BÖLÜM
18

PERİNATAL ENFEKSİYONLAR TANI VE TEDAVİ

Ayşegül BESTEL[1]

Giriş

Çocuklarda ve yetişkinlerde hastalığa neden olan enfeksiyonlar gebelik ve puerperal dönemde geçirildiğinde fetusta ciddi komplikasyonlara neden olabilmektedir. Bu geçişin hematojen yol (transplasental), asendan yol, vertikal yol (doğum esnasında), doğum sonrası (laktasyon) ve iatrojenik (invaziv girişimler) olarak gerçekleştiği kabul edilmektedir (1). Gebelik döneminde fetüs mikroorganizmalara oldukça hassas olduğundan abortus, yapısal anomaliler, intrauterin mort fetüs ve etkilenen fetusta ileri dönemde sekellere neden olabilmektedir (1).

Günümüz şartlarında gebelik öncesinde riskli grupta hastalık etkenlerinin taranması, mikrobiyolojik, immünolojik ve serolojik testlerle hastalığın tanısının konulması mümkündür. Fetusta anomali taraması ile etkilenme riski olan ve etkilenmiş fetusların takibi sağlanabilmektedir.

Perinatal enfeksiyonların taranması

Gebelik esnasında perinatal enfeksiyonların tarama programları sıklığına ve uygulanabilirliğine bağlı olarak ülkeden ülkeye değişiklik göstermektedir. Yenidoğanda ise konjenital enfeksiyon şüphesi durumunda patojenler için test yapılması önerilmektedir (2).

Toksoplazmozis

Toksoplazma zoonotik bulaşma veya gıda kontaminasyonu yoluyla insanları enfekte edebilmektedir. Çiğ veya az pişmiş etin tüketilmesi, yıkanmamış sebze ve meyve yenmesi, enfekte olmuş kedilerin dışkılarıyla atılan oositleri içeren suların içilmesi ve kedi kumu veya toprakla temas enfeksiyona neden olabilir (3).

Fetal enfeksiyon riski, enfeksiyonun geçirildiği gestasyonel yaş ile doğru orantılı olarak artar. Bu risk 13. Haftada % 15, 26. Haftada % 44 ve 36 haftada % 71 olarak bildirilmiştir (4). Fetal enfeksiyonun ciddiyeti ise patojenin fetusa bulaştığı gebelik haftası ile ters orantılıdır. İlk üç aylık dönemde, fetusta ciddi anormalliklere veya abortusa yol açabilir. Üçüncü trimesterde ise vakaların yaklaşık % 80'inde asemptomatik konjenital toksoplazmozis bulunmaktadır (5).

Gebelik döneminde geçirilmiş toxoplazma enfeksiyonunun transplasental yolla fetusa geçişi abortus, ölü doğum, nörolojik ve oküler defektle-

[1] Uzm. Dr. Ayşegül BESTEL, Sağlık Bilimleri Üniversitesi İstanbul Kanuni Sultan Süleyman Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Bölümü draysegulciftci@gmail. com

azaltmaktadır (94, 95). Antepartum, intrapartum ve fetusun profilaksisinin kombinasyonu, bulaşma riskini azaltmak ve gebelik boyunca maternal viral yükü azaltmak için önerilir (94, 96, 97). Perinatal bulaş riski maternal HIV viral yükün baskılanmasıyla azalmaktadır (98, 99). Erken dönemde başlanan antiretroviral tedavi viral yükün azalmasını ve buna bağlı olarak da perinatal bulaşın azalmasını sağlamaktadır(98, 100).

Gebelerde, antiretroviral rejim seçiminde virüsün direnç profili, ilaçların anne ve fetustaki güvenliliği ve etkililiği, rejimin uygunluğu ve bağlılık potansiyeli, diğer ilaçlarla etkileşim potansiyeli dikkate alınmalıdır. Bu ilaçların kullanımıyla birçok ülkede anneden bebeğe bulaş ihtimali oldukça azalmıştır.

