in pregnancy. Semin Perinatol 1998;22(4):277-83.
- Dugoff L, Hobbins JC, Malone FD, Vidaver J, Sullivan L, Canick JA, Lambert-Messerlian GM, Porter TF, Luthy DA, Comstock CH, Saade G, Eddleman K, Merkatz IR, Craigo SD, Timor-Tritsch IE, Carr SR, Wolfe HM, D'Alton ME; FASTER Trial Research Consortium. Quad screen as a predictor of adverse pregnancy outcome. Obstet Gynecol 2005 Aug;106(2):260-7.
- Duley L, Henderson-Smart D, King M. Antiplatelet agents for preventing pre-eclampsia and its complication. Cochrane Database Syst Rev 2007Feb;(2):CD004659.
- Duncan B, Ey J, Holberg CJ, Wright AL, Martinez FD, Taussig LM. Exclusive breastfeeding for at least 4 months protects against otitis media. Pediatrics 1993;91(5):867-72.
- Ecker JL, Frigoletto FD. Routine ultrasound screening in low-risk pregnancies: imperatives for further study. Obstet Gynecol 1999;93(4):607-10.
- Eddleman KA, Malone FD, Sullivan L, Dukes K, Berkowitz RL, Kharbutli Y, Porter TF, Luthy DA, Comstock CH, Saade GR, Klugman S, Dugoff L, Craigo SD, Timor-Tritsch IE, Carr SR, Wolfe

- HM, D'Alton ME. Pregnancy loss rates after midtrimester amniocentesis. Obstet Gynecol 2006 Nov;108(5):1067-72.
- Eik-Nes SH. The fetal examination. Ultrasound Obstet Gynecol 1993 Mar 1;3(2):83-5.
- Einarson TR, Einarson A. Newer antidepressants in pregnancy and rates of major malformations: a metaanalysis of prospective comparative studies. Pharmacoepidemiol Drug Saf 2005 Dec;14(12):823-
- Enders G, Miller E, Cradock-Watson J, Bolley I, Ridehalgh M. Consequences of varicella and herpes zoster in pregnancy: prospective study of 1739 cases. Lancet 1994;343(8912):1548-51.
- Englund J, Glezen WP, Piedra PA. Maternal immunization against viral disease. Vaccine 1998;16(14-15):1456-63.
- Engstrom JL, Work BA. Prenatal prediction of small- and large-for-gestational age neonates. J Obstet Gynecol Neonatal Nurs 1992;21(6):486-95.
- Engstrom JL. Quickening and auscultation of fetal heart tones as estimators of the gestational interval. J Nurse-Midwifery 1985;30(1):25-32.
- Entrekin K, Work B, Owen J. Does a high carbohydrate preparatory diet affect the 3-hour oral glucose tolerance test in pregnancy? J Matern Fetal Med 1998 Mar-Apr;7(2):68-71.
- Epperson CN, Terman M, Terman JS, Hanusa BH, Oren DA, Peindl KS, Wisner KL. Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings. J Clin Psychiatry 2004 Mar;65(3):421-5.
- Epperson CN. Postpartum major depression: detection and treatment. Am Fam Physician 1999 Apr 15;59(8):2247-54, 2259-60.
- Escobar GM, Jesus Obregon M, Escobar del Rey F. Is neuropsychological development relted to maternal hypothyroiism or to maternal hypothyroxinemia? J Clin Endocrinol Metab 2000;85:549-55.
- Evins GG, Theofrastous JP, Galvin SL. Postpartum depression: a comparison of screening and routine clinical evaluation. Am J Obstet Gynecol 2000 May;182(5):1080-2.
- Ewigman BG, Crane JP, Frigoletto FD, LeFevre ML, Bain RP, McNellis D. Effect of prenatal ultrasound screening on perinatal outcome. RADIUS Study Group. N Engl J Med 1993;329(12):821-7.
- Faich G, Strobos J. Sodium ferric gluconate complex in sucrose: safer intravenous iron therapy than iron dextrans. Am J Kidney Dis 1999;33:464–70.
- Fingar AR, Francis BJ. American College of Preventive Medicine Practice Policy Statement: adult immunizations. Am J Prev Med 1998;14(2):156-8.
- Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK. Herpes simplex virus type 2 in the United States, 1976 to 1994. N Engl J Med 1997Oct 16;337(16):1105-11.
- Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH; Fetal Medicine Foundation Second Trimester Screening Group. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med 2007 Aug 2;357(5):462-9.
- Frenkel JK. Prevention of taxoplasma infection in pregnant women and their fetuses. Clin Infect Dis 1995;20 (3):727-9.
- Friedman E, Neff R. Pregnancy Hypertension: A systematic evaluation of clinical diagnostic criteria. 1st ed. Littleton, MA:1977.
- Fries MH, Bashford M, Nunes M. Implementing prenatal screening for cystic fibrosis in routine obstetric practice. Am J Obstet Gynecol 2006 Mar;192(2): 527-34.
- Gabbe SG, Turner LP. Reproductive hazards of the American lifestyle: work during pregnancy. Am J Obstet Gynecol 1997;176 (4):826-32.

- Gardella C, Brown Z, Wald A, Selke S, Zeh J, Morrow RA, Corey L. Risk factors for herpes simplex virus transmission to pregnant women: a couples study. Am J Obstet Gynecol 2005 Dec;193(6):1891-9.
- Gardosi J, Vanner T, Francis A. Gestational age and induction of labour for prolonged pregnancy. Br J Obstet Gynaecol 1997 Jul;104(7):792-7.
- Garner P, Okun N, Keely E, Wells G, Perkins S, Sylvain J, Belcher J. A randomized controlled trial of strict glycemic control and tertiary level obstetric care versus routine obstetric care in the management of gestational diabetes: a pilot study. Am J Obstet Gynecol 1997;177 (1):190-5.
- Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, Brody S, Miller WC. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ). 2005 Feb;(119):1-8.
- Gazmararian JA, Lazorick S, Spitz AM, Ballard TJ, Saltzman LE, Marks JS. Prevalence of violence against pregnant women. JAMA 1996;27 (24):1915-20.
- Geirsson RT, Have G. Comparison of actual and ultrasound estimated second trimester gestational length in in-vitro fertilized pregnancies. Acta Obstet Gynecol Scand 1993 Jul;72(5):344-6.
- Gencay M, Koskiniemi M, Ammala P, Fellman V, Narvanen A. Chlamydia trachomatis seropositivity is associated both with stillbirth and preterm delivery. APMIS 2000;108(9):584-8.
- Gennaro S, Hendricks-Muñoz KD, <u>Chhun N</u>. Maternal periodontal disease, pregnancy, and neonat Dasanayake APal outcomes. MCN Am J Maternal Child Nurs 2008 Jan-Feb;33(1):45-9.
- Georgiopoulos AM, Bryan TL, Yawn BP, Houston MS, Rummans TA, Therneau TM. Population-based screening for postpartum depression. Obstet Gynecol 1999 May;93(5 Pt 1):653-7.
- Gjerdingen DK, Yawn BP. Postpartum depression screening: importance, methods, barriers, and recommendations for practice. J Am Board Fam Med 2007 May-Jun;20(3):280-8.
- Goh YI, Bollano E, Einarson TR, Koren G. Prenatal multivitamin supplementation and rates of pediatric cancers: a meta-analysis. Clin Pharmacol Ther 2007 May;81(5):685-91.
- Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. N Engl J Med 2000;342 (20):1500-7.
- Goldenberg RL, Iams JD, Das A, Mercer BM, Meis PJ, Moawad AH, Miodovnik M, VanDorsten JP, Caritis SN, Thurnau GR, Dombrowski MP, Roberts JM, McNellis D. The Preterm Prediction Study: sequential cervical length and fetal fibronectin testing for the prediction of spontaneous preterm birth. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 2000 Mar;182(3):636-43.
- Goldenberg RL, Mercer BM, Meis PJ, Copper RL, Das A, McNellis D. The preterm prediction study: fetal fibronectin testing and spontaneous preterm birth. National Institute of Child health and Human Development Maternal Fetal Medicine Units Network. Obstet Gynecol 1996;87(5 Pt 1):643-8.
- Grace SL, Evindar A, Stewart DE. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature. Arch Womens Ment Health 2003 Nov;6(4):263-74.
- Grant A, Hepburn M. Merits of an individualized approach to fetal movement counting compared with fixed-time and fixed-number methods. Br J of Obstet and Gynaecol 1984;91(11):1087-90.
- Grant R, Flint K. Prenatal Screening for Fetal Aneuploidy: a commentary by the Canadian Down Syndrome Society. J Obstet Gynaecol Can 2007 Jul;29(97):580-2.
- Gribble RK, Meier PR, Berg RL. The value of urine screening for glucose at each prenatal visit. Obstet Gynecol 1995;86(3):405-10.
- Griffin ME, Coffey M, Johnson H, Scanlon P, Foley M, Stronge J, O'Meara NM, Firth RG. Universal vs. risk factor-based screening for gestational diabetes mellitus: detection rates, gestation at diagnosis and outcome. Diabet Med 2000;17(1):26-32.

