

Health Advisory

NICOTINE RISKS FOR CHILDREN, TEENS, AND PREGNANT WOMEN

Updated February 2018

This advisory seeks to inform health care professionals and parents of the public health risks of nicotine exposure to children, teens, and pregnant women.

With increased use and expanding availability of nicotine products such as e-cigarettes, especially among youth, it is important to understand the facts about nicotine and its health effects. Nicotine is addictive and can be toxic at high doses. Evidence also supports that it can harm brain development during adolescence. Nicotine exposure is unsafe for youth.

Nicotine products pose a serious health risk for youth.

The use of e-cigarettes and other Electronic Nicotine Delivery Systems (ENDS; e.g. vape pens, hookah pens, and e-pipes) recently surpassed conventional cigarettes to become the most commonly used tobacco product among U.S. youth. [1] Given the use of e-cigarettes among teens increased dramatically during 2011-2015, [1] it is critical that public health officials and the general public understand the potential risks of using nicotine products for youth. Recent evidence suggests that, compared to youth who have never used them, youth who have tried e-cigarettes are twice as likely to start smoking in the future. [2] This relationship appears to be stronger for lower-risk adolescents, suggesting e-cigarettes may attract youth who otherwise would not have smoked. [3] Human clinical studies report similar findings—adolescent nicotine exposure leads to higher rates of smoking behavior in adulthood. [4-9] Accordingly, youth should avoid use of all nicotine containing products, including e-cigarettes.

Nicotine exposure can harm brain development during adolescence.

Adolescence (the transitional period between childhood and adulthood, typically ranging from 12-18 years of age) is a critical window for brain growth and development, when it is still "under construction." [10, 11] As a consequence, adolescents are especially at risk of harm caused by nicotine exposure.

Evidence indicates that exposure to nicotine during adolescence can have long-term effects on brain development, [1, 12-14] and may increase the risk of addiction to other substances by causing changes within the brain. [13, 15-28] Animal research has found that even in small doses, nicotine exposure in adolescence causes long-lasting changes in brain development. This could have negative implications for learning, memory, attention, behavioral problems, and future addiction in human adolescents. [14, 26, 29-33]

Nicotine is highly addictive.

Nicotine is the drug in tobacco that causes addiction. [34-38] Studies show that symptoms of nicotine addiction can appear among youth within only a few days or weeks after smoking initiation. [39, 40]

Nicotine stimulates reward pathways in the brain, and can be as addictive as heroin or cocaine. [18, 35, 41-47]

Because their brains are still developing, adolescents are especially vulnerable to nicotine addiction. [10, 13,

⁴⁸⁻⁵¹ While experimental studies testing the effects of nicotine addiction on the human adolescent brain do not exist due to ethical restrictions, researchers agree that results from animal studies do translate to humans^[1]. Existing animal studies show that adolescents are more sensitive to the rewarding effects of nicotine at lower doses than adults, and experience fewer negative side effects of higher-dose exposure.^[52, 53] Further, adolescents are less sensitive to the negative effects of withdrawal than adults, making them more susceptible to nicotine addiction. Human clinical reports confirm this pattern, showing adolescents are more likely to experience nicotine dependence at lower doses than adults.^[4-9]

Nicotine is harmful to the health of unborn children.

The U.S. Surgeon General has concluded that use of products containing nicotine poses danger to pregnant women and unborn children.^[1, 16] Fetal exposure to nicotine can have a variety of negative long-term consequences including sudden infant death syndrome, impaired brain and lung development, auditory processing problems, effects on behaviors and obesity, and deficits in attention and cognition.^[11-13, 16, 22-24, 54, 55] Studies also indicate that fetal nicotine exposure is associated with nicotine dependence in adolescence.^[11, 16, 56-65] Pregnant women and women who intend to become pregnant should avoid e-cigarettes to minimize unnecessary exposure to nicotine.^[1, 16]

Nicotine causes harmful physical effects and can be toxic in high doses.