Gebelik öncesi özellikle HIV enfeksiyonu açısından risk grubundaki hastaların uyuşturucu madde kullanımı ve birden çok partnerle korunmasız ilişki gibi değiştirilebilir alışkanlıkları değerlendirilmelidir (101-103). Cinsel yolla bulaşan hastalıklardan korunmak için cinsel ilişki sırasında kondom kullanımı önerilmelidir.

Gebeliğin ilk trimesterinde bir kombinasyon antiretroviral ilaç rejimi alan kadınlarda fetal anatominin ayrıntılı bir ikinci trimester ultrason değerlendirmesi önerilmektedir (104). Doğumdan önce, HIV ile enfekte kadına, anne sütüne HIV bulaşma riski ile ilgili endişeler nedeniyle emzirmenin tavsiye edilmediği konusunda bilgilendirilmelidir.

Sonuç

Perinatal enfeksiyonlar fetal ve neonatal morbidite ve mortalitesinde önemli nedenlerden biridir. Enfeksiyonların zamanında teşhisi ve uygun tedavinin başlatılması kritik değere sahiptir. Perinatal enfeksiyonların önlenmesi için gebelik öncesi ve gebelik döneminde ülkelerin belirlenmiş tarama programları kapsamında hareket edilmeli ve şüpheli durumlarda tanıya yönelik ileri değerlendirme yapılmalıdır. Ayrıca gebelik ve öncesi dönemde olası enfeksiyonlar açısından hastalar enfeksiyonu önleme konusunda bilgilendirilmelidir.

KAYNAKLAR

1. SAĞOL S. Fetal Enfeksiyonların Prenatal Tanısı. Journal of Clinical Obstetrics & Gynecology. 2002;12(5):419-30.
2. de Jong EP, Vossen AC, Walther FJ, Lopriore E. How to use... neonatal TORCH testing. Archives of Disease in Childhood-Education and Practice. 2013;98(3):93-8.
3. Joynson DH, Wreghitt TG. Toxoplasmosis: a comprehensive clinical guide: Cambridge University Press; 2005.
4. Thiébaut R, Leproust S, Chêne G, Gilbert R. Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients'data. The Lancet. 2007;369(9556):115-22.
5. Fricker-Hidalgo H, Bailly S, Brenier-Pinchart M-P, Dard C, Jean D, Coston A-L, et al. How to estimate time of infection with Toxoplasma gondii in pregnant women. Use of specific IgG and IgM kinetics by 7 techniques on 691 sera. Diagnostic microbiology and infectious disease. 2020;96(4):114987.
6. Davis SM, Anderson BL, Schulkin J, Jones K, Eng JV, Jones JL. Survey of obstetrician-gynecologists in the United States about toxoplasmosis: 2012 update. Archives of gynecology and obstetrics. 2015;291(3):545-55.
7. Paquet C, Yudin MH. No. 285-toxoplasmosis in pregnancy: prevention, screening, and treatment. Journal of Obstetrics and Gynaecology Canada. 2018;40(8):e687-e93.
8. El Bissati K, Levigne P, Lykins J, Adlaoui EB, Barkat A, Berraho A, et al. Global initiative for congenital toxoplasmosis: an observational and international comparative clinical analysis. Emerging microbes & infections. 2018;7(1):1-14.
9. Bigna JJ, Tochie JN, Tounouga DN, Bekolo AO, Ymele NS, Youda EL, et al. Global, regional, and country seroprevalence of Toxoplasma gondii in pregnant women: a systematic review, modelling and meta-analysis. Scientific reports. 2020;10(1):1-10.
10. Cortina-Borja M, Tan HK, Wallon M, Paul M, Prusa A, Buffolano W, et al. Prenatal treatment for serious neurological sequelae of congenital toxoplasmosis: an observational prospective cohort study. PLoS Med. 2010;7(10):e1000351.
11. McLeod R, Boyer K, Karrison T, Kasza K, Swisher C, Roizen N, et al. Toxoplasmosis Study Group. Outcome of treatment for congenital toxoplasmosis, 1981-2004: the National Collaborative ChicagoBased, Congenital Toxoplasmosis Study. Clin Infect Dis. 2006;42(10):1383-94.
12. Cvetković D, Bobić B, Jankovska G, Klun I, Panovski N, Djurković-Djaković O. Risk factors for Toxoplasma infection in pregnant women in FYR of Macedonia. Parasite. 2010;17(3):183-6.
13. Davis NL, King CC, Kourtis AP. Cytomegalovirus infection in pregnancy. Birth defects research.

