

How to Cite:

Almjalawi, B. S. A., Alabassi, H. M., & Alhesnawi, A. S. M. (2022). Effect of some factors on microbiota vitality and its reflection on the gut. *International Journal of Health Sciences*, 6(S3), 5854–5863. <https://doi.org/10.53730/ijhs.v6nS3.7277>

Effect of some factors on microbiota vitality and its reflection on the gut

Batool Shakir Abed Almjalawi

General Directorate of Education in Karbala, Karbala, Iraq

*Corresponding author email: batoolshakir5@gmail.com

Hazima Mossa Alabassi

University of Baghdad, College of Education for Pure Science-Ibn Alhaitham, Baghdad, Iraq

Email: Hazima.m.k@ihcoedu.uobaghdad.edu.iq

Asaad Sh. M. Alhesnawi

University of Kerbala/College of Applied Medical Sciences, Karbala, Iraq.

Email: asaad.sh@uokerbala.edu.iq

Abstract---The presence of microbiota in the Gut is very essential in the digestion process, and some factors may cause dysfunction in their activity. This review study is focused on effect of four factors on gut microbiota function, which includes; intake of, antibiotics, alcohol, smoking, and mental issues such as; depression, anxiety, tension. The study went through the findings of a lot of researchers and came up with some conclusions such as; incorrect using of the antibiotics affect the functions of the GI microbiota causing disorder in the digestion system, Smoking cause disease in different organs, affecting the general health of the human being which reflect on nutrition and digestion, alcohol effects microbiota leading to liver fibrosis, hepatitis that effects digestion system.

Keywords---microbiota, the gut, smoking, alcohol, antibiotic.

Introduction

Microorganisms are considered the most plentiful creatures on the surface of the earth and human life was modified according to the presence of these microbes, the researchers and scientists describe the microbiota and define it as a collection of microorganisms such as; viruses, bacteria, fungi and eukaryotes that presents in different sites of human body, and the name of microbiota usually combined with its location such as intestinal microbiota which represent their presence in the gut and intestinal tract ^(1, 2). In human beings, microbiota includes large and

various single cell microorganisms that live in the human body such as fungi, viruses, protozoa, and bacteria, while the gene inside this microbiota is called microbiome; however, most of the microbiota in the gut of human beings is useful in healthy bodies. The intestinal microbiome bacterium help in digesting food control and adjust the immune system and increases its protection against diseases and raise the production of vitamins such as B, and K ^(3, 4).

Since 2003 until 2015 Guarner ^(5, 6) was carried out a lot of researches and clinical experiments to find the correlation between gut and microbiota, he found that these microorganisms are very important to enhance the function of humans, improve digestion and lower the risk of diseases. This finding was supported in 2019 by Ananthakrishnan and his coworkers who enhance and recognized association between microbiota of gut and diseases ⁽⁷⁾. Recent studies confirm the association between gut microbiota and immune system of human body this is called (Immunity-Microbiome Dialogues) the researchers confirmed the correlation between the microbiota of gut and its impact on the function and the activity of the host which reflected on the metabolism of the host immunity and the risk of diseases ^(8, 9).

In (2005) Nicholson and his coworker describe the main bacterial gathering that is located in gastrointestinal tract (GI) of the host, as a microbiota that has many functions such as physiological, immunological, and nutritional that affected the life of human beings ⁽¹⁰⁾. In (2007) Frank *et al* ⁽¹¹⁾, explained that the composition of mucus-associated bacteria and epithelial crypts diverges widely from that of glossy and fecal content. Figure 1 shows this diversity.

