2. Ossenkoppele GJ, van de Loosdrecht AA, Schuurhuis GJ. Review of the relevance of aberrant antigen expression by flow cytometry in myeloid neoplasms. *Br J Haematol* 2011;153:421–436.
3. Röllig C, Ehninger G. How I treat hyperleukocytosis in acute myeloid leukemia. *Blood* 2015;125:3246–3252.
4. Azoulay E, Fieux F, Moreau D, Thiery G, Rousselot P, Parrot A, Le Gall JR, Dombret H, Schlemmer B. Acute monocytic leukemia presenting as acute respiratory failure. *Am J Respir Crit Care Med* 2003;167:1329–1333.
5. Montesinos P, Bergua JM, Vellenga E, Rayón C, Parody R, de la Serna J, León A, Esteve J, Milone G, Debén G, *et al*. Differentiation syndrome in patients with acute promyelocytic leukemia treated with all-trans retinoic acid and anthracycline chemotherapy: characteristics, outcome, and prognostic factors. *Blood* 2009;113:775–783.
6. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS; ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012;307:2526–2533.
7. Al Ameri A, Koller C, Kantarjian H, Ravandi F, Verstovsek S, Borthakur G, Pierce S, Mattiuzzi G. Acute pulmonary failure during remission induction chemotherapy in adults with acute myeloid leukemia or high-risk myelodysplastic syndrome. *Cancer* 2010;116:93–97.
8. Xu Y, McKenna RW, Wilson KS, Karandikar NJ, Schultz RA, Kroft SH. Immunophenotypic identification of acute myeloid leukemia with monocytic differentiation. *Leukemia* 2006;20:1321–1324.
9. Hashida H, Takabayashi A, Kanai M, Adachi M, Kondo K, Kohno N, Yamaoka Y, Miyake M. Aminopeptidase N is involved in cell motility and angiogenesis: its clinical significance in human colon cancer. *Gastroenterology* 2002;122:376–386.
10. Delclaux C, d'Ortho MP, Delacourt C, Lebargy F, Brun-Buisson C, Brochard L, Lemaire F, Lafuma C, Harf A. Gelatinases in epithelial lining fluid of patients with adult respiratory distress syndrome. *Am J Physiol* 1997;272:L442–L451.
11. Vahdat L, Maslak P, Miller WH Jr, Eardley A, Heller G, Scheinberg DA, Warrell RP Jr. Early mortality and the retinoic acid syndrome in acute promyelocytic leukemia: impact of leukocytosis, low-dose chemotherapy, PMN/RAR-alpha isoform, and CD13 expression in patients treated with all-trans retinoic acid. *Blood* 1994;84:3843–3849.
12. Rezaei A, Adib M, Mokarian F, Tebianian M, Nassiri R. Leukemia markers expression of peripheral blood vs bone marrow blasts using flow cytometry. *Med Sci Monit* 2003;9:CR359–CR362.
13. Piedfer M, Dauzonne D, Tang R, N'Guyen J, Billard C, Bauvois B. Aminopeptidase-N/CD13 is a potential proapoptotic target in human myeloid tumor cells. *FASEB J* 2011;25:2831–2842.
14. Löwenberg B, Morgan G, Ossenkoppele GJ, Burnett AK, Zachée P, Dührsen U, Dierickx D, Müller-Tidow C, Sonneveld P, Krug U, *et al*. Phase I/II clinical study of Tosedostat, an inhibitor of aminopeptidases, in patients with acute myeloid leukemia and myelodysplasia. *J Clin Oncol* 2010;28:4333–4338.

Carbon Monoxide Exposure in Workplaces, Including Coffee Processing Facilities

To the Editor:

We read the recent review of carbon monoxide (CO) poisoning by Rose and colleagues (1) with great interest. To their excellent summary, we would add mention of the burden of occupational CO exposure: 13% of nonfatal carbon monoxide poisoning cases seen in U.S. emergency departments during a 3-year period were exposed at work (2), and CO exposure is the leading cause of fatality resulting from acute chemical inhalation among US workers (3). Because CO is odorless and tasteless, patients may not be aware of workplace CO exposures. Thus, it is important for clinicians to be familiar with occupational sources of CO.