2017;109(5):336-46.
14. Buxmann H, Hamprecht K, Meyer-Wittkopf M, Friese K. Primary human cytomegalovirus (HCMV) infection in pregnancy. Deutsches Ärzteblatt International. 2017;114(4):45.
15. Hyde TB, Schmid DS, Cannon MJ. Cytomegalovirus seroconversion rates and risk factors: implications for congenital CMV. Reviews in medical virology. 2010;20(5):311-26.
16. Lazzarotto T, Guerra B, Gabrielli L, Lanari M, Landini M. Update on the prevention, diagnosis and management of cytomegalovirus infection during pregnancy. Clinical Microbiology and Infection. 2011;17(9):1285-93.
17. Picone O, Vauloup- Fellous C, Cordier A, Guitton S, Senat M, Fuchs F, et al. A series of 238 cytomegalovirus primary infections during pregnancy: description and outcome. Prenatal diagnosis. 2013;33(8):751-8.
18. Rawlinson WD, Boppana SB, Fowler KB, Kimberlin DW, Lazzarotto T, Alain S, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. The Lancet Infectious Diseases. 2017;17(6):e177-e88.
19. Istas AS, Demmler GJ, Dobbins JG, Stewart JA. Surveillance for congenital cytomegalovirus disease: a report from the National Congenital Cytomegalovirus Disease Registry. Clinical infectious diseases. 1995;20(3):665-70.
20. Obstetricians ACo, Gynecologists. Practice bulletin no. 151: Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy. Obstetrics and gynecology. 2015;125(6):1510.
21. Hughes BL, Gyamfi-Bannerman C, Medicine SfM-F. Diagnosis and antenatal management of congenital cytomegalovirus infection. American journal of obstetrics and gynecology. 2016;214(6):B5-B11.
22. Ornoy A, Diav-Citrin O. Fetal effects of primary and secondary cytomegalovirus infection in pregnancy. Reproductive Toxicology. 2006;21(4):399-409.
23. Guerra B, Lazzarotto T, Quarta S, Lanari M, Bovicelli L, Nicolosi A, et al. Prenatal diagnosis of symptomatic congenital cytomegalovirus infection. American journal of obstetrics and gynecology. 2000;183(2):476-82.
24. Azam A-Z, Vial Y, Fawer C-L, Zufferey J, Hohlfeld P. Prenatal diagnosis of congenital cytomegalovirus infection. Obstetrics & Gynecology. 2001;97(3):443-8.
25. Liesnard C, Donner C, Brancart F, Gosselin F, Delforge M-L, Rodesch F. Prenatal diagnosis of congenital cytomegalovirus infection: prospective study of 237 pregnancies at risk. Obstetrics & Gynecology. 2000;95(6):881-8.
26. Eggers M, Bäder U, Enders G. Combination of microneutralization and avidity assays: improved diagnosis of recent primary human cytomegalovirus infection in single serum sample of second trimester pregnancy. Journal of medical virology. 2000;60(3):324-30.
27. Lazzarotto T, Ripalti A, Bergamini G, Battista M, Spezzacatena P, Campanini F, et al. Development of a new cytomegalovirus (CMV) immunoglobulin M (IgM) immunoblot for detection of CMV-specific IgM. Journal of Clinical Microbiology. 1998;36(11):3337-41.