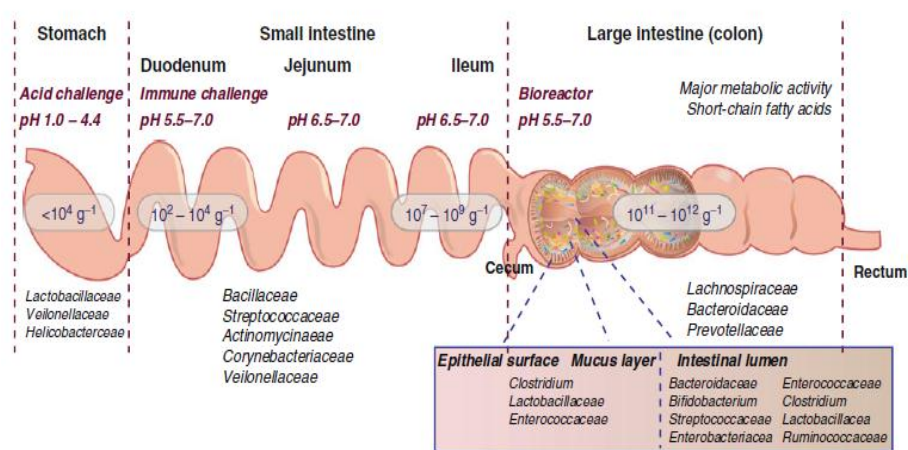


Figure 1. Diversity of microbiota in GI tract ⁽¹²⁾

In (2016) Gensollen and his coworkers ⁽¹³⁾ found that early colonization of the mucosal surfaces of host mammals plays a significant role in the maturation of immune system of the host ⁽¹³⁾, the researchers also concluded that the majority of the significant process in the development of the host immunity may occur throughout the early years of the mammal's life, where the composition of the microorganism (microbiota) shows the maximum variation between individuals. This finding was also previously found by (Bäckhed., et al 2015) ⁽¹⁴⁾. In general,

there were many factors affecting functions of the microbiota in GI tract and may reflects on the immune system and the causes of some diseases risks, among them are:

Incorrect using of antibiotics

In general, antibiotic has an effect not only on the infectious bacteria that cause illness and diseases, but it affected the useful microbiota inside the intestinal tract (gut microbiota) as well. Even though this side effect has been recognized a long time ago, the development and the advances in the inspection technologies make things easier for the researchers and enable them to achieve comprehensive studies and researches in particular the changes and the alteration that occurs in the microbiota of the guts ⁽¹⁵⁾. In 1928, Alexander Fleming discovered penicillin, and since that time, antibiotics were used in treating and managing infectious diseases and a lot of people lives were saved by using the penicillin ⁽¹⁶⁾. The misuse and overuse of the antibiotics was the concern of the scientists as well as the researchers for the last twenty years due to its serious affect on the health of the individuals, and one of the main concerns is Antibiotic Resistance (AR) which threatens the physicians in infectious diseases ⁽¹⁶⁾.

Even while irrational antibiotic usage was formerly thought to be an issue exclusively in developed nations, it has recently increased dramatically in middle and low-income countries ⁽¹⁷⁾. It's worth noting that de Jong et al. found that the antibiotic-resistant bacteria from animal farms can be cause of the therapeutic failure in individuals who live in rural regions in their observational study, a supposition that, of course, requires additional exploration ⁽¹⁸⁾. Yet, according to another research, urban areas had an 8-fold greater prevalence rate than rural areas, owing to the fact that antibiotic prescriptions were more common in towns with hospitals. In urban areas, in which individuals receive better quality hospital care, the incidence of antibiotic prescriptions was 46.8% ⁽¹⁹⁾. AR is becoming increasingly common in hospitals as the number of surgical procedures, patients, and interventions increase, all of associated with the increased utilization of the antibiotics in healthcare context.

Antibiotics are widely documented for the alteration of host's indigenous microbiota through choosing resistant bacteria which might be manifested as opportunistic pathogens ⁽²⁰⁾. Gut dysbiosis was associated with the intake of low-dosage antibiotic or sub-therapeutic antibiotic treatment (STAT) from the environment and foods. Also, the gut dysbiosis has deleterious impacts upon various host systems and processes. The microbiome of the gut was associated with various pathological conditions, and scientists were focused upon associations between the gut microbiota and antibiotics due to the fact that it could be "at the intersection of everything" ⁽²¹⁾. Antibiotics have been linked to gut microbiome disruptions, according to accumulating data primarily from animal research ^(22,23). Antibiotic use was linked to gut microbiome alterations, despite the fact that infectious disease morbidity and death were significantly decreased.