- Grimes-Dennis J, Berghella V. Cervical length and prediction of preterm delivery. Curr Opin Obstet Gynecol 2007 Apr;19(2):191-5.
- Grote NK, Bledsoe SE, Swartz HA, Frank E. Feasibility of Providing Culturally Relevant, Brief Interpersonal Psychotherapy for Antenatal Depression in an Obstetrics Clinic: a pilot study. Research on Social Work Practice 2004;14(6): 397-407.
- Grote NK, Frank E. Difficult-to-treat depression: the role of contexts and comorbidities. Biol Psychiatry 2003 Apr 15;53(8):660-70.
- Guidetti DA, Divon MY, Langer O. Postdate fetal surveillance: is 41 weeks too early? Am J Obstet Gynecol 1989; 161(1):91-3.
- Guidozzi F, Ballot D, Rothberg AD. Human B19 parvovirus infection in an obstetric population. A prospective study determining fetal outcome. J Reprod Med 1994;39(1):36-8.
- Gurewitsch ED, Smith-Levitin M, Mack J. Pregnancy following gastric bypass surgery for morbid obesity. Obstet Gynecol 1996;88:658-61.
- Gwinn ML, Lee NC, Rhodes PH, Layde PM, Rubin GL. Pregnancy, breast feeding, and oral contraceptives and the risk of epithelial ovarian cancer. J Clin Epidemiol 1990;43(6):559-68.
- Haddow JE, Bradley LA, Palomaki GE, Doherty RA. Issues in implementing prenatal screening for cystic fibrosis: results of a working conference. J Med Screen 1999;6(2):60-6.
- Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD, Klein RZ. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341 (8):549-55.
- Haddow JE, Palomaki GE, Knight GJ, Cunningham GC, Lustig LS, Boyd PA. Reducing the need for amniocentesis in women 35 years of age or older with serum markers for screening. N Engl J Med 1994;330(16):1114-8.
- Haddow JE, Palomaki GE, Knight GJ, Williams J, Pulkkinen A, Canick JA, Saller DN, Jr., Bowers GB. Prenatal screening for Down's syndrome with use of maternal serum markers. N Engl J Med 1992;327 (9):588-93.
- Hager WD, Schuchat A, Gibbs R, Sweet R, Mead P, Larsen JW. Prevention of perinatal group B streptococcal infection: current controversies. Obstet Gynecol 2000;9(1):141-5.
- Hammer RL, Perkins J, Parr R. Exercise during the childbearing year. J Perinat Educ 2000;9(1):1-13.
- Hammerschlag MR, Anderka M, Semine DZ, McComb D, McCormack WM. Prospective study of maternal and infantile infection with Chlamydia trachomatis. Pediatrics 1979;64(2):142-8.
- Handmaker NS, Miller WR, Manicke M. Findings of a pilot study of motivational interviewing with pregnant drinkers. J Stud Alcohol 1999;60(2):285-7.
- Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. Term Breech Trial Collaborative Group. Lancet 2000 Oct 21;356(9239):1375-83.
- Hanusa BH, Scholle SH, Haskett RF, Spadaro K, Wisner KL. Screening for depression in the postpartum period: a comparison of three instruments. J Womens Health (Larchmt) 2008 May;17(4):585-96.
- Hart G. Syphilis tests in diagnostic and therapeutic decision making. Ann Intern Med 1986;104(3):368-76.
- Hartely BM, O'Connor ME. Evaluation of the 'Best Start' breast-feeding education program. Arch Pediatr Adolesc Med 1996;150(8):868-71.
- Hatch MC, Shu XO, McLean DE, Levin B, Begg M, Reuss L, Susser M. Maternal exercise during pregnancy, physical fitness, and fetal growth. Am J Epidemiol 1993;137(10):1105-14.

- Hauth JC, Goldenber RL, Andrews WW, Dubbard MB, Copper RL. Reduced incidence of preterm delivery with metronidazole and erytromycin in women with bacterial vaginosis. N Engl J Med 1995;333:1732-6.
- Heath VC, Daskalakis G, Zagaliki A, Carvalho M, Nicolaides KH. Cervicovaginal fibronectin and cervical length at 23 weeks of gestation: relative risk of early preterm delivery. BJOG 2000;107(10):1276-81
- Heath VC, Souka AP, Erasmus I, Gibb DM, Nicolaides KH. Cervical length at 23 weeks of gestation: the value of Shirodkar suture for the short cervix. Ultrasound Obstet Gynecol 1998;12(5):318-22.
- Heath VC, Southall TR, Souka AP, Elisseou A, Nicolaides KH. Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery. Ultrasound Obstet Gynecol 1998;12(5):312-7.
- Heath VC, Southall TR, Souka AP, Novakov A, Nicolaides KH. Cervical length at 23 weeks of gestation: relation to demographic characteristics and previous obstetric history. Ultrasound Obstet Gynecol 1998;12(5):304-11.
- Heimstad R, Romundstad PR, Salvesen KA. Induction of labour for post-term pregnancy and risk estimates for intrauterine and perinatal death. Acta Obstet Gynecol Scand 2008;87(2):247-9.
- Hemminki E, Rimpelä U. A randomized comparison of routine versus selective iron supplementation. J Am Coll Nutr Feb;10(1):3-10.
- Henderson JL, Weiner CP. Congenital infection. Curr Opin Obstet Gynecol 1995;(2):130-4.
- Herron MA, Katz M, Creasy RK. Evaluation of a preterm birth prevention program: preliminary report. Obstet Gynecol 1982;59 (4):452-6.
- Hibbard JU, Shashoua A, Adamczyk C, Ismail M. Cervical ripening with prostaglandin gel and hygroscopic dilators. Infect Dis Obstet Gynecol 1998;6(1):18-24.
- Hibbard JU, Tart M, Moawad AH. Cervical length at 16-22 weeks' gestation and risk for preterm delivery. Obstet Gynecol 2000;96(6):972-8.
- Higgins AC, Moxley JE, Pencharz PB, Mikolainis D, Dubois S. Impact of the Higgins Nutrition Intervention Program on birth weight: a within-mother analysis. J Am Diet Assoc 1989;89(8):1097-103.
- Higgins DL, Galavotti C, O'Reilly KR, Schnell DJ, Moore M, Rugg DL, Johnson R. Evidence for the effects of HIV antibody counseling and testing on risk behaviors. JAMA 1991;26(17):2419-29.
- Hill PD, Humenick SS. Nipple pain during breastfeeding: the first two weeks and beyond. J Perinat Educ1993; (2):21-35.
- Hill PD. Predictors of breastfeeding duration among WIC and non-WIC mothers. Pub Health Nurs 1991;8 (1):46-52.
- Hoffman MS, Hill DA, Gordy LW, Lane J, Cavanagh D. Comparing the yield of the standard Papanicolaou and endocervical brush smears. J Reprod Med 1991;36(4):267-9.
- Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2006 Jul;(3):CD001059
- Hofmeyr GJ, Hannah ME. Planned Caesarean section for term breech delivery. Cochrane Database Syst Rev 2001;(1):CD 000166.
- Hofmeyr GJ, Kulier R. Cephalic version by postural management for breech presentation. Cochrane Database Syst Rev 2000;(3):CD0000051.
- Hofmeyr GJ, Kulier R. External cephalic version for breech presentation at term. Cochrane Database Syst Rev 2000;(2):CD0000083..
- Hofmeyr GJ, Kulier R. Hands/knees posture in late pregnancy or labour for fetal malposition (lateral or posterior). Cochrane Database Syst Rev 2005;(2):CD001063