28. Grangeot-Keros L, Mayaux MJ, Lebon P, Freymuth F, Eugene G, Stricker R, et al. Value of cytomegalovirus (CMV) IgG avidity index for the diagnosis of primary CMV infection in pregnant women. Journal of Infectious Diseases. 1997;175(4):944-6.
29. Leruez-Ville M, Sellier Y, Salomon LJ, Stirnemann JJ, Jacquemard F, Ville Y. Prediction of fetal infection in cases with cytomegalovirus immunoglobulin M in the first trimester of pregnancy: a retrospective cohort. Clinical infectious diseases. 2013;56(10):1428-35.
30. Barber V, Calvert A, Vandrevala T, Star C, Khalil A, Griffiths P, et al. Prevention of acquisition of cytomegalovirus infection in pregnancy through hygiene-based behavioral interventions: A systematic review and gap analysis. The Pediatric infectious disease journal. 2020;39(10):949-54.
31. Prasad VM, Klose T, Rossmann MG. Assembly, maturation and three-dimensional helical structure of the teratogenic rubella virus. PLoS pathogens. 2017;13(6):e1006377.
32. Best JM, editor Rubella. Seminars in fetal and neonatal medicine; 2007: Elsevier.
33. Miller E, Cradock-Watson J, Pollock T. Consequences of confirmed maternal rubella at successive stages of pregnancy. The Lancet. 1982;320(8302):781-4.
34. Webster WS. Teratogen update: congenital rubella. Teratology. 1998;58(1):13-23.
35. Morgan-Capner P, Miller E, Vurdien J, Ramsay M. Outcome of pregnancy after maternal reinfection with rubella. CDR (London, England: Review). 1991;1(6):R57-R9.
36. Best JM, O'Shea S, Tipples G, Davies N, Al-Khusaiby SM, Krause A, et al. Interpretation of rubella serology in pregnancy—pitfalls and problems. Bmj. 2002;325(7356):147-8.
37. Frey TK, Abernathy ES. Identification of strain-specific nucleotide sequences in the RA 27/3 rubella virus vaccine. Journal of Infectious Diseases. 1993;168(4):854-64.
38. Tanemura M, Suzumori K, Yagami Y, Katow S. Diagnosis of fetal rubella infection with reverse transcription and nested polymerase chain reaction: a study of 34 cases diagnosed in fetuses. American journal of obstetrics and gynecology. 1996;174(2):578-82.
39. Reef SE, Frey TK, Theall K, Abernathy E, Burnett CL, Icenogle J, et al. The changing epidemiology of rubella in the 1990s: on the verge of elimination and new challenges for control and prevention. Jama. 2002;287(4):464-72.
40. Bart SW, Stetler HC, Preblud SR, Williams NM, Orenstein WA, Bart KJ, et al. Fetal risk associated with rubella vaccine: an update. Clinical Infectious Diseases. 1985;7(Supplement_1):S95-S102.
41. Control CfD, Prevention. Revised ACIP recommendation for avoiding pregnancy after receiving a rubella-containing vaccine. MMWR Morbidity and mortality weekly report. 2001;50(49):1117.
42. Brown KE, Anderson SM, Young NS. Erythrocyte P antigen: cellular receptor for B19 parvovirus. Science. 1993;262(5130):114-7.

