NOTES FROM THE FIELD

Double Jeopardy: Methamphetamine Use and HIV as Risk Factors for COVID-19

Adam W. Carrico1,6 · Keith J. Horvath2 · Christian Grov3 · Judith T. Moskowitz4 · Savita Pahwa1 · Suresh Pallikkuth1 · Sabina Hirshfield5

Published online: 7 April 2020
© Springer Science+Business Media, LLC, part of Springer Nature 2020

Among men who have sex with men (MSM), the co-occurrence of methamphetamine (meth) use and HIV could create a double jeopardy for coronavirus disease 2019 (COVID-19). Co-occurring meth and HIV could amplify biological and behavioral risk for infection with the novel coronavirus (SARS-CoV-2), presenting unique challenges to halting community-level transmission. This confluence of bio-behavioral risk factors related to meth and HIV may also synergistically enhance vulnerability to COVID-19 progression. Below we provide an overview of important areas for further research regarding the potential implications of the intertwining epidemics of meth use and HIV for the COVID-19 pandemic in MSM.

The resurgence of meth use in MSM threatens to compromise biomedical approaches to HIV/AIDS prevention, such as treatment as prevention (TasP), and fuel the COVID-19 pandemic. The prevalence of stimulant use is twofold greater among MSM living with HIV [14], and stimulant use undermines the clinical and public health benefits of TasP. Our team and others have demonstrated that people living with HIV who use stimulants experience profound difficulties with navigating the HIV care continuum, including poorer antiretroviral therapy (ART) adherence and persistence, that lead to slower rates of viral suppression [15–18] and faster mortality [19, 20]. Even in the era of universal ART, stimulant users in a clinical cohort comprised mostly of MSM receiving HIV care at Zuckerberg San Francisco General Hospital reached viral suppression more slowly [15]. It is plausible that the COVID-19 pandemic will present new barriers to engagement along the HIV care continuum, which could disproportionately affect people who use stimulants. This could include difficulties with obtaining timely laboratory results or refilling ART medications. The difficulties that people who use stimulants experience with achieving and maintaining viral suppression could enhance biological vulnerability to SARS-CoV-2 infection as well as lead to faster COVID-19 progression.

HIV is already damaging the immune system even when people are virally suppressed, a phenomenon referred to as residual immune dysregulation [21], which meth use amplifies to create a double jeopardy for COVID-19.

* Adam W. Carrico
  a.carrico@miami.edu

1 University of Miami School of Medicine, Miami, FL, USA
2 San Diego State University Department of Psychology, San Diego, CA, USA
3 City University of New York Graduate School of Public Health, New York, NY, USA
4 Northwestern University Feinberg School of Medicine, Chicago, IL, USA
5 State University of New York – Downstate Health Sciences University, New York, NY, USA
6 University of Miami Department of Public Health Sciences, 1120 NW 14th St., Office 1005, Miami, FL 33136, USA
There is increasing evidence from our team and others that meth use can induce gut-immune dysregulation, even among those with treated HIV infection [22–26]. In our prior bio-behavioral research conducted with MSM with treated HIV infection who use meth, those who provided a urine sample that was reactive for stimulants (i.e., meth or cocaine) displayed differential expression of genes and 2-directional perturbation of pathways relevant to systemic immune activation and inflammation [25]. These perturbations in gene expression relevant to immune dysregulation among those providing a urine sample that was reactive for stimulants were paralleled by elevations in plasma tumor necrosis factor-alpha (TNF-α), an important marker of systemic inflammation. We also observed concomitant elevations in soluble CD14 (sCD14), a clinically relevant plasma marker of monocyte activation [27], in those providing a urine sample that was reactive for stimulants. This partially reflects stimulation of monocytes with lipopolysaccharide leaking from the gastrointestinal tract [26]. The clinical relevance of these findings is supported by the fact that markers of systemic immune activation and inflammation are implicated in multiple, chronic medical conditions such as cardiovascular disease in people living with HIV, which have been identified as key risk factors for COVID-19 progression [28, 29].

Meth use could also contribute local immune dysregulation as well as alter the expression of angiotensin-converting enzyme 2 (ACE-2) receptors, a key site for SARS-CoV-2 binding in the lungs and small intestine [30]. Smoking is a prevalent mode of administration for meth and crack-cocaine that could enhance local immune dysregulation in the lungs and modify the expression of ACE-2 receptors to increase vulnerability to SARS-CoV-2 infection and COVID-19 progression. There are also three plausible biological pathways for meth-associated exacerbation of microbial translocation (i.e., the leaky gut) that could serve as a primary driver of systemic immune dysregulation, particularly among those living with HIV. First, the meth decreases parasympathetic tone [31], which could increase intestinal permeability. Second, meth directly damages gut barrier integrity in self-administering HIV-1 transgenic rats [32]. Third, meth-associated indoleamine 2,3-dioxygenase upregulation in treated HIV infection damages gut barrier integrity [33]. These meth-induced alterations to the gastrointestinal tract may be partially responsible for systemic immune dysregulation in people living with HIV who use meth and further research is needed to determine if meth use alters ACE-2 receptor expression in the small intestine [30]. Taken together, pulmonary immune dysregulation, gut-immune dysregulation, and enhanced ACE-2 receptor expression are biologically plausible pathways whereby co-occurring meth use and HIV could heighten vulnerability to SARS-CoV-2 infection and COVID-19 progression.