Antibiotic resistance is increasing on a daily basis, not just in hospitals, yet also in a variety of other settings. Antibiotics are given to animals for a variety of reasons, including treating illnesses and achieving faster growth for the

commercial objectives. Furthermore, AR has been found in pathogens of the plants ⁽²⁴⁾. Antibiotics that are utilized in medicine and animal feed play the role in the antibiotic resistance that spreads in food and the environment ⁽²⁵⁾. Resistance is currently a common feature of practically all antibiotics that have been created. Unfortunately, because of the regulatory and economic barriers, the discovery of new antibiotics slowed drastically near the end of the twentieth century ⁽²⁶⁾. The human gut microbiota usually contributes in enhance the immunity system through metabolism and food digestion and taking antibiotics could contribute and leads to dysbiosis to the gut microorganism, affects immune system and threat the human health ^(27,28). Figure 2 shows the relationship between disease antibiotics and microbiota in the human gut system ⁽¹⁵⁾.

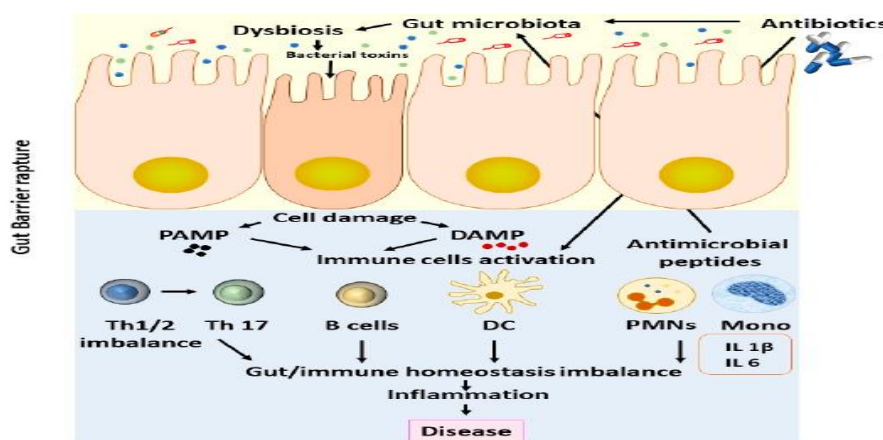


Figure 2. The effect of Antibiotics on gut system ⁽¹⁵⁾

Smoking

Cigarette smoking represents leading preventable mortality cause in the world. In spite of the widespread public awareness regarding the dangers of smoking, it's a worldwide epidemic, with 1.1 billion people globally currently smoking ⁽²⁹⁾. In addition, smoking is on the decline in advanced countries, but it is on the rise in many of the developing countries, particularly in Asia ⁽³⁰⁾. Approximately 50% of smokers will acquire major smoking-related disorders like COPD, cancer, and cardiovascular disease ^(29,31). Furthermore, secondhand smoking exposure raises the likelihood of pathogen infection and exacerbates other lung disorders like asthma ⁽³²⁾. In addition, cigarette smoking has a dual effect on the development of the IBD (i.e. inflammatory bowel disease). It hastens progression of Crohn's disease (CD) while alleviating ulcerative colitis (UC) symptoms ⁽³³⁾. Toxic components in the cigarette smoke had long been thought to be the leading cause of major diseases, and the pathological mechanisms that underpin them were extensively researched ⁽³⁴⁾. These mechanisms, yet, remain a mystery.