43. Anderson M, Higgins P, Davis L, Willman J, Jones S, Kidd I, et al. Experimental parvoviral infection in humans. Journal of Infectious Diseases. 1985;152(2):257-65.
44. Waldman M, Kopp JB. Parvovirus B19 and the kidney. Clinical Journal of the American Society of Nephrology. 2007;2(Supplement 1):S47-S56.
45. Goldstein A, Anderson M, Serjeant G. Parvovirus associated aplastic crisis in homozygous sickle cell disease. Archives of disease in childhood. 1987;62(6):585-8.
46. Rodis JF, Quinn DL, Gary Jr GW, Anderson LJ, Rosengren S, Cartter ML, et al. Management and outcomes of pregnancies complicated by human B19 parvovirus infection: a prospective study. American journal of obstetrics and gynecology. 1990;163(4):1168-71.
47. Gratacós E, Torres P-J, Vidal J, Antolín E, Costa J, Jimenez de Anta MT, et al. The incidence of human parvovirus B19 infection during pregnancy and its impact on perinatal outcome. Journal of Infectious Diseases. 1995;171(5):1360-3.
48. Jordan JA. Identification of human parvovirus B19 infection in idiopathic nonimmune hydrops fetalis. American journal of obstetrics and gynecology. 1996;174(1):37-42.
49. Enders M, Weidner A, Zoellner I, Searle K, Enders G. Fetal morbidity and mortality after acute human parvovirus B19 infection in pregnancy: prospective evaluation of 1018 cases. Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis. 2004;24(7):513-8.
50. Parilla BV, Tamura RK, Ginsberg NA. Association of parvovirus infection with isolated fetal effusions. American journal of perinatology. 1997;14(06):357-8.
51. Anand A, Gray ES, Brown T, Clewley JP, Cohen BJ. Human parvovirus infection in pregnancy and hydrops fetalis. New England Journal of Medicine. 1987;316(4):183-6.
52. Schwarz T, Roggendorf M, Hottenträger B, Deinhardt F, Enders G, Gloning K, et al. Human parvovirus B19 infection in pregnancy. Lancet (London, England). 1988;2(8610):566-7.
53. Enders M, Klingel K, Weidner A, Baisch C, Kandolf R, Schalasta G, et al. Risk of fetal hydrops and non-hydropic late intrauterine fetal death after gestational parvovirus B19 infection. Journal of clinical virology. 2010;49(3):163-8.
54. Bascietto F, Liberati M, Murgano D, Buca D, Iacovelli A, Flacco ME, et al. Outcome of fetuses with congenital parvovirus B19 infection: systematic review and meta- analysis. Ultrasound in Obstetrics & Gynecology. 2018;52(5):569-76.
55. Weiland H, Vermey-Keers C, Salimans M, Fleuren G, Verwey R, Anderson M. Parvovirus B19 associated with fetal abnormality. The Lancet. 1987;329(8534):682-3.
56. Katz VL, McCoy MC, Kuller JA, Hansen WF. An association between fetal parvovirus B19 infection and fetal anomalies: a report of two cases. American journal of perinatology. 1996;13(01):43-5.
57. Barton LL, Lax D, Shehab ZM, Keith JC. Congenital cardiomyopathy associated with human parvovirus B19 infection. The American heart journal. 1997;133(1):131-3.
58. Tiessen R, van Elsacker- Niele A, Vermeij- Keers C, Oepkes D, Van Roosmalen J, Gorsira M. A fetus with a parvovirus B19 infection and congenital anomalies. Prenatal diagnosis. 1994;14(3):173-6.
59. Vogel H, Kornman M, Ledet SC, Rajagopalan L, Taber L, McClain K. Congenital parvovirus infection. Pediatric Pathology & Laboratory Medicine. 1997;17(6):903-12.
60. Miyagawa S, Takahashi Y, Nagai A, Yamamoto Y, Nakagawa A, Hori K, et al. Angio- oedema in a neonate with IgG antibodies to parvovirus B19 following intrauterine parvovirus B19 infection. British Journal of Dermatology. 2000;143(2):428-30.
61. Saarinen UM, Chorba TL, Tattersall P, Young NS, Anderson LJ, Palmer E, et al. Human parvovirus B19-induced epidemic acute red cell aplasia in patients with hereditary hemolytic anemia. 1986.
62. Rothart HA. Human parvovirus infections. Annual review of medicine. 1990;41(1):25-34.
63. Mielk G, Enders G. Late onset of hydrops fetalis following intrauterine parvovirus B19 infection. Fetal diagnosis and therapy. 1997;12(1):40-2.
64. Török TJ, Wang Q-Y, Gary Jr GW, Yang C-F, Finch TM, Anderson LJ. Prenatal diagnosis of intrauterine infection with parvovirus B19 by the polymerase chain reaction technique. Clinical Infectious Diseases. 1992;14(1):149-55.
65. Clewley J. Polymerase chain reaction assay of parvovirus B19 DNA in clinical specimens. Journal of Clinical Microbiology. 1989;27(12):2647-51.
66. Yamakawa Y, Oka H, Hori S, Aral T, Izumi R. Detection of human parvovirus B19 DNA by nested polymerase chain reaction. Obstetrics & Gynecology. 1995;86(1):126-9.
67. Cosmi E, Mari G, Delle Chiaie L, Detti L, Akiyama M, Murphy J, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia resulting from parvovirus infection. American journal of obstetrics and gynecology. 2002;187(5):1290-3.
68. Bizjak G, Blondin D, Hammer R, Kozlowski P, Siegmann H, Stressig R. Acute infection with parvovirus B19 in early pregnancy. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2009;34(2):234-5.
69. Borna S, Mirzaie F, Hanthoush- Zadeh S, Khazardoost S, Rahimi- Sharbaf F. Middle cerebral artery peak systolic velocity and ductus venosus velocity in the investigation of nonimmune hydrops. Journal of Clinical Ultrasound. 2009;37(7):385-8.
70. Berry SM, Stone J, Norton ME, Johnson D, Berghella V, Medicine SfM-F. Fetal blood sampling. American journal of obstetrics and gynecology. 2013;209(3):170-80.
71. Nicolaides K, Clewell W, Mibashan R, Soothill P, Rodeck C, Campbell S. Fetal haemoglobin measurement in the assessment of red cell isoimmunisation. The Lancet. 1988;331(8594):1073-5.
72. Hook III EW, Marra CM. Acquired syphilis in adults.

