Fact Sheet 2: Nicotine, the Heart & the Cardiovascular System

Renee Bittoun [1,2.] and Matt Akehurst [2.]

1. Nicotine Addiction Unit, Lifestyle Medicine, Avondale University
2. School of Medicine, Notre Dame University, Australia

For at least a century it has been known that nicotine has a profound effect on human cardiovasculature. By 1926, predating the oral cancer warnings he received, Sigmund Freud's physician suggested he give up cigars because nicotine had caused his heart disease. With the advent and promotion of Electronic Cigarettes and Vaping devices that contain nicotine, this Fact Sheet is a reminder of the effects that nicotine has on the heart and the vasculature and that these effects are not benign.
It is important to note that different modalities and speed of delivery of nicotine effect the vasculature in different ways.
As described in Fact Sheet 1, there is a hierarchical effect on the vasculature, such that the faster or sharper the bolus of nicotine delivered into the bloodstream, the greater the physiological effect. Hence steady state nicotine delivery, such as through nicotine transdermal patches, has little to no vascular effect, whereas nicotine acutely delivered via the lungs as a bolus, such as by inhaling cigarette smoke or vaping, has a significant cardiovascular effect on smokers and non-smokers alike.
Below is a list of important effects of nicotine from the foetal and perinatal though to the adult cardiovasculature and some references to the cardiac safety of nicotine containing smoking cessation products.

GENERAL CARDIOVASCULAR SYSTEM

1. Nicotine increases heart rate & blood pressure, exacerbates angina in coronary patients, diminishes left ventricular performance and promotes arrythmias (US Surgeon General's Report, 1983).

2. Acute nicotine exposure is sympathoexcitatory, leading to increased heart rate and blood pressure (Garcia, Gornbein & Middlekauff, 2020).

3. Nicotine exposure impairs endothelial cell function and increases levels of markers for oxidative stress (Carnevale et al., 2016), substantially contributing to the development of arteriosclerotic cardiovascular disease (Zheng et al., 2021).

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

4. Nicotine mediated catecholamine release promotes coronary artery constriction, reducing blood and oxygen supply to the myocardium (Benowitz & Gourlay, 1997).

5. Nicotine elevates plasma levels of neuropeptide Y, which is a powerful vasoconstrictor and promotes endothelial dysfunction (Zheng et al., 2021).

6. Chronic nicotine exposure chronically elevates cardiac sympathetic activation without generating elevations in heart rate and blood pressure (Garcia, Gornbein & Middlekauff, 2020).

7. A single vaping session of electronic nicotine delivery systems in rats impairs arterial flow mediated dilation comparably to combusted cigarettes (Rao et al., 2022).

PERINATAL

8. Foetuses exposed to nicotine in early pregnancy are at increased risk of developing postnatal cardiac hypertrophy (Aoyagi et al., 2020).

9. Prenatal nicotine exposure promotes long term dysfunction of autonomic cardiovascular control (Nordenstam, 2021).

10. There is increased risk of hypertension and dyslipidaemia in children born to women who smoked during pregnancy (Somm et al., 2009).

11. Cotinine, nicotine's main metabolite, may cause enduring cardiovascular system abnormalities in exposed infants, such as bradycardia, hypotension, adrenergic hypocontractility & endothelial dysfunction.(Bastianini et al., 2018)

12. Postnatal exposure to nicotine through breast milk impairs autonomic cardiovascular control in infants, resulting in reduced heart rate variability which is associated with sympathetic system predominance and increased risk of ischaemic heart disease (Dahlström et al., 2008)

13. Nicotine exposure to mice foetuses decreases foetal blood flow through the dorsal aorta, carotid artery, and umbilical artery, reducing blood flow to all foetal organs and promoting intrauterine growth restriction (Aoyagi et al., 2020).

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

ADOLESCENCE

14. Nicotine exposure in adolescents causes a reduction in heart rate variability in non-smoking adolescents, a factor which is associated with increased risk of major adverse cardiac events in later life (Guo et al., 2022).

ADULTHOOD

15. Nicotine exposure increases the likelihood of myocardial infarction in adults, independent of smoking and other risk factors (Alzharani et al., 2018).

16. Nicotine exposure is associated with erectile dysfunction in adulthood, independent of age, cardiovascular disease and other risk factors (El-Shahawy et al., 2022).

17. Nicotine stimulates pathological angiogenesis in pre-clinical models of carcinomas, atherosclerosis, and age-related macular degeneration (Lee & Cooke, 2012).

18. Inhalation of nicotine in adults causes increased arterial stiffness directly following exposure for approximately thirty minutes (Antoniewicz et al., 2019).