In early March of 2020, epidemiologic experts warned that as much as 70% of the population could become infected with SARS-CoV-2 without broad implementation of social distancing such as restrictions on interactions in large groups [34]. Recent forecasting models and data strongly suggest that the number of COVID-19 cases will grow exponentially in countries that do not achieve high rates of adherence to social distancing guidelines [35]. Because meth use has been consistently linked to sexual risk taking behaviors among MSM [1], it is likely that people who use meth will experience greater difficulties with adhering to COVID-19 social distancing guidelines. Men will continue to seek out partners for substance use and sex, which will potentiate COVID-19 clusters among MSM and present a key challenge to halting community-level transmission. In fact, there are reports of meth-fueled sex parties among MSM during the COVID-19 lockdown in Spain [36] and COVID-19 clusters from a recent Miami circuit party [37]. Further research is needed to examine meth use and other behavioral correlates of adherence to social distancing guidelines. This represents a critical first step to informing targeted deployment of limited public health resources to “flatten the curve” of the COVID-19 pandemic.

It is also clear that the COVID-19 pandemic represents a chronic, uncontrollable stressor that could exacerbate psychiatric disorders and increase risk for SARS-CoV-2 infection. Those living with stimulant use disorders could experience new barriers to accessing and remaining engaged in substance use disorder treatment programs as well as 12-step self-help groups, increasing risk for relapse [38]. Furthermore, the stress and social isolation individuals experience during social distancing could serve as a potent trigger for alcohol and other substance use. There is a clear need for scalable, mHealth interventions to address the psychiatric burden of the COVID-19 pandemic. We have previously demonstrated the efficacy of a positive affect intervention for improving psychological adjustment and achieving durable reductions in viral load for people living with HIV [39], including MSM living with HIV who use methamphetamine [40, 41]. We have also demonstrated that it is feasible and acceptable to deliver this positive affect intervention to various populations in a self-guided, online format [42–45]. Furthermore, there is other evidence to support the potential benefits of text messaging for reducing condomless sex [46] and mHealth applications for improving ART adherence in MSM who use meth [47]. Further clinical research is needed to characterize the psychiatric consequences of the COVID-19 pandemic and test novel mHealth approaches to improve adherence to social distancing guidelines in MSM who use meth and other stimulants.

The COVID-19 pandemic is rapidly evolving, leaving more questions than answers regarding how best to mitigate its devastating effects. At this stage, there clearly is
an urgent need for research to examine the implications of co-occurring meth use and HIV for SARS-CoV-2 acquisition as well as COVID-19 progression. Identifying the behavioral mechanisms that could account for the potential double jeopardy experienced by those living with co-occurring meth use and HIV will inform efforts to halt community-level SARS-CoV-2 transmission and reduce risk for COVID-19 progression. It is also clear that the COVID-19 pandemic presents unique challenges to engagement along the HIV care continuum as well as engagement in substance use disorder treatment that warrant further study. Finally, the COVID-19 pandemic underscores the urgent need for mHealth approaches to reach high priority populations to “flatten the curve” of the COVID-19 pandemic. Efforts to stem the tide of the COVID-19 pandemic will require a sustained, coordinated response that integrates behavioral and biomedical approaches much like we have witnessed in over three decades of the HIV/AIDS epidemic.