Cigarette smoke has been specified as complicated chemical mix containing aldehydes, nicotine, nitrosamines, polycyclic aromatic hydro-carbons (PAH), heavy metals, and other substances that is inhaled as aerosol particles or as gaseous state into the lungs ^(35,36). In vivo, such toxic compounds enhance oxidative stress and lipid peroxidation, reduce endogenous antioxidants, and raise pro-

inflammatory factor levels in host's blood ⁽³⁷⁾. Furthermore, toxicants in the cigarette smoke absorbed into GI tract cause the GI microbiota dysbiosis via various mechanisms, which include antimicrobial activities and intestinal micro-environment regulation ⁽³⁸⁾.

Around two billions of people around the world are smokers using tobacco, nargile or cigarettes for smoking, four millions of them were died every year due to the diseases that resulted from smoking such as lung diseases, cardiovascular diseases, brain diseases as well as cancer ^(39,40). Many studies show that smoking indirectly or directly, as well as environmental factors, influence the efficacy, shape, and function of microbial communities linked with humans, gut microbiota, and immune responses ^(41,42,43). The microbiota of the human gut comprises a wide range of micro-organisms (such as viruses, bacteria, and fungi) that form a mutually beneficial connection with the host under hygienic conditions; nevertheless, both environmental variables and the host alter the active balance. Smoking causes changes in microbiota of lungs, gut, and microbiota, which might result in a variety of diseases like asthma, Crohn's disease, ulcerative colitis, gingivitis, COPD, and various cancer types. Yet, the precise correlation between changes in the smoking and human microbiota is still unknown, and more research is needed ^(44,45). Figure 3 shows the correlation between diseases that are caused due to smoking and their effect on microbiota ⁽⁴⁶⁾.

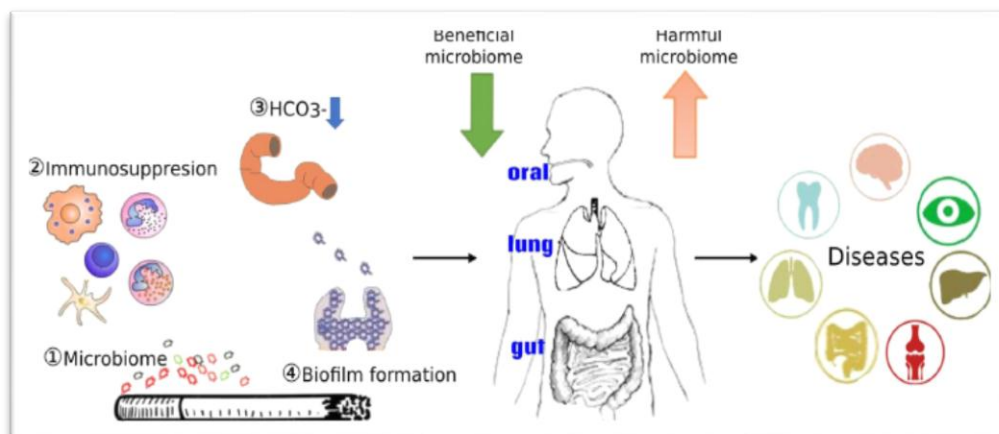


Figure 3. Correlation between smoking, diseases and gut microbiota ⁽⁴⁶⁾

Effect of alcohol on gut microbiota

Alcohol consumption is a prominent cause of global disease and one of the major risk factors for a variety of social and health problems. Alcohol is absorbed through the gastrointestinal tract (GIT) and then metabolized in the lungs and liver. Ethanol and its metabolites create health problems such as oxidative stress, direct toxicity, and the accumulation of fatty acid ethyl esters during this process ⁽⁴⁷⁾. Acetaldehyde can be defined as one of the toxic substances that was once thought to be a primary cause of diseases brought on by alcohol consumption ⁽⁴⁸⁾. Another theory has lately been raised: gut microbiota that has been altered

via alcohol consumption is involved in the development of alcohol-related disorders, and that such illnesses could be relieved by recovery of the changes in gut microbial composition resulting from alcohol.