Nicotine affects the cardiovascular and central nervous systems, causing blood vessels to constrict, raising the pulse and blood pressure. [34,66] Eating, drinking, or otherwise absorbing nicotine at high enough doses can lead to nicotine poisoning, especially in children. [16] Symptoms of poisoning include nausea, vomiting, seizures and respiratory depression. [67,68] In high enough doses, nicotine can be fatal. [69]

There has been a significant rise in the number of calls to poison control centers for exposures to liquids used in e-cigarettes. [70] Nationally, the number of calls rose from one per month in September 2010 to 215 per month in February 2014, with over half (51.5%) occurring among children aged 0-5 years. [71] Similarly, calls increased in Minnesota, with e-cigarette-related poisonings among children 0-5 years increasing from just 1 in 2011 to 62 in 2014. Many cases involve children and toddlers who ingested e-cigarette liquids left unattended.

The amount of nicotine in products may vary widely. Nicotine levels in e-cigarettes have been found to range from 0 to 34 mg/mL,^[72] and studies have found discrepancies between the labeled and measured nicotine content in some e-cigarette products.^[73] Because of the lack of quality and manufacturing standards for e-cigarettes and other ENDS, it is difficult for the consumer to know how much nicotine is contained in these products, increasing the risk of a toxic exposure. The U.S. Food and Drug Administration now has the authority to address the varying nicotine levels in tobacco products, including e-cigarettes, but has not yet done so.

Recommendations for Parents of Young Children

Keep nicotine-containing products out-of-reach

- Nicotine-containing cartridges and bottles are a potential source of poisoning through ingestion, skin or eye contact. Store these materials out of the reach of young children.
- For products kept in the home, ensure that they are kept in child-resistant packaging, which is required for all liquid nicotine sold in Minnesota and nationwide. [74]
- Call 1-800-222-1222 for poison emergencies.

Recommendations for Health Care Professionals

Educate and Advise

- Advise that **nicotine exposure is unsafe** for children, teens, and pregnant women.
 - The nicotine contained in products such as e-cigarettes is highly addictive.
 - Accidental exposure to liquids contained in e-cigarettes and similar products can result in nicotine poisoning at high enough doses, especially in children.
- Advise that exposure to nicotine can harm the developing adolescent brain.
- Advise pregnant women to avoid using nicotine products.

Adults interested in quitting tobacco can receive free resources, including nicotine replacement therapies like patches or gum, from QUITPLAN® Services at www.quitplan.com or by calling 1-888-354-7526.

Protect Children from Nicotine Poisoning

 Inform parents and nicotine users that nicotine-containing cartridges and bottles are a potential source of poisoning through ingestion, skin, or eye contact. Store these materials out of the reach of children, and call the Minnesota Poison Control System at 1-800-222-1222 for expert help in case of accidental exposure.

Minnesota Department of Health Tobacco Prevention and Control 651-201-3535 tobacco@state.mn.us www.health.state.mn.us/nicotine

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To obtain this information in a different format, call: 651-201-3535. Printed on recycled paper.