- Honest H, Bachmann LM, Coomarasamy A, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervical transvaginal sonography in predicting preterm birth: a systematic review. Ultrasound Obstet Gynecol 2003 Sep;22(3):305-22.
- Honest H, Bachmann LM, Gutpa JK, Kleijnen J, Khan K. Accuracy of cervicovaginal fetal fibronectin test in predicting spontaneous preterm birth: systematic review. BJM 2002 Aug 10;325(7359): 301-4.
- Honest H, Sharma S, Khan KS. Rapid tests for group B Streptococcus colonization in laboring women: A systematic review. Pediatrics 2006 Apr;117(4):1055-66.
- Hooper DE. Detecting GD and preeclampsia. Effectiveness of routine urine screening for glucose and protein. J Reprod Med 1996;41(12):885-8.
- Horrigan TJ, Piazza NJ, Weinstein L. The substance abuse subtle screening inventory is more cost effective and has better selectivity than urine toxicology for the detection of substance abuse in pregnancy. J Perinatol 1996; 16(5):326-30.
- Horstmann DM, Schluederberg A, Emmons JE, Evans BK, Randolph MF, Andiman WA. Persistence of vaccine-induced immune responses to rubella: comparison with natural infection. Rev Infect Dis 1985;7 (Suppl 1):S80-5.
- Howard H, Martlew V, McFadyen I, Clarke C, Duguid J, Bromilow I, Eggington J. Consequences for fetus and neonate of maternal red cell allo-immunisation. Arch Dis Child Fetal Neonatal Ed 1998;78(1):F62-6.
- Howell EM, Heiser N, Harrington M. A review of recent findings on substance abuse treatment for pregnant women. J Subst Abuse Treat 1999;16(3):195-219.
- Howie PW, Forsyth JS, Ogston SA, Clark A, du V Florey C. Protective effect of breastfeeding against infection. BMJ 1990;300(6716):11-6.
- Hughes A. A dilation on dilatation. Lancet 1993 Apr 3;341(8849):867.
- Humenick SS, Hill PD, Wilhelm S. Postnatal factors encouraging sustained breastfeeding among primiparas and multiparas. J Perinatal Education 1997;6(3):33-45.
- Hunter AG, Cappelli M, Humphreys L, Allanson JE, Chiu TT, Peeters C, Moher D, Zimak A. A randomized trial comparing alternative approaches to prenatal diagnosis counseling in advanced maternal age patients. Clin Genet 2005 Apr;67(4):303-13.
- Iams JD, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A, Thom E, McNellis D, Copper RL, Johnson F, Roberts JM. The length of the cervix and the risk of spontaneous premature delivery. National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. N Engl J Med 1996; 334 (9):567-72.
- Iams JD, Goldenberg RL, Mercer BM, Moawad A, Thom E, Meis PJ, McNellis D, Caritis SN, Miodovnik M, Menard MK, Thurnau GR, Bottoms SE, Roberts JM. The Preterm Prediction Study: recurrence risk of spontaneous preterm birth. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 1998;178(5):1035-40.
- Iams JD, Goldsmith LT, Weiss G. The preterm prediction study: maternal serum relaxin, sonographic cervical length, and spontaneous preterm birth in twins. J Soc Gynecol Investig 2001;8(1):39-42.
- Iams JD, Stilson R, Johnson FF, Williams RA, Rice R. Symptoms that precede preterm labor and preterm premature rupture of the membranes. Am J Obstet Gynecol 1990;162(2):486-90.
- Ickovics JR, Kershaw TS, Westdahl C, Magriples U, Massey Z, Reynolds H, Rising SS. Group prenatal care and perinatal outcomes: a randomized controlled trial. Obstet Gynecol 2007;110(2 Pt 1):330-9.
- Institute for Clinical Systems Improvement (ICSI), Immunizations 2001; Available from: ICSI:Bloomington MN.

- Institute of Medicine (U.S.). Subcommittee on Nutritional Status and Weight Gain during Pregnancy., Institute of Medicine (U.S.). Subcommittee on Dietary Intake and Nutrient Supplements during Pregnancy. Nutrition during pregnancy: part I, weight gain: part II, nutrient supplements. Washington, D.C.: National Academy Press; 1990. 1-222 p.
- Institute of Medicine (US). Iron deficiency anemia: recommended guidelines for the prevention, detection, and management among U.S. children and women of childbearing age. Washington, DC: National Academy Press; 1993. 1-126p.
- Jazayeri A, Heffron JA, Harnetty P, Jazayeri M, Gould SF. Antepartum and postpartum Papanicolaou smears. Are they both necessary? J Reprod Med 1999;44(10):879-82.
- Jesse DE, Swanson MS. Risks and resources associated with antepartum risk for depression among rural southern women. Nurs Res 2007 Nov-Dec;56(6):378-86.
- Jimenez JM, Tyson JE, Reisch JS. Clinical measures of gestational age in normal pregnancies. Obstet Gynecol 1983;61 (4):438-43.
- Johnson-Spear MA, Yip R. Hemoglobin difference between black and white women with comparable iron status: justification for race-specific anemia criteria. Am J Clin Nutr 1994;60:117–21.
- Jones KL, Johnson KA, Chambers CD. Offspring of women infected with varicella during pregnancy: a prospective study. Teratology 1994;49 (1):29-32.
- Katz M, Goodyear K, Creasy RK. Early signs and symptoms of preterm labor. Am J Obstet Gynecol 1990;162 (5):1150-3.
- Kellner LH, Weiss RR, Weiner Z, Neuer M, Martin GM, Schulman H, Lipper S. The advantages of using triple-marker screening for chromosomal abnormalities. Am J Obstet Gynecol 1995;172 (3):831-6
- Kelly A, Kevany J, de Onis M, Shah PM. A WHO collaborative study of maternal anthropometry and pregnancy outcomes. Int J Gynaecol Obstet 1997;5(1):1-15.
- Kent T, Gregor J, Deardorff L, Katz V. Edema of pregnancy: a comparison of water aerobics and static immersion. Obstet Gynecol 1999;94(5 Pt 1):726-9.
- Kieler H, Ahlsten G, Haglune B, Salvesen K, Axelsson O. Routine ultrasound screening in pregnancy and the children's subsequent neurologic development. Obstet Gynecol 1998;91(5 Pt 1):750-6.
- Koonings PP, Dickinson K, d'Ablaing G, III, Schlaerth JB. A randomized clinical trial comparing the Cytobrush and cotton swab for Papanicolaou smears. Obstet Gynecol 1992;80(2):241-5.
- Kozer E, Costei A, Boskovic R, Nulman I, Nikfar S, Koren G. Effects of aspirin consumption during pregnancy on pregnancy outcomes: meta-analysis. Birth Defects Research 2003Feb;68(1):70-84.
- Kragt H, Keirse MJ. How accurate is a woman's diagnosis of threatened preterm delivery? Br J Obstet Gynaecol 1990;97(4):317-23.
- Kramer MS, McDonald SW. Aerobic exercise for women during pregnancy. Cochrane Database Syst Rev 2006;(3):CD000180.
- Kramer MS. Balanced protein/energy supplementation in pregnancy. Cochrane Database Syst Rev 2003;(4):CD000032.
- Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. Bull World Health Organ 1987;65(5):663-737.
- Kramer MS. Energy/protein restriction for high weight-for-height or weight gain during pregnancy. Cochrane Database Syst Rev 2000;(2):CD000080.
- Kramer MS. High protein supplementation in pregnancy. Cochrane Database Syst Rev 2000;(2):CD000105.