Microbes in the gut had previously been linked to the risk of intestinal disorders such as the inflammatory bowel disease, irritable bowel syndrome, and colorectal cancer ⁽⁴⁹⁾. Since the first commercialization of next-generation sequencing (NGS) assay in 2004 ⁽⁵⁰⁾, study on the gut microbes was actively undertaken on all of the micro-organisms in an environment, in other words, microbiota, and microbiome that refers to collection of their genomes ⁽⁵¹⁾. The study of the microbiota of the gut revealed fresh evidence linking it to cardiovascular diseases, obesity, neuropsychiatric disorders, and nonalcoholic fatty liver disease, emphasizing its significance in human health ⁽⁴⁹⁾. Alcohol has an effect on the organs of the human systems causing diseases in all of them such as diseases in liver that ranged from steatosis to hepatitis passing through inflammation and cirrhosis and also caused fibrosis in liver ^(52,53).

In 2021 a study made by Lee and Lee ⁽⁵⁴⁾ about the effect of alcohol on gut microbiota, they find that alcohol affects the function of gut microbiota causing disorder and changes in its activity ⁽⁵³⁾. Taking alcohol can also lead to illness, morbidity, and may end with death. A research carried out in 2017 by Dubinkina and his coworkers find that taking alcohol causes damage to the tissues and to all gut tract including the microbiota leading to a lot of changes in their digestion functions causing diseases that associate with alcohol (alcohol-associated diseases) ^(54,55). Figure 4 shows the correlation between alcohol and gut diseases.

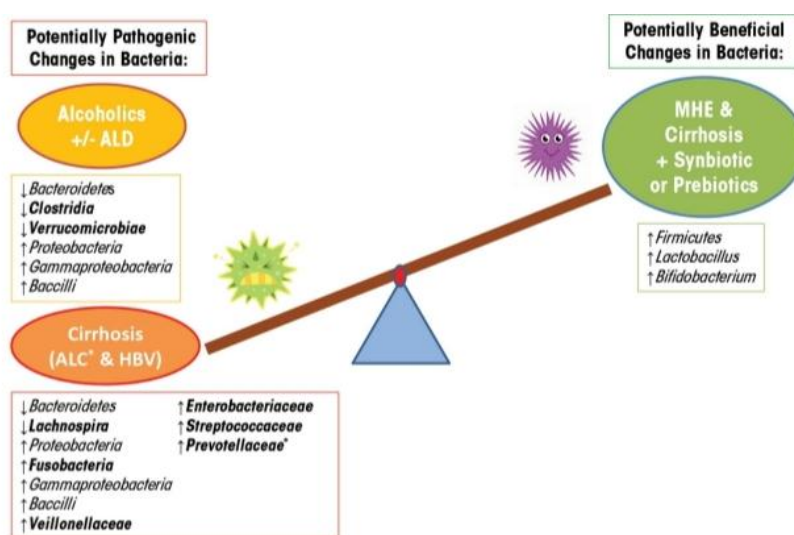


Figure 4. The imbalance in microbiota caused by alcohol intakes ⁽⁵²⁾

Conclusions

GI microbiota has essential useful role in digestion of the food, Any dysfunction in GI microbiota can affect the immunity system causing diseases in many human

organs, Incorrect use of the antibiotics may affect the functions of the GI microbiota leading to disorders in the digestion system, Smoking cause disease in different organs, such as lung disease that affect the general health of the human being which reflect on nutrition and digestion, Alcohol affects microbiota and affects liver leading to liver fibrosis, hepatitis that has an effect on digestion system and weakens the human immunity.