Occupations that are known to have greater risk for CO poisoning include jobs that require working around combustion sources such as engines and fires and include mechanics, firefighters, longshore workers, diesel engine and forklift operators, and tunnel or toll booth attendants (3). Other occupations that have been largely overlooked but also carry risk for CO exposure include those as varied as warehouse workers, who use propane or diesel forklifts, and restaurant workers, such as charcoal meat grillers and indoor barbeque workers (4).

People who work at coffee processing facilities that make coffee extract are also at risk for CO poisoning (5, 6). Six workers at a coffee extract facility in Japan become symptomatic after they entered or approached a tank that stored coffee extract. One of these workers died and at autopsy was found to have a carboxyhemoglobin level of 26% (5). Subsequent measurement of CO inside the storage tank showed concentrations of 10,000–100,000 ppm, levels at which lethal carboxyhemoglobin saturation could be achieved in as little as a few minutes (5). At a coffee extract facility in the United States, a worker who entered a storage tank collapsed and was initially resuscitated with oxygen on site; his carboxyhemoglobin level was 27% at the hospital. CO concentration inside the tank was found to be 7,500 ppm (6).

We recently evaluated the potential for CO exposure at a coffee processing facility that makes whole bean and ground coffee, rather than coffee extract. Interestingly, the biggest source of CO was not from the roaster, a combustion source, but rather from the roasted beans themselves. High CO levels were observed where coffee beans were stored or ground. Notably, grinding provides a greater surface area for the off-gassing of CO that occurs after roasting (6). We found workers with personal CO exposure levels that ranged from 7 to 30 ppm when averaged over a shift, with a peak CO level of 584 ppm when a worker was standing next to an open hopper of ground coffee. Although not as high as the concentrations inside coffee extract storage tanks, as noted earlier, these exposures approach or exceed the levels recommended by the National Institute for Occupational Safety and Health (7) and, as Rose and colleagues point out, have potential health effects (1).

Recognizing an occupational source of CO has diagnostic and therapeutic implications for a patient with CO poisoning and provides an opportunity for prevention in coworkers. We encourage clinicians to consider workplace CO exposure when evaluating patients with symptoms and signs compatible with CO poisoning. Our data indicate that coffee processors should be added to the list of occupations at risk. ■

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References

1. Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, Gladwin MT. Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy. *Am J Respir Crit Care Med* 2017;195:596–606.
2. Annest JL, Howell J, Yip F, Stock A, Lucas M, Igbal S; Centers for Disease Control and Prevention (CDC). Aug 22, 2008. Nonfatal, unintentional, non-fire-related carbon monoxide exposures: United States, 2004–2006. *MMWR Morb Mortal Wkly Rep* 2008;57:896–899.
3. Henn SA, Bell JL, Sussell AL, Konda S. Occupational carbon monoxide fatalities in the US from unintentional non-fire related exposures, 1992-2008. *Am J Ind Med* 2013;56:1280–1289.
4. Sari I, Zengin S, Ozer O, Davutoglu V, Yildirim C, Aksoy M. Chronic carbon monoxide exposure increases electrocardiographic P-wave and QT dispersion. *Inhal Toxicol* 2008;20:879–884.
5. Nishimura F, Abe S, Fukunaga T. Carbon monoxide poisoning from industrial coffee extraction. *JAMA* 2003;290:334.
6. Newton J. Carbon monoxide exposure from coffee roasting. *Appl Occup Environ Hyg* 2002;17:600–602.
7. National Institute for Occupational Safety and Health (NIOSH) Education and Information Division. NIOSH pocket guide to chemical hazards: carbon monoxide [updated 2016 Apr 11; accessed 2017 Mar]. Available from: https://www.cdc.gov/niosh/npg/npgd0105.html

Reply

From the Authors:

We appreciate the important data presented by Dr. Hawley and colleagues regarding occupational exposure to carbon monoxide (CO) in a number of work settings, including coffee processing facilities. As highlighted by Hawley and colleagues, CO is the most frequent cause of acute chemical exposure fatality in the workplace, and although there are myriad sources of CO, the most common exposure is from motor vehicles (1). Generators are also a very common cause of CO poisoning in the occupational setting, accounting for 13% of occupational CO-related deaths from 1992 to 2008 in one study (1–3). Of note, generators, along with gas grills and heaters operated inappropriately indoors, are the main contributors to the increase in CO poisoning during storm-related and natural disaster–related power outages (3).