References

- 1. U.S. Department of Health and Human Services, *E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General.* 2016, U. S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta, GA.
- 2. Watkins, S.L., S.A. Glantz, and B.W. Chaffee, Association of Noncigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015. JAMA Pediatr, 2018.
- 3. Wills, T.A., et al., *E-cigarette use is differentially related to smoking onset among lower risk adolescents*. Tob Control, 2016. **26**(5): p. 534-539.
- 4. Chen, J. and W.J. Millar, *Age of smoking initiation: implications for quitting.* Health Rep, 1998. **9**(4): p. 39-46(Eng); 39-48(Fre).
- 5. Adelman, W.P., *Tobacco use cessation for adolescents.* Adolesc Med Clin, 2006. **17**(3): p. 697-717; abstract xii.
- 6. DiFranza, J.R. and R.J. Wellman, *A sensitization-homeostasis model of nicotine craving, withdrawal, and tolerance: integrating the clinical and basic science literature.* Nicotine Tob Res, 2005. **7**(1): p. 9-26.
- 7. DiFranza, J.R. and R.J. Wellman, *Sensitization to nicotine: how the animal literature might inform future human research.* Nicotine Tob Res, 2007. **9**(1): p. 9-20.
- 8. Ginzel, K.H., et al., *Critical review: nicotine for the fetus, the infant and the adolescent?* J Health Psychol, 2007. **12**(2): p. 215-24.
- 9. Nelson, D.E., et al., Long-term trends in adolescent and young adult smoking in the United States: metapatterns and implications. Am J Public Health, 2008. **98**(5): p. 905-15.
- 10. Spear, L.P., *The adolescent brain and age-related behavioral manifestations*. Neurosci Biobehav Rev, 2000. **24**(4): p. 417-63.
- 11. England, L.J., et al., *Nicotine and the Developing Human: A Neglected Element in the Electronic Cigarette Debate.* Am J Prev Med, 2015.
- 12. Dwyer, J.B., R.S. Broide, and F.M. Leslie, *Nicotine and brain development*. Birth Defects Res C Embryo Today, 2008. **84**(1): p. 30-44.
- 13. Goriounova, N.A. and H.D. Mansvelder, *Short- and long-term consequences of nicotine exposure during adolescence for prefrontal cortex neuronal network function*. Cold Spring Harb Perspect Med, 2012. **2**(12): p. a012120.
- 14. England, L.J., et al., *Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products.* Neurosci Biobehav Rev, 2017. **72**: p. 176-189.
- 15. U.S. Department of Health and Human Services, National Institutes of Health, and National Cancer Institute. *Smoke-free Teens: Health Effects*. 2014 [cited 2014 November 6]; Available from: http://teen.smokefree.gov/yourHealthEffects.aspx#.VFu27PnF-pl
- 16. U.S. Department of Health and Human Services, *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta, GA.
- 17. Centers for Disease Control and Prevention, *Incidence of initiation of cigarette smoking--United States, 1965-1996.* MMWR Morb Mortal Wkly Rep, 1998. **47**(39): p. 837-40.

- 18. United States Public Health Service, et al., *Preventing tobacco use among youth and young adults : a report of the Surgeon General.* 2012, Atlanta, Ga.: U.S. Dept. of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion For sale by the Supt. of Docs., U.S. G.P.O. xiv, 899 p.
- 19. Dwyer, J.B., S.C. McQuown, and F.M. Leslie, *The dynamic effects of nicotine on the developing brain.* Pharmacol Ther, 2009. **122**(2): p. 125-39.
- 20. Schochet, T.L., A.E. Kelley, and C.F. Landry, *Differential expression of arc mRNA and other plasticity-related genes induced by nicotine in adolescent rat forebrain.* Neuroscience, 2005. **135**(1): p. 285-97.
- 21. Polesskaya, O.O., et al., *Nicotine causes age-dependent changes in gene expression in the adolescent female rat brain.* Neurotoxicol Teratol, 2007. **29**(1): p. 126-40.
- 22. Duncan, J.R., et al., *Prenatal nicotine-exposure alters fetal autonomic activity and medullary neurotransmitter receptors: implications for sudden infant death syndrome.* J Appl Physiol (1985), 2009. **107**(5): p. 1579-90.
- 23. Poorthuis, R.B., et al., *Nicotinic actions on neuronal networks for cognition: general principles and long-term consequences.* Biochem Pharmacol, 2009. **78**(7): p. 668-76.
- 24. Bublitz, M.H. and L.R. Stroud, *Maternal smoking during pregnancy and offspring brain structure and function: review and agenda for future research.* Nicotine Tob Res, 2012. **14**(4): p. 388-97.
- 25. Trauth, J.A., F.J. Seidler, and T.A. Slotkin, *An animal model of adolescent nicotine exposure:* effects on gene expression and macromolecular constituents in rat brain regions. Brain Res, 2000. **867**(1-2): p. 29-39.
- 26. Counotte, D.S., et al., *Long-lasting cognitive deficits resulting from adolescent nicotine exposure in rats.* Neuropsychopharmacology, 2009. **34**(2): p. 299-306.
- 27. Alajaji, M., et al., *Early adolescent nicotine exposure affects later-life cocaine reward in mice.* Neuropharmacology, 2016. **105**: p. 308-17.
- 28. Reed, S.C. and S. Izenwasser, *Nicotine produces long-term increases in cocaine reinforcement in adolescent but not adult rats.* Brain Res, 2017. **1654**(Pt B): p. 165-170.
- 29. Abreu-Villaca, Y., et al., Short-term adolescent nicotine exposure has immediate and persistent effects on cholinergic systems: critical periods, patterns of exposure, dose thresholds. Neuropsychopharmacology, 2003. **28**(11): p. 1935-49.
- 30. Abreu-Villaca, Y., et al., *Nicotine is a neurotoxin in the adolescent brain: critical periods, patterns of exposure, regional selectivity, and dose thresholds for macromolecular alterations.* Brain Res, 2003. **979**(1-2): p. 114-28.
- 31. Slikker, W., Jr., et al., Mode of action: disruption of brain cell replication, second messenger, and neurotransmitter systems during development leading to cognitive dysfunction--developmental neurotoxicity of nicotine. Crit Rev Toxicol, 2005. **35**(8-9): p. 703-11.
- 32. Slotkin, T.A., *Nicotine and the adolescent brain: insights from an animal model.* Neurotoxicol Teratol, 2002. **24**(3): p. 369-84.
- 33. Gould, T.J. and P.T. Leach, *Cellular, molecular, and genetic substrates underlying the impact of nicotine on learning.* Neurobiol Learn Mem, 2014. **107**: p. 108-32.
- 34. U.S. Department of Health and Human Services, *How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the Surgeon General.* 2010, U.S. Department of Health and Human Services, CDC: Atlanta, GA.