References

1. The Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature*. 2012; 486: 207–214. <https://doi.org/10.1038/nature11234>.
2. Thursby E, Juge N. Introduction to the human gut microbiota. *Biochemical Journal*. 2017; 474: 1823–1836. DOI: 10.1042/BCJ20160510.
3. Bull MJ, Plummer NT. Part 1: The Human Gut Microbiome in Health and Disease. *Integr Med (Encinitas)*. 2014;13(6):17–22.
4. Rowland I, Gibson G, Heinken A, et al. Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr*. 2018;57(1):1–24. doi:10.1007/s00394-017-1445-8
5. Guarner, F., and Malagelada, J. R. (2003). Gut flora in health and disease. *Lancet*. 361, 512–519. doi: 10.1016/S0140-6736(03)12489-0
6. Guarner, F. (2015). The gut microbiome: what do we know? *Clin. Liver Dis. (Hoboken)*. 5, 86–90. doi: 10.1002/cld.454
7. Ananthakrishnan AN, Singal AG, Chang L. The gut microbiome and digestive health - a new frontier. *Clin. Gastroenterol. Hepatol*. 2019; 17: 215–217. doi: 10.1016/j.cgh.2018.10.040
8. Valitutti F, Cucchiara S, Fasano A. Celiac disease and the microbiome. *Nutrients*. 2019; 11: 2403.
9. Sender, R., Fuchs, S. & Milo, R. Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell* 164, 337–340 (2016).
10. Nicholson JK, Holmes E, Wilson ID. Gut microorganisms, mammalian metabolism and personalized health care. *Nat Rev Microbiol*. 2005; 3: 431–438
11. Frank DN, Amand ALS, Feldman RA, Boedeker EC, Harpaz N, Pace NR. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci. USA*. 2007; 104: 13780–13785
12. Kovatcheva-Datchary P, Tremaroli V, Bäckhed F. The gut microbiota. In: Rosenberg E, ed. *The Prokaryotes: Human Microbiology*. Springer Berlin Heidelberg, Berlin, Heidelberg. 2013. DOI: [10.1007/978-3-642-30144-5_87](https://doi.org/10.1007/978-3-642-30144-5_87)
13. Gensollen T, Iyer SS, Kasper DL, Blumberg RS. How colonization by microbiota in early life shapes the immune system. *Science*. 2016; 352: 539–544.
14. Bäckhed F, Roswall J, Peng Y, Feng Q, Jia H, et al. Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. *Cell Host Microbe*. 2015; 17(5): 690–703. doi: 10.1016/j.chom.2015.04.004.
15. Konstantinidis T, Tsigalou C, Karvelas A, Stavropoulou E, Voidarou C, Berirtzoglou E. Effects of antibiotics upon the gut microbiome: a review of the literature. *Biomedicines*. 2020; 8(11): 502. doi: 10.3390/biomedicines8110502.