Fire is one of the most common sources for CO, and perhaps the most lethal (2, 4). In one study looking at risk factors for acute mortality, more than half of CO deaths occurred from a fire source of CO (4). The National Fire Protection Association reports that in 2015, there were 1,345,000 fires reported in the United States, causing 15,700 civilian injuries and 3,280 deaths (5). Inhalational injury occurs concomitantly in more than two-thirds of lethal cases (2).

Almost 15,000 individuals suffer CO poisoning intentionally each year. Between 1999 and 2014, more than 70% of CO related deaths were from intentional versus unintentional poisonings (6). Intentional CO poisoning deaths declined in the past decade, thought to be partially a result of improving regulations for vehicle CO emissions (6), which make it more difficult to asphyxiate in a sealed environment with a motor vehicle running. More than 25% of occupational fatalities from non–fire-related CO poisoning from 1992 to 2008 were a result of intentional poisoning (1).

Education and prevention efforts are critical to controlling CO exposure (1–3). The catalytic converter has reduced CO emissions by automobiles by 75% since 1975, which has reduced unintentional motor vehicle-related CO death rates by more than 80% (2). Although there have been multiple public campaigns and regulatory measures to increase the placement of CO alarms, there has been no study demonstrating the efficacy of CO alarms to reduce the morbidity or mortality of CO poisoning (2). Although preventing CO exposure is of critical importance, after exposure there remains no quickly administered, widely available, portable antidote for CO poisoning available (2).

For severe cases, in addition to hyperbaric oxygen therapy, discussed in detail in our review, aggressive interventions have been tested in humans, such as extracorporeal membrane oxygenation (2, 7). An ideal treatment would be a portable, quickly administered antidotal agent that could be given immediately at the site of rescue or at the emergency department (2). Roderique and colleagues have presented work in which intravenous hydroxycobalamin can increase the clearance of CO from the bloodstream (2, 8). Our group recently demonstrated a mutationally engineered recombinant neuroglobin molecule that binds to CO avidly, scavenging CO from hemoglobin (2, 9). CO scavenging may have applicability in very severe CO poisoning exposures, as recombinant neuroglobin infusion improved survival significantly by reversing hemodynamic collapse in a lethal model of severe poisoning in mice (2, 9).

The many known and new emerging sources of CO exposure, such as coffee processing facilities, demonstrate the global burden of CO poisoning. Despite increasing safety regulations and public awareness, more than 1,200 individuals die each year from CO poisoning of any source in the United States alone (6). ■

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References

1. Henn SA, Bell JL, Sussell AL, Konda S. Occupational carbon monoxide fatalities in the US from unintentional non-fire related exposures, 1992-2008. *Am J Ind Med* 2013;56:1280–1289.
2. Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, Gladwin MT. Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy. *Am J Respir Crit Care Med* 2017;195:596–606.
3. Hampson NB, Piantadosi CA, Thom SR, Weaver LK. Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. *Am J Respir Crit Care Med* 2012;186:1095–1101.
4. Hampson NB, Hauff NM. Risk factors for short-term mortality from carbon monoxide poisoning treated with hyperbaric oxygen. *Crit Care Med* 2008;36:2523–2527.
5. National Fire Protection Association. NFPA Reports – Fires in the US March 13, 2017. Quincy, MA: National Fire Protection Association [accessed 2017 April 12]. Available from: http://www.nfpa.org/news-and-research/fire-statistics-and-reports/fire-statistics/fires-in-the-us
6. Hampson NB. U.S. mortality due to carbon monoxide poisoning, 1999-2014: accidental and intentional deaths. *Ann Am Thorac Soc* 2016;13:1768–1774.
7. McCunn M, Reynolds HN, Cottingham CA, Scalea TM, Habashi NM. Extracorporeal support in an adult with severe carbon monoxide poisoning and shock following smoke inhalation: a case report. *Perfusion* 2000;15:169–173.