19. Nicotine decreases exercise time to angina by increasing myocardial oxygen demand and by decreasing myocardial oxygen delivery (Aronow & Cassidy, 1975)

20. Following administration of intravenous adenosine, nicotine enhanced the stimulatory effect of adenosine on angina like chest pain (Sylven et al., 1990)

NICOTINE REPLACEMENT THERAPY

21. The use of nicotine replacement therapy poses no increased risk of cardiovascular disease in smokers with cardiovascular diagnoses (Ford & Zlabek, 2005).

22. The commencement of nicotine replacement therapy for smokers hospitalized with acute myocardial infarction or coronary heart disease is not associated with any increase in inpatient mortality (Pack et al., 2018).

23. Amongst patients with cardiac disease, transdermal nicotine replacement therapy does not cause a significant increase in risk of adverse cardiovascular events (Joseph et al., 1996).

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

24. There is no evidence from human studies that nicotine replacement therapy increases the risk of healing related or cardiovascular complications in the perioperative period (Nolan et al., 2015)

25. Smoking cessation with nicotine replacement therapy reverses endothelial dysfunction, arterial stiffness, and inflammation (Xue et al., 2019).

26. Cigarette smoking gives rise to a high peak concentration of nicotine in blood, whilst the use of nicotine-rich dermal patches leads to a high peak concentration of nicotine in the liver (Gajewska et al., 2014).

27. "…minimal amounts of nicotine are excreted into breast milk so nicotine replacement can be safely used by breast-feeding mothers." – (Dempsey & Benowitz, 2001)

ACKNOWLEDGMENTS:

Reviewer: Professor David Celermajer, Professor of Cardiology at Sydney University and Royal Prince Alfred Hospital, Sydney.

Commentary: Tracey Greenberg, NSW Ministry of Health Tobacco Cessation Trainer

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

REFERENCE LIST

Alzahrani, T., Pena, I., Temesgen, N., & Glantz, S. A. (2018). Association between electronic cigarette use and myocardial infarction. *Am J Prev Med, 55*(4), 455-461. https://doi.org/10.1016/j.amepre.2018.05.004

Antoniewicz, L., Brynedal, A., Hedman, L., Lundbäck, M., & Bosson, J. A. (2019). Acute effects of electronic cigarette inhalation on the vasculature and the conducting airways. *Cardiovasc Toxicol, 19*(5), 441-450. https://doi.org/10.1007/s12012-019-09516-x

Aoyagi, Y., Momoi, N., Kanai, Y., Go, H., Abe, Y., Miyazaki, K., . . . Hosoya, M. (2020). Prenatal nicotine exposure affects cardiovascular function and growth of the developing fetus. *J Obstet Gynaecol Res, 46*(7), 1044-1054. https://doi.org/10.1111/jog.14294

Aronow, W. S., & Cassidy, J. (1975). Effect of smoking marihuana and of a high-nicotine cigarette on angina pectoris. *Clin Pharmacol Ther, 17*(5), 549-554. https://doi.org/10.1002/cpt1975175549

Bastianini, S., Lo Martire, V., Silvani, A., Zoccoli, G., Berteotti, C., Lagercrantz, H., . . . Cohen, G. (2018). Long-term cardiovascular reprogramming by short-term perinatal exposure to nicotine's main metabolite cotinine. *Acta Paediatr, 107*(4), 638-646. https://doi.org/10.1111/apa.14181

Carnevale, R., Sciarretta, S., Violi, F., Nocella, C., Loffredo, L., Perri, L., . . . Frati, G. (2016). Acute impact of tobacco vs electronic cigarette smoking on oxidative stress and vascular function. *Chest, 150*(3), 606-612. https://doi.org/10.1016/j.chest.2016.04.012

Dahlström, A., Ebersjö, C., & Lundell, B. (2008). Nicotine in breast milk influences heart rate variability in the infant. *Acta Paediatr, 97*(8), 1075-1079. https://doi.org/10.1111/j.1651-2227.2008.00785.x

Dempsey, D. A., & Benowitz, N. L. (2001). Risks and benefits of nicotine to aid smoking cessation in pregnancy. *Drug Saf, 24*(4), 277-322. https://doi.org/10.2165/00002018-200124040-00005

El-Shahawy, O., Shah, T., Obisesan, O. H., Durr, M., Stokes, A. C., Uddin, I., . . . Blaha, M. J. (2022). Association of e-cigarettes with erectile dysfunction: The population assessment of tobacco and health study. *Am J Prev Med, 62*(1), 26-38. https://doi.org/10.1016/j.amepre.2021.08.004