16. Gaynes R. The Discovery of Penicillin—New Insights after More Than 75 Years of Clinical Use. *Emerg. Infect. Dis.* 2017; 23: 849–853.
17. Aslam, B.; Wang, W.; Arshad, M.I.; Khurshid, M.; Muzammil, S.; Rasool, M.H.; Nisar, M.A.; Alvi, R.F.; Aslam, M.A.; Qamar, M.U.; et al. Antibiotic resistance: A rundown of a global crisis. *Infect. Drug Resist.* 2018, 11, 1645–1658. [[CrossRef](#)] [[PubMed](#)]
18. De Jong, J.; Bos, J.H.J.; de Vries, T.W.; de Jong-van den Berg, L.T.W. Use of antibiotics in rural and urban regions in The Netherlands: An observational drug utilization study. *BMC Public Health* 2014, 14, 677. [[CrossRef](#)] [[PubMed](#)]
19. Russo, V.; Monetti, V.M.; Guerriero, F.; Trama, U.; Guida, A.; Menditto, E.; Orlando, V. Prevalence of antibiotic prescription in southern Italian outpatients: Real-world data analysis of socioeconomic and sociodemographic variables at a municipality level. *ClinicoEcon. Outcomes Res.* 2018, 10, 251–258. [[CrossRef](#)]
20. Bezirtzoglou, E.; Stavropoulou, E. Immunology and probiotic impact of the newborn and young children intestinal microflora. *Anaerobe* 2011, 17, 369–374. [[CrossRef](#)]
21. Cani, P.D. Gut microbiota—At the intersection of everything? *Nat. Rev. Gastroenterol. Hepatol.* 2017, 14, 321–322. [[CrossRef](#)]
22. Leong, K.S.W.; Derraik, J.G.B.; Hofman, P.L.; Cutfield, W.S. Antibiotics, gut microbiome and obesity. *Clin. Endocrinol.* 2018, 88, 185–200. [[CrossRef](#)]
23. Belizário, J.E.; Faintuch, J. Microbiome and Gut Dysbiosis. *Exp. Suppl.* 2018, 109, 459–476. [[CrossRef](#)]
24. Stavropoulou, E.; Tsigalou, C.; Bezirtzoglou, E. Spreading of Antimicrobial Resistance (AMR) across clinical borders. *Erciyes Med. J.* 2019, 41, 238–243. [[CrossRef](#)]
25. Bezirtzoglou, P.E.; Alexopoulos, A.; Voidarou, C. Apparent antibiotic misuse in environmental ecosystems and food. *Microb. Ecol. Health Dis.* 2008, 20, 197–198. [[CrossRef](#)]
26. Bartlett, J.G.; Gilbert, D.N.; Spellberg, B. Seven ways to preserve the miracle of antibiotics. *Clin. Infect. Dis.* 2013, 56, 1445–1450. [[CrossRef](#)] [[PubMed](#)]
27. Goldenberg JZ, Mertz D, Johnston BC. Probiotics to Prevent Clostridium difficile Infection in Patients Receiving Antibiotics. *JAMA* 2018; 320: 499.
28. Ruppé E, Ghozlane A, Tap J, Pons N, et al. Prediction of the intestinal resistome by a three-dimensional structure-based method. *Nat. Microbiol.* 2019; 4: 112–123. doi: 10.1038/s41564-018-0292-6.
29. Huxley, R. R., and Woodward, M. (2011). Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. *Lancet* 378, 1297–1305. doi: 10.1016/S0140-6736(11)60781-2.
30. Rom, O., Avezov, K., Aizenbud, D., and Reznick, A. Z. (2013). Cigarette smoking and inflammation revisited. *Respir. Physiol. Neurobiol.* 187, 5–10.
31. Csordas, A., and Bernhard, D. (2013). The biology behind the atherothrombotic effects of cigarette smoke. *Nat. Rev. Cardiol.* 10, 219–230. doi: 10.1038/nrcardio.2013.8.
32. Öberg, M., Jaakkola, M. S., Woodward, A., Peruga, A., and Prüss-Ustün, A. (2011). Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. *Lancet* 377, 139–146. doi: 10.1016/S0140-6736(10)61388-8.