New England Journal of Medicine. 1992;326(16):1060-9.
73. Chapel TA. The signs and symptoms of secondary syphilis. Sexually transmitted diseases. 1980;7(4):161-4.
74. Rac MW, Revell PA, Eppes CS. Syphilis during pregnancy: a preventable threat to maternal-fetal health. American journal of obstetrics and gynecology. 2017;216(4):352-63.
75. Trivedi S, Williams C, Torrone E, Kidd S. National trends and reported risk factors among pregnant women with syphilis in the United States, 2012–2016. Obstetrics and gynecology. 2019;133(1):27.
76. Newman L, Kamb M, Hawkes S, Gomez G, Say L, Seuc A, et al. Global estimates of syphilis in pregnancy and associated adverse outcomes: analysis of multinational antenatal surveillance data. PLoS Med. 2013;10(2):e1001396.
77. Cheng J, Zhou H, Hong F, Zhang D, Zhang Y, Pan P, et al. Syphilis screening and intervention in 500 000 pregnant women in Shenzhen, the People's Republic of China. Sexually Transmitted Infections. 2007;83(5):347-50.
78. Hossain M, Broutet N, Hawkes S. The elimination of congenital syphilis: a comparison of the proposed World Health Organization action plan for the elimination of congenital syphilis with existing national maternal and congenital syphilis policies. Sexually transmitted diseases. 2007;34(7):S22-S30.
79. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recommendations and reports: Morbidity and mortality weekly report Recommendations and reports. 2015;64(RR-03):1.
80. Klein VR, Cox SM, Mitchell MD, Wendel Jr GD. The Jarisch-Herxheimer reaction complicating syphilotherapy in pregnancy. Obstetrics and gynecology. 1990;75(3 Pt 1):375-80.
81. Hollier LM, Harstad TW, Sanchez PJ, Twickler DM, Wendel Jr GD. Fetal syphilis: clinical and laboratory characteristics. Obstetrics & Gynecology. 2001;97(6):947-53.
82. Rac MW, Bryant SN, McIntire DD, Cantey JB, Twickler DM, Wendel Jr GD, et al. Progression of ultrasound findings of fetal syphilis after maternal treatment. American journal of obstetrics and gynecology. 2014;211(4):426. e1-. e6.
83. Benedetti J, Corey L, Ashley R. Recurrence rates in genital herpes after symptomatic first-episode infection. Annals of internal medicine. 1994;121(11):847-54.
84. Bernstein DI, Bellamy AR, Hook III EW, Levin MJ, Wald A, Ewell MG, et al. Epidemiology, clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women. Clinical infectious diseases. 2013;56(3):344-51.
85. Schillinger JA, McKinney CM, Garg R, Gwynn RC, White K, Lee F, et al. Seroprevalence of herpes simplex virus type 2 and characteristics associated with undiagnosed infection: New York City, 2004. Sexually transmitted diseases. 2008;35(6):599-606.
86. Corey L, Adams HG, Brown ZA, Holmes KK. Genital herpes simplex virus infections: clinical manifestations, course, and complications. Annals of internal medicine. 1983;98(6):958-72.
87. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. Jama. 2003;289(2):203-9.
88. Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labor. New England Journal of Medicine. 1991;324(18):1247-52.