References

1. Colfax G, Santos GM, Chu P, Vittinghoff E, Plummerman A, Kumar S, et al. Amphetamine-group substances and HIV. Lancet. 2010;376(9739):458–74.
2. Colfax G, Shoptaw S. The methamphetamine epidemic: implications for HIV prevention and treatment. Curr HIV/AIDS Rep. 2005;2(4):194–9.
3. Shoptaw S, Montgomery B, Williams CT, El-Bassel N, Aramattana A, Metsch L, et al. Not just the needle: the state of HIV-prevention science among substance users and future directions. J Acquir Immune Defic Syndr. 2013;63(Suppl 2):S174–S178.
4. Carrico AW, Flentje A, Gruber VA, Woods WJ, Discipola MV, Dilworth SE, et al. Community-based harm reduction substance abuse treatment with methamphetamine-using men who have sex with men. J Urban Health. 2014;91(3):555–67.
5. Shoptaw S, Klausner JD, Reback CJ, Tierney S, Stansell J, Hare DB, et al. Public health response to the methamphetamine epidemic: the implementation of contingency management to treat methamphetamine dependence. BMC Public Health. 2006;6:214.
6. Nanin JE, Parsons JT, Bimbì DS, Grov C, Brown JT. Community reactions to campaigns addressing crystal methamphetamine use among gay and bisexual men in New York City. J Drug Educ. 2006;36(4):297–315.
7. Robles P. Meth. The Forgotten killer, is back. And it’s everywhere. New York Times. 2018 02/14/2018.
8. CDC. HIV infection risk, prevention, and testing behaviors among men who have sex with men—National HIV Behavioral Surveillance, 20 U.S. Cities, 2014. 2016.
9. Hoenigl M, Chaillon A, Moore DJ, Morris SR, Smith DM, Little SJ. Clear links between starting methamphetamine and increasing sexual risk behavior: a cohort study among men who have sex with men. J Acquir Immune Defic Syndr. 2016;71(5):551–7.
10. (NDEWS) NDEWS. Annual Project Report. 2015
11. Mimiga MJ, Reisner SL, Fontaine YM, Bland SE, Driscoll MA, Isenberg D, et al. Walking the line: stimulant use during sex and HIV risk behavior among Black urban MSM. Drug Alcohol Depend. 2010;110(1–2):30–7.
12. Carrico AW, Storholm ED, Flentje A, Arnold EA, Pollack LM, Neilands TB, et al. Spirituality/religiosity, substance use, and HIV testing among young black men who have sex with men. Drug Alcohol Depend. 2017;174:106–12.
13. Carrico AW, Zepf R, Meanley S, Batchelder A, Stall R. Critical review: when the party is over: a systematic review of behavioral interventions for substance-using men who have sex with men. J Acquir Immune Defic Syndr. 2016;73(3):299–306.
14. Vu NT, Maher L, Zablotska I. Amphetamine-type stimulants and HIV infection among men who have sex with men: implications on HIV research and prevention from a systematic review and meta-analysis. J Int AIDS Soc. 2015;18:19273.
15. Carrico AW, Hunt PW, Neilands TB, Dilworth SE, Martin JN, Deeks SG, et al. Stimulant use and viral suppression in the era of universal antiretroviral therapy. J Acquir Immune Defic Syndr. 2019;80:89–93.
16. Carrico AW, Riley ED, Johnson MO, Charlebois ED, Neilands TB, Remien RH, et al. Psychiatric risk factors for HIV disease progression: the role of inconsistent patterns of antiretroviral therapy utilization. J Acquir Immune Defic Syndr. 2011;56(2):146–50.
17. Ellis RJ, Childers ME, Chernew M, Lazzaretto D, Letendre S, Grant I, et al. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. J Infect Dis. 2003;188(12):1820–6.
18. Horvath KJ, Carrico AW, Simoni J, Boyer EW, Amico KR, Petroll AE. Engagement in HIV medical care and technology use among stimulant-using and nonstimulant-using men who have sex with men. AIDS Res Treat. 2013:2013:121352.
19. Cook JA, Burke-Miller JK, Cohen MH, Cook RL, Vlahov D, Wilson TE, et al. Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. AIDS. 2008;22(11):1355–63.
20. Carrico AW, Shoptaw S, Cox C, Stall R, Li X, Ostrow DG, et al. Stimulant use and progression to AIDS or mortality after the initiation of highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2014;67(5):508–13.
21. Lederman MM, Funderburg NT, Sekaly RP, Klatt NR, Hunt PW. Residual immune dysregulation syndrome in treated HIV infection. Adv Immunol. 2013;119:51–83.
22. Cabral GA. Drugs of abuse, immune modulation, and AIDS. J Neuroimmune Pharmacol. 2006;1(3):280–95.
23. Mata MM, Napier TC, Graves SM, Mahmood F, Raesici S, Baum LL. Methamphetamine decreases CD4 T cell frequency and alters pro-inflammatory cytokine production in a model of drug abuse. Eur J Pharmacol. 2015;752:26–33.
24. Fulcher JA, Shoptaw S, Magkoeng SB, Elliott J, Ibarroand FJ, Ragsdale A, et al. Brief review: recent methamphetamine use is associated with increased rectal mucosal inflammatory cytokines, regardless of HIV-1 serostatus. J Acquir Immune Defic Syndr. 2018;78(1):119–23.
25. Carrico AW, Flentje A, Kober K, Lee S, Hunt P, Riley ED, et al. Recent stimulant use and leukocyte gene expression in methamphetamine users with treated HIV infection. Brain Behav Immun. 2018;71:108–15.
26. Carrico AW, Cherenack EM, Roach ME, Riley ED, Oni O, Dilworth SE, et al. Substance-associated elevations in monocyte activation among methamphetamine users with treated HIV infection. AIDS. 2018;32(6):767–71.
27. Hunt PW, Sinclair E, Rodriguez B, Shive C, Clagett B, Funderburg N, et al. Gut epithelial barrier dysfunction and innate immune activation predict mortality in treated HIV infection. J Infect Dis. 2014;210(8):1228–38.
28. Nou E, Lo J, Grinspoon SK. Inflammation, immune activation, and cardiovascular disease in HIV. AIDS. 2016;30(10):1495–509.
29. Zhou F, Yu T, Du R, Fain G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with
COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.

30. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS Coronavirus. J Virol. 2020;94(7):e0012720.

31. Henry BL, Minassian A, Perry W. Effect of methamphetamine dependence on heart rate variability. Addict Biol. 2012;17(3):648–58.

32. Persons AL, Bradaric BD, Dodiya HB, Ohene-Nyako M, Forsyth CB, Keshavarzian A, et al. Colon dysregulation in methamphetamine self-administering HIV-1 transgenic rats. PLoS ONE. 2018;13(1):e0190078.

33. Favre D, Mold J, Hunt PW, Kanwar B, Loke P, Seu L, et al. Typtophan catabolism by indoleamine 2,3-dioxygenase 1 alters the balance of TH17 to regulatory T cells in HIV disease. Sci Transl Med. 2010;2(32):32ra6.

34. Axelrod J. Coronavirus may infect up to 70% of world’s population, expert warns. 2020 https://www.cbsnews.com/news/coronavirus-infection-outbreak-worldwide-virus-expert-warning-today-2020-03-02/

35. Elmousalami HH, Hassanien AB. Day level forecasting for Coronavirus Disease (COVID-19) spread: analysis, modeling and recommendations. arXiv preprint. 2020: arXiv:2003.07778

36. Dollimore L. 8 Men arrested for hosting drug-fuelled orgy during coronavirus lockdown in Spain. 2020. https://www.theolivepress.es/spain-news/2020/03/22/8-men-arrested-for-hosting-drug-fuelled-orgy-during-coronavirus-lockdown-in-spain/

37. Bollinger A. 3 more gay men who went to the Winter Party test positive for coronavirus & others are getting sick. 2020. https://www.lgbtqnation.com/2020/03/3-gay-men-went-winter-party-test-positive-coronavirus-others-getting-sick/

38. Hoffman J. With meetings banned, millions struggle to stay sober on their own. New York Times. 2020.

39. Moskwitz JT, Carrico AW, Duncan LG, Cohn MA, Cheung EO, Batchelder A, et al. Randomized controlled trial of a positive affect intervention for people newly diagnosed with HIV. J Consult Clin Psychol. 2017;85(5):409–23.

40. Carrico AW, Gomez W, Jain J, Shoptaw S, Discipola MV, Olem D, et al. Randomized controlled trial of a positive affect intervention for methamphetamine users. Drug Alcohol Depend. 2018;192:8–15.

41. Carrico AW, Neilands TB, Dilworth SE, Evans JL, Gomicronmez W, Jain JP, et al. Randomized controlled trial of a positive affect intervention to reduce HIV viral load among sexual minority men who use methamphetamine. J Int AIDS Soc. 2019;22(12):e25436.

42. Addington EL, Cheung EO, Bassett SM, Kwok I, Schuette SA, Shiu E, et al. The MARIGOLD study: feasibility and enhancement of an online intervention to improve emotion regulation in people with elevated depressive symptoms. J Affect Disord. 2019;257:352–64.

43. Bassett SM, Cohn M, Cotten P, Kwok I, Moskwitz JT. Feasibility and acceptability of an online positive affect intervention for those living with comorbid HIV depression. AIDS Behav. 2019;23(3):753–64.

44. Cheung EO, Cohn MA, Dunn LB, Melisko ME, Morgan S, Penedo FJ, et al. A randomized pilot trial of a positive affect skill intervention (lessons in linking affect and coping) for women with metastatic breast cancer. Psychooncology. 2017;26(12):2101–8.

45. Cohn MA, Pietrucha ME, Raslow LR, Hult JR, Moskwitz JT. An online positive affect skills intervention reduces depression in adults with type 2 diabetes. J Posit Psychol. 2014;9(6):523–34.

46. Reback CJ, Fletcher JB, Swendeman DA, Metzner M. Theory-based text-messaging to reduce methamphetamine use and HIV sexual risk behaviors among men who have sex with men: automated unidirectional delivery outperforms bidirectional peer interactive delivery. AIDS Behav. 2019;23(1):37–47.

47. Horvath KJ, Lammert S, MacLehose RF, Danh T, Baker JV, Carrico AW. A pilot study of a mobile app to support HIV antiretroviral therapy adherence among men who have sex with men who use stimulants. AIDS Behav. 2019;23(11):3184–98.

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.