- Kramer MS. Isocaloric balanced protein supplementation in pregnancy. Eur J Clin Nutr 2000Feb;54(2):180.
- Kroenke K R, Spitzer RL, Williams JB. The Patient Health Questionnaire 2 Validity of a two item depression screener. Med Care 2003 Nov 41(11):1284 92.
- Krogh V, Duffy LC, Wong D, Rosenband M, Riddlesberger KR, Ogra PL. Postpartum immunization with rubella virus vaccine and antibody response in breast-feeding infants. J Lab Clin Med 1989;113(6):695-9.
- Kuo VS, Koumantakis G, Gallery ED. Proteinuria and its assessment in normal and hypertensive pregnancy. Am J Obstet Gynecol 1993 dec;169(6):1654.
- Langer O, Brustman L, Anyaegbunam A, Mazze R. The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. Am J Obstet Gynecol 1987;157(3):758-63.
- LaPolla JP, O'Neil C, Wetrich D. Colposcopic management of abnormal cervical cytology in pregnancy. J Reprod Med 1988;33(3):301-6.
- Layde PM, Webster LA, Baughman AL, Wingo PA, Rubin GL, Ory HW. The independent associations of parity, age at first full term pregnancy, and duration of breastfeeding with the risk of breast cancer. J Clin Epidemiol 1989;42(10):963-73.
- LeFevre ML, Bain RP, Ewigman BG, Frigoletto FD, Crane JP, McNellis D. A randomized trial of prenatal ultrasonographic screening: impact on maternal management and outcome. RADIUS (Routine Antenatal Diagnostic Imaging with Ultrasound). Am J Obstet Gynecol 1993 Sep;169(3):483-9.
- Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Hisslein P. Bacterial Vaginosis as a Risk Factor for Preterm Delivery. Am J Obst Gynecol 2003 Jul;189(1) 139-47.
- Leitich H, Egarter C, Kaider A, Hohlagschwandtner M, Berghammer P, Husslein P. Cervicovaginal fetal fibronectin as a marker for preterm delivery: a meta-analysis. Am J Obstet Gynecol 1999;180(5):1169-76.
- Lennon CA, Gray DL. Sensitivity and specificity of ultrasound for the detection of neural tube and ventral wall defects in a high-risk population. Obstet Gynecol 1999 Oct;94(4):562-6
- Lettieri L, Vintzileos AM, Rodis JF, Albini SM, Salafia CM. Does "idiopathic" preterm labor resulting in preterm birth exist? Am J Obstet Gynecol 1993;168(5):1480-5.
- Leu RH. Complications of coexisting chlamydial and gonococcal infections. Postgrad Med 1991;89(7):56-60.
- Levinson-Castiel R, Merlob P, Linder N, Sirota L, Klinger G. Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. Arch Pediatr Adolesc Med 2006 Feb;160(2):173-6.
- Li XM, Shi MF, Yang YB, Shi ZJ, Hou HY, Shen HM, Teng BQ. Effect of hepatitis B immunoglobulin on interruption of HBV intrauterine infection. World J Gastroenterol 2004 Nov 1;10:3215-7.
- Lin FY, Brenner RA, Johnson YR, Azimi PH, Philips JBr, Regan JA, Clark P, Weisman LE, Rhoads GG, Kong F, Clemens JD. The effectiveness of risk-based intrapartum chemoprophylaxis for the prevention of early-onset neonatal group B streptococcal disease. Am J Obstet Gynecol 2001;184(6):1204-10.
- Lindhard A, Nielsen PV, Mouritsen LA, Zachariassen A, Sorensen HU, Roseno H. The implications of introducing the symphyseal-fundal height- measurement. A prospective randomized controlled trial. Br J Obstet Gynaecol 1990;97(8):675-80.
- Lindsay MK, Graves W, Klein L. The relationship of one abnormal glucose tolerance test value and pregnancy complications. Obstet Gynecol 1989;7(1):103-6.
- Londo R, Bjelland T, Girod C, Glasser M. Prenatal and postpartum Pap smears: do we need both? Fam Pract Res J 1994;14(4):359-67.

- Louik C, Lin AE, Werler MM, Hernández-Díaz S, Mitchell AA. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. N Engl J Med 2007 Jun 28;356(26):2675-83.
- Luke B, Mamelle N, Keith L, Munoz F, Minogue J, Papiernik E, Johnson TR. The association between occupational factors and preterm birth: a United States nurses' study. Research Committee of the Association of Women's Health, Obstetric, and Neonatal Nurses. Am J Obstet Gynecol 1995;173(3 Pt 1):849-62.
- Lumley J, Oliver SS, Chamberlain C, Oakley L. Interventions for promoting smoking cessation during pregnancy. Cochrane Database Syst Rev 2004 Oct 18;(4):CD001055.
- Lumley J, Watson L, Watson M, Bower C. Periconceptional supplementation with folate and/oprmultivitamins for preventing neural tube defects. Cochrane Database Syst Rev 2001(3):CD001056.
- Lumley J. The epidemiology of preterm birth. Baillieres Clin Obstet Gynaecol 1993 Sep;7(3):477-98.
- Lurain JR, Gallop DG. Management of abnormal Papanicolaou smears in pregnancy. Obstet Gynecol 1979;53 (4):484-8.
- Lydon-Rochelle M, Albers L, Gorwoda J, Craig E, Qualls C. Accuracy of Leopold maneuvers in screening for malpresentation: a prospective study. Birth 1993;20(3):132-5.
- Mahomed K, Gulmezoglu AM. Pyridoxine (vitamin B6) supplementation in pregnancy. Cochrane Database Syst Rev 2001b;(2):CD000179.
- Mahomed K, Gulmezoglu AM. Vitamin D supplementation in pregnancy. Cochrane Database Syst Rev 2000;(2):CD000228.
- Mahomed K. Folate supplementation in pregnancy. Cochrane Database Syst Rev 2000c;(2):CD000183.
- Mahomed K. Iron supplementation in pregnancy. Cochrane Database Syst Rev 2000d;(2):CD001135.
- Main EK, Slagle T. Prevention of early-onset invasive neonatal group B streptococcal disease in a private hospital setting: the superiority of culture-based protocols. Am J Obstet Gynecol 2000;182(6):1344-54.
- Malone FD, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, Berkowitz RL, Gross SJ, Dugoff L, Craigo SD, Timor-Tritsch IE, Carr SR, Wolfe HM, Dukes K, Bianchi DW, Rudnicka AR, Hackshaw AK, Lambert-Messerlian G, Wald NJ, D'Alton ME; First- and Second-Trimester Evaluation of Risk (FASTER)Research Consortium. First-trimester or second-trimester screening, or both, for Down's syndrome. N Engl J Med 2005 Nov 10;353(19)2068-70.
- Malone FD, Wald NJ, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, Berkowitz RL, Gross SJ, Dugoff L, Craigo SD, Timor-Tritsch IE, Carr SR,M, Dukes K, Bianchi DW, Rudnicka AR, Hackshaw AK, Lambert-Messerlian G, Wald NJ, D'Alton ME; First- and second-trimester evaluation of risk (FASTER) trial: principal results of the NICHD multicenter Down syndrome screening study. Am J Obstet Gynecol 2003;189:(suppl 1):s56.
- Manning FA, Snijders R, Harman CR, Nicolaides K, Menticoglou S, Morrison I. Fetal biophysical profile score. VI. Correlation with antepartum umbilical venous fetal pH. Am J Obstet Gynecol 1993;169(4):755-63.
- Martin-Hirsch P, Lilford R, Jarvis G, Kitchener HC. Efficacy of cervical-smear collection devices; a systematic review and meta-analysis. Lancet 1999 Nov 20;354(9192):1763-70.
- Mast EE, Margolis HS, Fiore AE, Brind EW, Goldstein ST, Wang SA, Moyer LA, Bell BP, Alter MJ, Advisory Committee on Immunization Practices (ACIP). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. MMWR Recomm Rep 2005 Dec 23;54(RR-16):1-31.
- Mathai M, Jairaj P, Muthurathnam S. Screening for light-for-gestational age infants: a comparison of three simple measurements. Br J Obstet Gynaecol 1987;94(3):217-21.