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

Ford, C. L., & Zlabek, J. A. (2005). Nicotine replacement therapy and cardiovascular disease. *Mayo Clin Proc, 80*(5), 652-656. https://doi.org/10.4065/80.5.652

Gajewska, M., Worth, A., Urani, C., Briesen, H., & Schramm, K. W. (2014). The acute effects of daily nicotine intake on heart rate--a toxicokinetic and toxicodynamic modelling study. *Regul Toxicol Pharmacol, 70*(1), 312-324. https://doi.org/10.1016/j.yrtph.2014.07.015

Garcia, P. D., Gornbein, J. A., & Middlekauff, H. R. (2020). Cardiovascular autonomic effects of electronic cigarette use: a systematic review. *Clin Auton Res, 30*(6), 507-519. https://doi.org/10.1007/s10286-020-00683-4

Guo, Q. N., Wang, J., Liu, H. Y., Wu, D., & Liao, S. X. (in press). Nicotine ingestion reduces heart rate variability in young healthy adults. *Biomed Res Int,* 4286621. https://doi.org/10.1155/2022/4286621

Joseph, A. M., Norman, S. M., Ferry, L. H., Prochazka, A. V., Westman, E. C., Steele, B. G., McGovern, P. G. (1996). The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. *N Engl J Med, 335*(24), 1792-1798. https://doi.org/10.1056/nejm199612123352402

Nolan, M. B., & Warner, D. O. (2015). Safety and efficacy of nicotine replacement therapy in the perioperative period: A narrative review. *Mayo Clin Proc, 90*(11), 1553-1561. https://doi.org/10.1016/j.mayocp.2015.08.003

Nordenstam, F. (2021). Prenatal nicotine exposure was associated with long-term impact on the cardiovascular system and regulation. *Review. Acta Paediatrica, 110*(9), 2536-2544. doi: https://doi.org/10.1111/apa.15914

Pack, Q. R., Priya, A., Lagu, T. C., Pekow, P. S., Atreya, A., Rigotti, N. A., & Lindenauer, P. K. (2018). Short-term safety of nicotine replacement in smokers hospitalized with coronary heart disease. *J Am Heart Assoc, 7*(18), e009424. https://doi.org/10.1161/jaha.118.009424

Rao, P., Han, D. D., Tan, K., Mohammadi, L., Derakhshandeh, R., Navabzadeh, M., . . . Springer, M. L. (in press). Comparable impairment of vascular endothelial function by a wide range of electronic nicotine delivery devices. *Nicotine Tob Res*. https://doi.org/10.1093/ntr/ntac019

Somm, E., Schwitzgebel, V. M., Vauthay, D. M., Aubert, M. L., & Hüppi, P. S. (2009). Prenatal nicotine exposure and the programming of metabolic and cardiovascular disorders. *Mol Cell Endocrinol, 304*(1-2), 69-77. https://doi.org/10.1016/j.mce.2009.02.026

PROFESSOR RENEE BITTOUN: NICOTINE ADDICTION UNIT – LIFESTYLE MEDICINE AND HEALTH RESEARCH CENTRE

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL

U.S. Department of Health and Human Services. (1983). *The health consequences of smoking: Cardiovascular disease* (DHHS Publication No. 84-50204). https://profiles.nlm.nih.gov/101584932X318c

Xue, C., Chen, Q. Z., Bian, L., Yin, Z. F., Xu, Z. J., Zhang, A. L., . . . Wang, C. Q. (2019). Effects of smoking cessation with nicotine replacement therapy on vascular endothelial function, arterial stiffness, and inflammation response in healthy smokers. *Angiology, 70*(8), 719-725. https://doi.org/10.1177/0003319719853458

Zheng, Y. L., Wang, W. D., Li, M. M., Lin, S., & Lin, H. L. (2021). Updated role of neuropeptide Y in nicotine-induced endothelial dysfunction and atherosclerosis. *Front Cardiovasc Med*, 8, 630968. https://doi.org/10.3389/fcvm.2021.630968

PROFESSOR RENEE BITTOUN: NICOTINE ADDICTION UNIT – LIFESTYLE MEDICINE AND HEALTH RESEARCH CENTRE

© 2022. This work is licensed under a CC BY NC ND 4.0 license.

WANT TO LEARN MORE? CALL +61 2 49802377 TO ENQUIRE ABOUT AVONDALE UNIVERSITY'S POST-GRADUATE "NICOTINE ADDICTION & SMOKING CESSATION" MICRO-CREDENTIAL