- 35. United States, et al., *The Health Consequences of Smoking: Nicotine Addiction: A Report of the Surgeon General.* 1988: Rockville, MD.
- 36. Stolerman, I.P. and M.J. Jarvis, *The scientific case that nicotine is addictive*. Psychopharmacology (Berl), 1995. **117**(1): p. 2-10; discussion 14-20.
- 37. Royal College of Physicians, *Nicotine Addiction in Britain*. 2000, Royal College of Physicians: London.
- 38. Balfour, D.J., The neurobiology of tobacco dependence: a preclinical perspective on the role of the dopamine projections to the nucleus accumbens [corrected]. Nicotine Tob Res, 2004. **6**(6): p. 899-912.
- 39. DiFranza, J.R., et al., *Initial symptoms of nicotine dependence in adolescents*. Tob Control, 2000. **9**(3): p. 313-9.
- 40. U.S. Department of Health and Human Services, *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. 2014, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health: Atlanta.
- 41. Henningfield, J.E. and R.M. Keenan, *Nicotine delivery kinetics and abuse liability.* J Consult Clin Psychol, 1993. **61**(5): p. 743-50.
- de Wit, H. and J.P. Zacny, *Abuse potential of nicotine replacement therapies*. CNS Drugs, 1995. **4**(6): p. 456-468.
- 43. Stitzer, M.L. and H. de Wit, *Abuse liability of nicotine*, in *Nicotine Safety and Toxicity*, N.L. Benowitz, Editor. 1998, Oxford University Press: New York. p. 119-131.
- 44. Rose, J.E., et al., *Arterial nicotine kinetics during cigarette smoking and intravenous nicotine administration: implications for addiction.* Drug Alcohol Depend, 1999. **56**(2): p. 99-107.
- 45. Benowitz, N.L., *Neurobiology of nicotine addiction: implications for smoking cessation treatment.* Am J Med, 2008. **121**(4 Suppl 1): p. S3-10.
- 46. Benowitz, N.L., *Nicotine addiction*. N Engl J Med, 2010. **362**(24): p. 2295-303.
- 47. Psychology Today. Nicotine. 2014 November 24, 2014 [cited 2015 March 12].
- 48. Chambers, R.A., J.R. Taylor, and M.N. Potenza, *Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability.* Am J Psychiatry, 2003. **160**(6): p. 1041-52.
- 49. Casey, B.J., et al., *Imaging the developing brain: what have we learned about cognitive development?* Trends Cogn Sci, 2005. **9**(3): p. 104-10.
- 50. Ernst, M., et al., Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. Neuroimage, 2005. **25**(4): p. 1279-91.
- 51. Ernst, M. and J.L. Fudge, A developmental neurobiological model of motivated behavior: anatomy, connectivity and ontogeny of the triadic nodes. Neurosci Biobehav Rev, 2009. **33**(3): p. 367-82.
- 52. Torres, O.V., et al., *Enhanced vulnerability to the rewarding effects of nicotine during the adolescent period of development.* Pharmacol Biochem Behav, 2008. **90**(4): p. 658-63.
- 53. O'Dell, L.E., *A psychobiological framework of the substrates that mediate nicotine use during adolescence.* Neuropharmacology, 2009. **56 Suppl 1**: p. 263-78.
- 54. Thompson, B.L., P. Levitt, and G.D. Stanwood, *Prenatal exposure to drugs: effects on brain development and implications for policy and education.* Nat Rev Neurosci, 2009. **10**(4): p. 303-12.