- McDonald HM, Brocklehurst P, Gordon A., Antibiotics for Treating Bacterial Vaginosis in Pregnancy. Cochrane Database Syst. Rev 2007 Jan 24:(1):CD000262.
- McElhaney RD, Jr., Ringer M, DeHart DJ, Vasilenko P. Rubella immunity in a cohort of pregnant women. Infect Control Hosp Epidemiol 1999;20(1):64-6.
- McFarlane J, Greenberg L, Weltge A, Watson M. Identification of abuse in emergency departments: effectiveness of a two-question screening tool. J Emerg Nurs 1995;21(5):391-4.
- McFarlane J, Malecha A, Gist J, Schultz P, Willson P, Fredland N. Indicators of intimate partner violence in women's employment: implications for workplace action. AAOHN J 2000 May;48(5):215-20.
- McFarlane J, Parker B, Soeken K, Bullock L. Assessing for abuse during pregnancy. Severity and frequency of injuries and associated entry into prenatal care. JAMA 1992; 267(23):3176-8.
- McGregor JA, French JI, Richter R, Franco-Buff A, Johnson A, Hillier SL, Judson FN, Todd JK. Antenatal microbiologic and maternal risk factors associated with prematurity. Am J Obstet Gynecol 1990;163(5 pt 1):1465-73.
- Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, Spong CY, Hauth JC, Miodovnik M, Varner MW, Leveno KJ, Caritis SN, Iams JD, Wapner RJ, Conway D, O'Sullivan MJ, Carpenter M, Mercer B, Ramin SM, Thorp JM, Peaceman AM, Gabbe S; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network.et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003 Jun 12;348(24):2379–85.
- Michalowicz BS, Hodges JS, DiAngelis AJ, Lupo VR, Novak MJ, Ferguson JE, Buchanan W, Bofill J, Papapanou PN, Mitchell DA, Matseoane S, Tschida PA; OPT Study. Treatment of Periodontal Disease and the Risk of Preterm Birth. N Engl J Med 2006 Nov2; 355(18):1885-94.
- Michielsen PP, Van Damme P. Viral hepatitis and pregnancy. Acta Gastroenterol Belg 1999 Jan-Mar;62(1):21-9.
- Midanik LT, Zahnd EG, Klein D. Alcohol and drug CAGE screeners for pregnant, low-income women: the California Perinatal Needs Assessment. Alcohol Clin Exp Res 1998;22(1)121-5.
- Millar L, DeBuque L, Leialoha C, Grandinetti A, Killeen J. Rapid enzymatic urine screening test to detect bacteriuria in pregnancy. Obstet Gynecol 2000;95(4):601-4.
- Milman N, Bergholt T, Byg KE, Eriksen L, Graudal N. Iron status and iron balance during pregnancy. A critical reappraisal of iron supplementation. Acta Obstet Gynecol Scand 1999;78(9):749-57.
- Misri S, Kendrick K. Treatment of perinatal mood and anxiety disorders: a review. Can J Psychiatry 2007 Aug;52(8):489-98.
- Misri S, Reebye P, Corral M, Milis L. The use of paroxetine and cognitive-behavioral therapy in postpartum depression and anxiety: a randomized controlled trial. J Clin Psychiatry 2004 Sep;65(9):1236-41.
- Mongelli M, Gardosi J. <u>Gestation-adjusted projection of estimated fetal weight.</u> Acta Obstet Gynecol Scand 1996 Jan;75(1):28-31.
- Moore TR, Piacquadio K. A prospective evaluation of fetal movement screening to reduce the incidence of antepartum fetal death. Am J Obstetr and Gynecol 1989;160(5, Pt 1):1075-80.
- Morris SN, Johnson NR. Exercise during pregnancy: a critical appraisal of the literature. J Repro Med 2005 Mar;50(3):181-8.
- Morrison JC. Preterm birth: a puzzle worth solving. Obstet Gynecol 1990;7(1 Suppl):5S-12S.
- Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: a meta-analysis. Obstet Gynecol 2000;95(4):623-35.

- Mul T, Mongelli M, Gardosi J. A comparative analysis of second-trimester ultrasound dating formulae in pregnancies conceived with artificial reproductive techniques. Ultrasound Obstet Gynecol 1996 Dec;8(6):397-402.
- Nadel AS, Green JK, Holmes LB, Frigoletto FD, Jr., Benacerraf BR. Absence of need for amniocentesis in patients with elevated levels of maternal serum alpha-fetoprotein and normal ultrasonographic examinations. N Engl J Med 1990;323(9):557-61.
- National Center on Shaken Baby Syndrome. Available at: www.dontshake.com.
- National Diabetes Data Group (NDDG). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes Care 1979; 28(12):1039-105.
- National Institute for Health and Clinical Excellence (NICE) 2003. Guideline on Antenatal care: routine care for the healthy pregnant woman, NICE clinical guideline 2003; 62. Available at: www.nice.org.uk
- National Institute for Health and Clinical Excellence (NICE) 2007 Antenatal and postnatal mental health: clinical management and service guidance. NICE clinical guideline 2007; 45. Available at: www.nice.org.uk
- National Institutes of Health, National Heart, Lung, and Blood Institute. National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 1990 Nov;163(5 Pt 1):1691-712.
- National Institutes of Health, National Heart, Lung, and Blood Institute. National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. July 2000; Publication No. 003029.
- National Institutes of Health, State-of-the-Science Conference Statement on cesarean delivery on maternal request. NIH Consens State Sci Statements 2006 Mar 27-29;23(1):1-29.
- Naylor CD, Sermer M, Chen E, Farine E. Selective screening for gestational diabetes mellitus. Toronto Tri-Hospital Gestational Diabetes Investigators. N Engl J Med 1997;337(22):1591-6.
- Neilson JP. Ultrasound for routine fetal assessment in early pregnancy. Cochrane database Syst Rev 2000;(2):CD000182.
- Neldam, S. Fetal movement as an indicator of fetal well-being. Lancet 1980;1(8180):1222-4.
- New York State Department of Health, 2006. New York State Department of Health: Practice guidelines on oral health care during pregnancy and early childhood: New York State Department of Health.
- Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchaltranslucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. BMJ 1992;304:867–9.
- Nicolaides KH. Nuchal translucency and other first trimester sonographic markers of chromosomal abnormalities. Am J Obstet Gynecol 2004;191:45–67.
- Nielsen PE, Howard BC, Hill CC, Larson PL, Holland RH, Smith PN. Comparison of elective induction of labor with favorable Bishop scores versus expectant management: a randomized clinical trial. J Matern Fetal Neonatal Med 2005 Jul;18(1):59-64.
- Norton LB, Peipert JF, Zierler S, Lima B, Hume L. Battering in pregnancy: an assessment of two screening methods. Obstet Gynecol 1995;85(3):321-5.
- O'Brien KO, Zavaleta N, Caulfield LE, Yang DX, Abrams SA. Influence of prenatal iron and zinc supplements on supplemental iron absorption, red blood cell iron incorporation, and iron status in pregnant Peruvian women. Am J Clin Nutr 1999;69(3):509-15.
- Oncken CA, Kranzler HR. Pharmacotherapies to enhance smoking cessation during pregnancy. Drug Alcohol Rev 2003 Jun;22(2):191-202.
- Oregon Evidence-based Practice Center (Oregon Health and Science University). Screening for iron deficiency anemia in childhood and pregnancy: update of the 1996 U.S. Preventive Task Force