33. Opstelten, J. L., Plassais, J., van Mil, S. W. C., Achouri, E., Pichaud, M., Siersema, P. D., et al. (2016). Gut microbial diversity is reduced in smokers with crohn's disease. *Inflamm. Bowel. Dis.* 22, 2070–2077.
34. Smith, C. J., Perfetti, T. A., Morton, M. J., Rodgman, A., Garg, R., Selassie, C. D., et al. (2002). The relative toxicity of substituted phenols reported in cigarette mainstream smoke. *Toxicol. Sci.* 69, 265–278. doi: 10.1093/toxsci/69.1.265.
35. Theron, A. J., Tintinger, G. R., and Anderson, R. (2012). Harmful interactions of non-essential heavy metals with cells of the innate immune system. *J. Clin. Toxic.* 3, S3:005. doi: 10.4172/2161-0495.S3-005.
36. Lee, S. H., Yun, Y., Kim, S. J., Lee, E. J., Chang, Y., Ryu, S., et al. (2018). Association between cigarette smoking status and composition of gut microbiota: population-based cross-sectional study. *J. Clin. Med.* 7:282. doi: 10.3390/jcm7090282.
37. Roy, J., Palapati, P., Bettaieb, A., and Averill-Bates, D. A. (2010). Acrolein induces apoptosis through the death receptor pathway in a549 lung cells: role of p53. *Can. J. Physiol. Pharmacol.* 88, 353–368. doi: 10.1139/y09-134.
38. Bueno, S., Alvarez, M., Berkowitz, L., Pardo-Roa, C., Salazar, G., Salazar-Echegarai, F., et al. (2019). Mucosal exposure to cigarette components induces intestinal inflammation and alters antimicrobial response in mice. *Front. Immunol.* 10:2289. doi: 10.3389/fimmu.2019.02289.
39. DeMarini DM. Genotoxicity of tobacco smoke and tobacco smoke condensate: a review. *Mutat Res.* 2004; 567: 447–74.
40. Durazzo TC, Mattsson N, Weiner MW. Alzheimer's disease neuroimaging I: smoking and increased Alzheimer's disease risk: a review of potential mechanisms. *Alzheimers Dement.* 2014; 10: S122–145.
41. Shiloah J, Patters MR, Waring MB. The prevalence of pathogenic periodontal microflora in healthy young adult smokers. *J Periodontol.* 2000; 71:562–7.
42. Brook I, Gober AE. Recovery of potential pathogens and interfering bacteria in the nasopharynx of smokers and nonsmokers. *Chest.* 2005;127: 2072–2075.
43. Brook I, Gober AE. Recovery of potential pathogens in the nasopharynx of healthy and otitis media-prone children and their smoking and nonsmoking parents. *Ann Otol Rhinol Laryngol.* 2008; 117: 727–30.
44. Zhang R, Chen L, Cao L, Li KJ, Huang Y, Luan XQ, Li G. Effects of smoking on the lower respiratory tract microbiome in mice. *Respir Res.* 2018; 19: 253.
45. Valles Y, Inman CK, Peters BA, Ali R, Wareth LA, et al. Types of tobacco consumption and the oral microbiome in the United Arab Emirates Healthy Future (UAEHFS) Pilot Study. *Sci Rep.* 2018; 8: 11327.
46. Huang C, Shi G. Smoking and microbiome in oral, airway, gut and some systemic diseases. *J Transl Med.* 2019; 17: 225. <https://doi.org/10.1186/s12967-019-1971-7>.
47. Guo R, Ren J: Alcohol and acetaldehyde in public health: from marvel to menace. *Int J Environ Res Public Health* 2010, 7:1285-1301.
48. Salaspuro M: Key role of local acetaldehyde in upper GI tract carcinogenesis. *Best Pract Res Clin Gastroenterol* 2017, 31:491-499.
49. Chang CS, Kao CY: Current understanding of the gut microbiota shaping mechanisms. *J Biomed Sci* 2019, 26:59.

50. Alekseyev YO, Fazeli R, Yang S, Basran R, Maher T, Miller NS, Remick D: A next-generation sequencing primer-how does it work and what can it do? *Acad Pathol* 2018, 5:2374289518766521.
51. Malla MA, Dubey A, Kumar A, Yadav S, Hashem A, Abd Allah EF: Exploring the human microbiome: The potential future role of next-generation sequencing in disease diagnosis and treatment. *Front Immunol* 2018, 9:2868.
52. Engen PA, Green SJ, Voigt RM, Forsyth CB, Keshavarzian A. The Gastrointestinal Microbiome: Alcohol Effects on the Composition of Intestinal Microbiota. *Alcohol Res.* 2015; 37(2): 223-236.
53. Bajaj, J.S. Alcohol, liver disease and the gut microbiota. *Nat Rev Gastroenterol Hepatol.* 2019; 16: 235–246. <https://doi.org/10.1038/s41575-018-0099-1>
54. Lee E, Lee J-E. Impact of drinking alcohol on gut microbiota: recent perspectives on ethanol and alcoholic beverage. *Current opinion in food science.* 2021; 37: 91-97. <https://doi.org/10.1016/j.cofs.2020.10.001>.
55. Dubinkina VB, Tyakht AV, Odintsova VY, et al. Links of gut microbiota composition with alcohol dependence syndrome and alcoholic liver disease. *Microbiome.* 2017; 5: 141. <https://doi.org/10.1186/s40168-017-0359-2>.