- 55. Slotkin, T.A., *Fetal nicotine or cocaine exposure: which one is worse?* J Pharmacol Exp Ther, 1998. **285**(3): p. 931-45.
- 56. Maritz, G.S., *Nicotine and lung development*. Birth Defects Res C Embryo Today, 2008. **84**(1): p. 45-53.
- 57. Pierce, R.A. and N.M. Nguyen, *Prenatal nicotine exposure and abnormal lung function*. Am J Respir Cell Mol Biol, 2002. **26**(1): p. 10-3.
- 58. Sekhon, H.S., et al., *Prenatal nicotine increases pulmonary alpha7 nicotinic receptor expression and alters fetal lung development in monkeys.* J Clin Invest, 1999. **103**(5): p. 637-47.
- 59. Sekhon, H.S., et al., *Prenatal nicotine exposure alters pulmonary function in newborn rhesus monkeys.* Am J Respir Crit Care Med, 2001. **164**(6): p. 989-94.
- 60. Sekhon, H.S., et al., *Maternal nicotine exposure upregulates collagen gene expression in fetal monkey lung. Association with alpha7 nicotinic acetylcholine receptors.* Am J Respir Cell Mol Biol, 2002. **26**(1): p. 31-41.
- 61. Gupta, P.C. and S. Subramoney, *Smokeless tobacco use, birth weight, and gestational age: population based, prospective cohort study of 1217 women in Mumbai, India.* BMJ, 2004. **328**(7455): p. 1538.
- 62. Gupta, P.C. and S. Subramoney, *Smokeless tobacco use and risk of stillbirth: a cohort study in Mumbai, India*. Epidemiology, 2006. **17**(1): p. 47-51.
- Baba, S., et al., *Influence of smoking and snuff cessation on risk of preterm birth*. Eur J Epidemiol, 2012. **27**(4): p. 297-304.
- 64. England, L.J., et al., Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: a case-control study. Acta Obstet Gynecol Scand, 2013. **92**(6): p. 648-55.
- 65. De Genna, N.M., et al., *Prenatal tobacco exposure, maternal postnatal nicotine dependence and adolescent risk for nicotine dependence: Birth cohort study.* Neurotoxicol Teratol, 2017.
- 66. Benowitz, N.L., *Cigarette smoking and cardiovascular disease: pathophysiology and implications for treatment.* Prog Cardiovasc Dis, 2003. **46**(1): p. 91-111.
- 67. Benowitz, N.L., et al., *Prolonged absorption with development of tolerance to toxic effects after cutaneous exposure to nicotine*. Clin Pharmacol Ther, 1987. **42**(1): p. 119-20.
- 68. Okamoto, M., et al., *Tolerance to the convulsions induced by daily nicotine treatment in rats.* Jpn J Pharmacol, 1992. **59**(4): p. 449-55.
- 69. Cameron, J.M., et al., *Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions*. Tob Control, 2014. **23**(1): p. 77-8.
- 70. Cantrell, F.L., *Adverse effects of e-cigarette exposures.* J Community Health, 2014. **39**(3): p. 614-6.
- 71. Chatham-Stephens, K., et al., *Notes from the field: calls to poison centers for exposures to electronic cigarettes--United States, September 2010-February 2014.* MMWR Morb Mortal Wkly Rep, 2014. **63**(13): p. 292-3.
- 72. Schroeder, M.J. and A.C. Hoffman, *Electronic cigarettes and nicotine clinical pharmacology.* Tob Control, 2014. **23 Suppl 2**: p. ii30-5.
- 73. Goniewicz, M.L., et al., *Nicotine levels in electronic cigarettes.* Nicotine Tob Res, 2013. **15**(1): p. 158-66.
- 74. U. S. Congress. *Child Nicotine Poisoning Prevention Act of 2015*. 2016 [cited 2017 March 21]; Available from: https://www.congress.gov/bill/114th-congress/senate-bill/142.