- review. Agency for Healthcare Research and Quality. Available at: AHRQ, Publication No. 06-0590-EF-1. Rockville, MD:2006.
- Oren DA, Wisner KL, Spinelli M, Epperson CN, Peindl KS, Terman JS, Terman M. An open trial of morning light therapy for treatment of antepartum depression. Am J Psychiatry 2002 Apr;159(4):666-9.
- Panjari M, Bell R, Bishop S, Astbury J, Rice G, Doery J. A randomized controlled trial of a smoking cessation intervention during pregnancy. Aust N Z J Obstet Gynaecol 1999;39(3):312-7.
- Papiernik E, Bouyer J, Collin D, Winisdoerffer G, Dreyfus J. Precocious cervical ripening and preterm labor. Obstet Gynecol 1986;67(2):238-42.
- Parker B, McFarlane J, Soeken K, Silva C, Reel S. Testing an intervention to prevent further abuse to pregnant women. Res Nurs Health 1999;22(1):59-66.
- Parsons MT, Spellacy WN. Prospective randomized study of x-ray pelvimetry in the primigravida. Obstet Gynecol 1985;66(1):76-9.
- Partridge CA, Holman JR. Effects of a reduced-visit prenatal care clinical practice guideline. J Am Board Fam Pract 2005 Nov-Dec;18(6):555-60.
- Pastuszak AL, Levy M, Schick B, Zuber C, Feldkamp M, Gladstone J, Bar-Levy F, Jackson E, Donnenfeld A, Meschino W, et al. Outcome after maternal varicella infection in the first 20 weeks of pregnancy. N Engl J Med 1994;330(13):901-5.
- Pati S, Cullins V. Female sterilization. Obstet and Gynecol Clin North Am 2000;27(4):859-99.
- Patrick J, Campbell K, Carmichael L, Natale R, Richardson B. Patterns of gross fetal body movements over 24 hour observation intervals during the last 10 weeks of pregnancy. Am J Obstet Gynecol 1982;142(4):363-71.
- Pattinson RC. Pelvimetry for fetal cephalic presentations at term. Cochrane database Syst Rev 2000;(2):CD000161.
- Pearce JM, Campbell S. A comparison of symphysis-fundal height and ultrasound as screening tests for light-for-gestational age infants. Br J Obstet Gynaecol 1987;94(2):100-4.
- Pearson JF, Weaver JB. Fetal activity and fetal wellbeing: an evaluation. Br Med J 1976 May 29;1(6021):1305-7.
- Peek MJ, Devonald KJ, Beilby R, Ellwood D. The value of routine early pregnancy ultrasound in the antenatal booking clinic. Aust N Z J Obstet Gynaecol 1994 May;34(2):140-3.
- Peindl KS, Wisner KL, Hanusa BH. Identifying depression in the first postpartum year: guidelines for office-based screening and referral. J Affect Disord 2004 May;80(1):37-44.
- Pena-Rosa JP, Viteri FE. Effects of routine oral iron supplementation with or without folic acidfor women during pregnancy. Cocharane Database Syst Rev 2006 Jul 19;(3):CD004736.
- Perez EM, Hendricks MK, Beard JL, Murray-Kolb LE, Berg A, Tomlinson M, Irlam J, Isaccs W, Njengele T, Sive A, Vernon-Feagans L.Mother-infant interactions and infant development are altered by maternal iron deficiency anemia. J Nutr 2005 Apr;135(4):850–5.
- Perry GS, Byers T, Yip R, Margen S. Iron nutrition does not account for the hemoglobin differences between blacks and whites. J Nutr 1992 Jul;122(7):1417–24.
- Pop VJ, DeVries E, van Baar AL, Waelkens JJ, de Rooy HA, Horsten M, Donkers MM, Komproe IH, van Son MM, Vader HL. Maternal thyroid peroxidase antibodies during pregnancy: a marker of impaired child development. J Clin Endocrinal Metab 1995;80(12):3561.
- Prema K, Ramalakshmi BA, Babu S. Diuretic therapy in pregnancy induced hypertension and pregnancy edema. Indian J Med Res 1982 Apr;75:545-53.

- Quaranta P, Currell R, Redman CW, Robinson JS. Prediction of small-for-dates infants by measurement of symphysial-fundal-height. Br J Obstet Gynaecol 1981;88(2):115-9.
- Ramsay J, Richardson J, Carter YH, Davidson LL, Feder G. Should health professionals screen women for domestic violence? Systematic review. BMJ 2002 Aug;325(7359):314.
- Ramsey PS, Andrews WW. Biochemical predictors of preterm labor: fetal fibronectin and salivary estriol. Clin Perinatol 2003 Dec;30(4):701-33.
- Rarick TL, Tchabo JG. Timing of the postpartum Papanicolaou smear. Obstet Gynecol 1994 Oct;83(5 Pt 1):761-5.
- Read JS, Klebanoff MA. Sexual intercourse during pregnancy and preterm delivery: effects of vaginal microorganisms. The Vaginal Infections and Prematurity Study Group. Am J Obstet Gynecol 1993;168 (2):514-9.
- Renker PR, Tonkin P. Postpartum women's evaluations of an audio/video computer-assisted perinatal violence screen. Comput Inform Nurs 2007 May-Jun;25(3):139-47.
- Resta RG. Changing demographics of advanced maternal age (AMA) and the impact on the predicted incidence of Down syndrome in the United States: Implications for prenatal screening and genetic counseling. Am J Med Genet A 2005;133:31–6.
- Revah A, Hannah ME, Sue-A-Quan AK. Fetal fibronectin as a predictor of preterm birth: an overview. Am J Perinatol 1998;15(11):613-21.
- Reveiz L, Gyte GM, Cuervo LG. Treatments for iron-deficiency anaemia in pregnancy. Cochrane Database Sys Rev 2007 Apr 18;(2):CD003094.
- Reynolds KD, Coombs DW, Lowe JB, Peterson PL, Gayoso E. Evaluation of a self-help program to reduce alcohol consumption among pregnant women. Int J Addict 1995;30(4):427-43.
- Riggs MA, Klebanoff MA. Treatment of vaginal infections to prevent preterm birth: a meta-analysis. Clin Obstet Gynecol 2004 Dec:47(4):796-807.
- Righetti-Veltema M, Bousquet A, Manzano J. Impact of postpartum depressive symptoms on mother and her 18-month-old infant. Eur Child Adolesc Psychiatry 2003 Apr;12(2):75-83.
- Rising SS, Kennedy HP, Klima C. Redesigning prenatal care through Centering Pregnancy. J Midwifery Womens Health 2004 Sep-Oct;49(5):398-404.
- Rolfs RT, Galaid EI, Zaidi AA. Pelvic inflammatory disease: trends in hospitalizations and office visits, 1979 through 1988. Am J Obstet Gynecol 1992;166(3):983-90.
- Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC, Bracken M. Meta-analysis of the relationship between asymptomatic bacteriuria and preterm delivery/low birth weight. Obstet Gynecol 1989;73(4):576-82.
- Rosen DJ, Michaeli G, Markov S, Greenspoon JS, Goldberger SB, Fejgin MD. Fetal surveillance. Should it begin at 40 weeks' gestation in a low-risk population? J Reprod Med 1995;40(2):135-9.
- Rosenfeld JA, Everett KD. Factors related to planned and unplanned pregnancies. J Fam Pract 1996 Aug;43(2):161-6.
- Ross MG, Hobel CJ, Bragonier JR, Bear MB, Bemis RL. A simplified risk-scoring system for prematurity. Am J Perinatol 1986;3(4):339-44.
- Rutherford SE, Phelan JP, Smith CV, Jacobs N. The four-quadrant assessment of amniotic fluid volume: an adjunct to antepartum fetal heart rate testing. Obstet Gynecol 1987;70(3 Pt 1):353-6.
- Ryan D, Milis L, Misri N. Depression during pregnancy. Can Fam Physician. 2005 Aug;51:1087-93.
- Saari-Kemppainen A, Karjalainen O, Ylostalo P, Heinonen OP. Ultrasound screening and perinatal mortality: controlled trial of systematic one-stage screening in pregnancy. The Helsinki ultrasound trial. Lancet 1990 Aug 18;336(8712):387-91