89. Obstetricians ACo, Gynecologists. Management of Genital Herpes in Pregnancy: ACOG Practice Bulletinacog Practice Bulletin, Number 220. Obstetrics and gynecology. 2020;135(5):e193-e202.
90. Watts DH, Brown ZA, Money D, Selke S, Huang ML, Sacks SL, et al. A double-blind, randomized, placebo-controlled trial of acyclovir in late pregnancy for the reduction of herpes simplex virus shedding and cesarean delivery. American journal of obstetrics and gynecology. 2003;188(3):836-43.
91. Caviness AC, Demmler GJ, Selwyn BJ. Clinical and laboratory features of neonatal herpes simplex virus infection: a case-control study. The Pediatric infectious disease journal. 2008;27(5):425-30.
92. Piot P. AIDS: from crisis management to sustained strategic response. The Lancet. 2006;368(9534):526-30.
93. Quinn TC. Global burden of the HIV pandemic. The lancet. 1996;348(9020):99-106.
94. Cooper E. Women and Infants'Transmission Study Group. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. J Acquir Immune Defic Syndr. 2002;29:484-94.
95. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006. Aids. 2008;22(8):973-81.
96. Chou R, Cantor AG, Zakher B, Bougatsos C. Screening for HIV in pregnant women: systematic review to update the 2005 US Preventive Services Task Force recommendation. Annals of internal medicine. 2012;157(10):719-28.
97. Forbes J, Alimenti A, Singer J, Brophy J, Bitnun A, Samson L, et al. Canadian Pediatric AIDS Research Group (CPARG). A national review of vertical HIV transmission AIDS. 2012;26(6):757-63.
98. Mandelbrot L, Tubiana R, Le Chenadec J, Dollfus C, Faye A, Pannier E, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. Clinical Infectious Diseases. 2015;61(11):1715-25.
99. Ioannidis JP, Abrams EJ, Ammann A, Bulterys M, Goedert JJ, Gray L, et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA virus loads< 1000 copies/ml. The Journal of infectious diseases. 2001;183(4):539-45.
100. Townsend CL, Byrne L, Cortina-Borja M, Thorne C, de Ruiter A, Lyall H, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission

rates, 2000–2011. Aids. 2014;28(7):1049-57.
101. Matheson PB, Thomas PA, Abrams EJ, Pliner V, Lambert G, Bamji M, et al. Heterosexual behavior during pregnancy and perinatal transmission of HIV-1. New York City Perinatal HIV Transmission Collaborative Study Group. AIDS (London, England). 1996;10(11):1249-56.
102. Rodriguez EM, Mofenson LM, Chang B-H, Rich KC, Fowler MG, Smeriglio V, et al. Association of maternal drug use during pregnancy with maternal HIV culture positivity and perinatal HIV transmission. Aids. 1996;10(3):273-82.
103. Bulterys M, Landesman S, Burns DN, Rubinstein A, Goedert JJ. Sexual behavior and injection drug use during pregnancy and vertical transmission of HIV-1. JAIDS Journal of Acquired Immune Deficiency Syndromes. 1997;15(1):76-82.
104. Committee APRS. Antiretroviral Pregnancy Registry international interim report for 1 January 1989 through 31 July 2012. Wilmington, NC, Registry Coordinating Center. 2012.