- Sadovsky E, Yaffe H. Daily fetal movement recording and fetal prognosis. Obstet Gynecol 1973;41(6):845-50.
- Sady SP, Carpenter MW, Thompson PD, Sady MA, Haydon B, Coustan DR. Cardiovascular response to cycle exercise during and after pregnancy. J Appl Physiol 1989;66(1):336-41.
- Sanchez-Ramos L, Olivier F, Delke I, Kaunitz AM.Labor induction versus expectant management for postterm pregnancies: a systematic review with meta-analysis. Obstet Gynecol 2003 Jun;101(6):1312-8.
- Sangfelt P, Reichard O, Lidman K, von Sydow M, Forsgren M. Prevention of hepatitis B by immunization of the newborn infant--a long- term follow-up study in Stockholm, Sweden. Scand J Infect Dis 1995;27(1):3-7.
- Saslow D, Runowicz CD, Solomon D, Moscicki AB, Smith RA, Eyre HJ, Cohen C; American Cancer Society. American Cancer Society guideline for the early detection of cervical neoplasia and cancer. CA Cancer J Clin. 2002 Nov-Dec;52(6):342-62.
- Schoub BD, Johnson S, McAnerney JM, Blackburn NK, Guidozzi F, Ballot D, Rothberg A. Is antenatal screening for rubella and cytomegalovirus justified? S Afr Med J 1993;83(2):108-10.
- Sebire NJ, Jolly M, Harris J, Regan L, Robinson S. Is maternal underweight really a risk factor for adverse pregnancy outcome? A population-based study in London. BJOG 2001Jan; 2001(108):1:61-6.
- Seeds AE. Current concepts of amniotic fluid dynamics. Am J Obstet and Gynecol 1980;138:575-86.
- Shetty A, Burt R, Rice P, Templeton A. Women's perceptions, expectations and satisfaction with induced labour--a questionnaire-based study. Eur J Obstet Gynecol Reprod Biol. 2005 Nov 1;123(1):56-61.
- Sims ME, Walther FP. Neonatal morbidity and mortality and long-term outcome of postdate infants. Clin Obstet Gynecol 1989 Jun;32(2):289-93.
- Sladkevicius P, Saltvedt S, Almström H, Kublickas M, Grunewald C, Valentin L. Ultrasound dating at 12-14 weeks of gestation. A prospective cross-validation of established dating formulae in in-vitro fertilized pregnancies. Ultrasound Obstet Gynecol 2005 Oct;26(5):504-11.
- Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Sys Rev 2001;(2):CD000490.
- Smaill F. Intrapartum antibiotics for group B streptococcal colonisation Cochrane Database Sys Rev 2000;(2):CD000115.
- Smith WJ, Jackson LA, Watts DH, Koepsell TD. Prevention of chickenpox in reproductive-age women: cost-effectiveness of routine prenatal screening with postpartum vaccination of susceptibles. Obstet Gynecol 1998;92(4 Pt 1):535-45.
- Smith-Bindman R, Hosmer W, Felstein VA, Deeks JJ, Goldberg JD. Second-trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. JAMA 2001;285(8):1044-55.
- Snijders RJ, Thom EA, Zachary JM, Platt LD, Greene N, Jackson LG, Sabbagha RE, Filkins K, Silver RK, Hogge WA, Ginsberg NA, Beverly S, Morgan P, Blum K, Chilis P, Hill LM, Hecker J, Wapner RJ. First-trimester trisomy screening: nuchal translucency measurement training and quality assurance to correct and unify technique. Ultrasound Obstet Gynecol 2002 Apr;19(4):353–9.
- Society of Obstetricians and Gynaecologists of Canada (SOGC). Guidelines for ultrasound as a routine part of prenatal care. J Soc Obstet Gynaecol Can 1999;21(9):874-9
- Soliman MH. Impact of antenatal counseling on couples' knowledge and practice of contraception in Mansoura, Egypt. East Mediterr Health J 1999 Sep;5(5):1002-13.
- Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. Am J Psychiatry 2003 Mar;160(3):555-62.

- Spinelli MG. Interpersonal psychotherapy for depressed antepartum women: a pilot study. Am J Psychiatry 1997 Jul;154(7):1028-30.
- St Pierre A, Mark PM, Michelson R, Condon LM, Nelson AF, Rolnick SJ. Alcohol and other drugs of abuse in pregnancy. HMO Pract 1996;10(3):114-8.
- Steece RS, Talley MS, Skeels MR, Lanier GA. Comparison of enzyme-linked immunosorbent assay, hemagglutination inhibition, and passive latex agglutination for determination of rubella immune status. J Clin Microbiol 1985;21(1):140-2.
- Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal weight, pregnancy weight gain, and the risk of antepartum stillbirth. Am J Obstet Gynecol 2001;184(3):463-9.
- Stephenson MJ. Screening for gestational diabetes mellitus: a critical review. J Fam Pract 1993;37(3):277-83.
- Stergachis A, Scholes D, Heidrich FE, Sherer DM, Holmes KK, Stamm WE. Selective screening for Chlamydia trachomatis infection in a primary care population of women. Am J Epidemiol 1993;138(3):143-53.
- Sternfeld B, Quesenberry CP, Jr., Eskenazi B, Newman LA. Exercise during pregnancy and pregnancy outcome. Med Sci Sports Exerc 1995;27(5):634-40.
- Strobino B, Pantel-Silverman J. Gestational vaginal bleeding and pregnancy outcome. Am J Epidemiol 1989;129 (4):806-15.
- Stubbs TM, Van Dorsten JP, Miller MC, 3rd. The preterm cervix and preterm labor: relative risks, predictive values, and change over time. Am J Obstet Gynecol 1986;155 (4):829-34.
- Summers AM, Farrell SA, Huang T, Meier C, Wyatt PR. Maternal serum screening in Ontario using the triple marker test. J Med Screen 2003;10:107–11.
- Taipale P, Hiilesmaa V. Sonographic measurement of uterine cervix at 18-22 weeks' gestation and the risk of preterm delivery. Obstet Gynecol 1998;92(6):902-7.
- Tamura T, Goldenberg RL, Hou J, Johnston KE, Cliver SP, Ramey SL, Nelson KG. Cord serum ferritin concentrations and mental and psychomotor development of children at five years of age. J Pediatr 2002;140(2):165–70.
- Teitelman AM, Welch LS, Hellenbrand KG, Bracken MB. Effect of maternal work activity on preterm birth and low birth weight. Am J Epidemiol 1990;131(1):104-13.
- Tekesin I, Marek S, Hellmeyer L, Reitz D, Schmidt S. Assessment of rapid fetal fibronectin in predicting preterm delivery. Obstet Gynecol 2005;105:280-4.
- Thorp JM, Jr., Jenkins T, Watson W. Utility of Leopold maneuvers in screening for malpresentation. Obstet Gynecol 1991;78(3 Pt 1):394-6.
- Tookey PA, Gibb DM, Ades AE, Duong T, Masters J, Sherr L, Peckham CS, Hudson CN. Performance of antenatal HIV screening strategies in the United Kingdom. J Med Screen 1998;5(3):133-6.
- Trincado DE, Rawlinson WD. Congenital and perinatal infections with cytomegalovirus. J Paediatr Child Health 2001;37(2):187-92.
- U.S. Army Medical Command, Circular 40-18. Vaginal Birth After Cesarean Delivery. Jan 2005.
- U.S. Preventive Services Task Force (USPSTF). Guide to Clinical Preventive Services. 2nd edition. Baltimore: Williams and Wilkins, 1996.
- U.S. Preventive Services Task Force Screening for Cervical Cancer, Topic Page. January 2003. U.S. Preventive Services Task Force. Agency for Healthcare Research and Quality, Rockville, MD. Available at: http://www.ahrq.gov/clinic/uspstf/uspscerv.htm

- U.S. Preventive Services Task Force. Screening for Asymptomatic Bacteriuria: Recommendation Statement. Rockville, MD: Agency for Healthcare Research and Quality; 2004. Available at: www.ahrq.gov/clinic/uspstf/uspsbact.htm
- U.S. Preventive Services Task Force. Screening for Bacterial Vaginosis in Pregnancy, Topic Page. February 2008. U.S. Preventive Services Task Force. Agency for Healthcare Research and Quality, Rockville, MD. Available at: http://www.ahrq.gov/clinic/uspstf/uspsbvag.htm.
- U.S. Preventive Services Task Force. United States. Office of Disease Prevention and Health Promotion. Chapter 54: Counseling to prevent tobacco use. In, Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. 2nd ed. Washington, DC: U.S. Dept. of Health and Human Services Office of Public Health and Science Office of Disease Prevention and Health Promotion: Supt. of Docs. U.S. G.P.O. distributor; 1996; p. 425-32.
- U.S. Preventive Services Task Force., United States. Office of Disease Prevention and Health Promotion.
 Chapter 37: Screening for preeclampsia. In, Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. 2nd edn. Washington, DC: U.S. Dept. of Health and Human Services Office of Public Health and Science Office of Disease Prevention and Health Promotion: Supt. of Docs. U.S. G.P.O. distributor; 1996; p. 419-24.
- U.S. Preventive Services Task Force., United States. Office of Disease Prevention and Health Promotion. Chapter 38: Screening for D (Rh) incompatibility. In, Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. 2nd edn. Washington, DC: U.S. Dept. of Health and Human Services Office of Public Health and Science Office of Disease Prevention and Health Promotion: Supt. of Docs. U.S. G.P.O. distributor; 1996; p. 425-32.
- Urbaniak SJ. The scientific basis of antenatal prophylaxis. Br J Obstet Gynaecol 1998;105(Suppl 18):11-8.
- Utiger RD. Maternal hypothyroidism and fetal development. N Engl J Med 1999;341(8):601-2.
- van Zonneveld M, van Nunen AB, Niesters HG, de Man RA,Schalm SW,Janssen HL. Lamivudine treatment during pregnancy to prevent perinatal transmission of hepatitis B virus infection. J Viral Hepat 2003;10:294-7.
- Varma R, Gupta J. Antibiotic treatment of bacterial vaginosis in pregnancy: multiple meta-analyses and dilemmas in Interpretation. Eur Jl Obstet Gynecol Reprod Biol 2006 Jan 1;124(1):10-4.
- Veterans Health Administration and Department of Defense (VHA/DoD). Management of Substance Use Disorders in the Primary and Specialty Care. Washington, DC: Office of Quality and Performance and the Veterans Affairs and Department of Defense Development Work Group, Veterans Health Administration, Department of Veterans Affairs; September 2001.
- Villar J, Carroli G, Khan-Neelofur D, Piaggio G, Gulmezoglu M. Patterns of routine antenatal care for low-risk pregnancy. Cochrane Database Syst Rev 2001;4:CD000934
- Viswanathan M, Visco AG, Hartmann K, Wechter, ME, Gartlehner G, Wu JM, Palmieri R, Funk MJ, Lux, LJ, Swinson T, Lohr KN. Cesarean Delivery on Maternal Request. Evid RepTechnol Assess (Full Rep). 2006 Mar;(133):1-138.
- Vuylsteke B, Laga M, Alary M, Gerniers MM, Lebughe JP, Nzila N, Behets F, Van Dyck E, Piot P. Clinical algorithms for the screening of women for gonococcal and chlamydial infection: evaluation of pregnant women and prostitutes in Zaire. Clin Infect Dis 1993;17(1):82-8.
- Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. J Med Screen 1997;4:181–246.
- Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM. First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). Health Techol Assess 2003;7(11):1-77.
- Waldenstrom U, Axelsson O, Nilsson S, Eklund G, Fall O, Lindeberg S, Sjodin Y. Effects of routine one-stage ultrasound screening in pregnancy: a randomised controlled trial. Lancet 1988;2(8611):585-8.

- Walker D, Rising SS. Revolutionizing prenatal care: new evidence-based prenatal care delivery models. J of NY State Nurses Assoc. 2004 fall-2005 Winter;35(2):18-21.
- Walker JL. Methyclothiazide in excessive weight gain and edema of pregnancy. Obstet Gynecol 1966;27(2):247-51.
- Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. BMJ 1999;318(7197):1511-4.
- Wapner R, Thom E, Simpson JL, Pergament E, Silver R, Filkins K, Platt L, Mahoney M, Johnson A, Hogge WA, Wilson RD, Mohide P, Hershey D, Krantz D, Zachary J, Snijders R, Greene N, Sabbagha R, MacGregor S, Hill L, Gagnon A, Hallahan T, Jackson L; First Trimester Maternal Serum Biochemistry and Fetal Nuchal Translucency Screening (BUN) Study Group. al. First-trimester screening for trisomies 21 and 18. First Trimester Maternal Serum Biochemistry and Fetal Nuchal Translucency Screening (BUN) Study Group. N Engl J Med 2003 Oct 9;349(15):1405-13.
- Wathen CN, MacMillan HL. Interventions for violence against women: scientific review. JAMA 2003 Feb 5;289(5):589–600.
- Watson PE, McDonald BW. Seasonal variation of nutrient intake in pregnancy: effects on infant measures and possible influence on diseases related to season of birth. Eur J Clin Nutr 2007 Nov;61(11):1271-80.
- Watson WJ. Screening for glycosuria during pregnancy. South Med J 1990;83(2):156-8.
- Wax JR, Pinette MG, Cartin A, Blackstone J. Female reproductive issues following bariatric surgery. Obstet Gynecol Surv 2007 Sep 62(9):595-604.
- Weiss BD, Senf JH, Udall W. The postpartum Papanicolaou smear. J Amer Board of Fam Pract 1989;2 (1):4-9.
- Wen SW, Goldenberg RL, Cutter GR, Hoffman HJ, Cliver SP. Intrauterine growth retardation and preterm delivery: prenatal risk factors in an indigent population. Am J Obstet Gynecol 1990;162(1):213-8.
- Werler MM, Hayes C, Louik C, Shapiro S, Mitchell AA. Multivitamin supplementation and risk of birth defects. Am J Epidemiol 1999 Oct 1;150(7):675-82.
- Whitley RJ, Corey L, Arvin A, Lakeman FD, Sumaya CV, Wright PF, Dunkle LM, Steele RW, Soong SJ, Nahmias AJ, et al. et al. Changing presentation of herpes simplex virus infection in neonates. J Infect Dis 1988 Jul; 158(1):109-16.
- Wilailak S, Suthutvoravut S, Cherng-sa-ad P, Herabutya Y, Chaturachinda K. Assessment of fetal well-being: Fetal movement count versus non stress test. Int J Gynecol Obstet 1992;39(1):23-7.
- Wilcox M, Gardosi J, Mongelli M, Ray C, Johnson I. Birth weight from pregnancies dated by ultrasonography in a multicultural British population. BMJ 1993 Sep 4;307(6904):588-91.
- Williams CB, Iqbal S, Zawacki CM, Yu D, Brown MB, Herman WH. Effect of selective screening for gestational diabetes. Diabetes Care 1999;22(3):418-21.
- Williams M, Iams JD. Cervical length measurement and cervical cerclage to prevent preterm birth. Clin Obstet Gynecol 2004 Dec;47(4):775-83; discussion 881-2.
- Wisborg K, Henriksen TB, Jespersen LB, Secher NJ. Nicotine patches for pregnant smokers: a randomized controlled study. Obstet Gynecol 2000;96(6):967-71.
- Wise D, Engstrom JL. The predictive validity of fundal height curves in the identification of small- and large-for-gestational age infants. J Obstet Gynecol Neonatal Nurs 1985;14(2):87-92.
- Wong SY, Remington JS. Toxoplasmosis in pregnancy. Clin Infect Dis 1994;18(6):853-62.
- Wright TC Jr, Massad LS, Dunton CJ, spitzer M, Wilkinson EJ, Solomon D; 2006 ASCCP-Sponsored Consensus Conference. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol 2007 Oct;197(4):346-55.

- Xiong, X. Beckens, P Fraser, WD, Beck, J, Offenbacher, S. Periodontal disease and adverse pregnancy outcomes: a systematic review. BJOG 2006 Jul;113(7):135-143.
- Xu WM, Cui YT, Wang L, Yang H, Liang ZQ, Li XM, Mao X. Efficacy and safety of lamivudine in late pregnancy for the prevention of mother-child transmission of hepatitis B; a multicentre, randomised, double-blind, placebo- controlled study [abstract]. Hepatology 2004;40(suppl 1):272A-3A.
- Young GL, Jewell D. Interventions for varicosities and leg oedema in pregnancy. Cochrane Database Syst Rev 2000;(2):CD001066.
- Yuan J, Lin J, Xu A, Li H, Hu B, Chen J, Yao J, Dong H, Jiang M. Antepartum immunoprophylaxis of three doses of hepatitis B immunoglobulin is not Effective: A Single-Centre Randomized Study . J Viral Hepat. 2006;13(9):597-604.
- Zhu Q,Yu G,Yu H,Lu Q,Gu X,Dong Z,et al. A randomized controlled trial on interruption of HBV transmission in utero. Chinese Med J 2003 May;116(5):685-7
- Ziaei S, Norrozi M, Faghigzadeh S, Jafarbegloo, E. A randomized placebo-controlled trial to determine the effect of iron supplementation on pregnancy outcome in pregnant women with haemoglobin > or =13.2 g/dl. BJOG 2007 Oct;114(6);684-8.