Pulmonary hypertension (PH) is defined by the presence of elevated pulmonary artery (PA) pressures, with a commonly employed threshold being a mean PA pressure greater than 25 mmHg. Many different types of patients can present with PH, including those with left-sided heart disease, chronic intrinsic lung disease and chronic thromboembolic disease. However, a much more discrete group of patients, said to have pulmonary arterial hypertension (PAH) has been found to share common pathophysiological features directly involving the pulmonary arterial tree, and to lack evidence of elevated left-heart filling pressures, intrinsic lung disease or thromboembolism. Such patients also tend to share a positive response to PAH-specific therapies. This group of patients includes those with idiopathic (IPAH) and familial (FPAH) forms of PAH, as well as those with PAH associated with connective tissue diseases, chronic hepatic or congenital heart disease, hemoglobin disorders, HIV infection and selected toxic exposures.

Pulmonary arterial structural and functional abnormalities frequently seen in PAH include vasoconstriction, medial hypertrophy, fibrosis, inflammation, cellular proliferation, in situ thrombosis and formation of plexiform lesions. These combine to increase pulmonary vascular resistance and right ventricular afterload. Without therapy, right heart failure and early morbidity and mortality are inevitable.

PAH remains relatively rare and its presenting signs and symptoms are notoriously non-specific. Accordingly, it is often confused with other diagnoses, and proper diagnosis and therapy are unacceptably delayed. It is the hope that increased awareness on the part of health professionals and the general public will help rectify this.
A recent study strongly suggested methamphetamine use is associated with the occurrence of idiopathic pulmonary arterial hypertension (IPAH). In fact, in that study, individuals with IPAH were 10 times more likely to have used stimulants than individuals with PAH associated with other known risk factors. Interestingly, this risk ratio was similar to that found in studies of individuals who developed PAH associated with use of appetite stimulants (anorexigens). In the above-mentioned study, use of cocaine alone was not sufficiently frequent to allow for meaningful conclusions; however, there are other studies that do suggest an increased risk of developing PAH in individuals who use cocaine.

Because of the retrospective nature of the above study, and the inherent limitations of such a study, it should be considered preliminary (or observational); however, it does raise the issue of a strong association between stimulant use and PAH.

If, in fact, there is an association between these two entities, the exact mechanism remains unknown. However, pharmacological similarities between amphetamines and the anorexigen fenfluramine suggest that a common receptor or pathway may be at play. Similar to fenfluramine, amphetamines increase neurotransmitter release via substrate-mediated exchange and disruption of intracytoplasmic storage vesicles. Fenfluramine is specific for the serotonin transporter protein (SERT), whereas methamphetamine and amphetamine are more potent activators of norepinephrine and dopamine transporters with less activity on the serotonin transporter. Both serotonin and norepinephrine are thought to contribute to the development of PAH because their transporters are found in the pulmonary vasculature and each causes vasoconstriction and proliferation of smooth muscle cells.

A high rate of stimulant use (methamphetamine or cocaine depending on the region of the country) is common among individuals who are both HIV infected and afflicted with PAH. Since the mechanism by which infection with HIV increases the risk of PAH is unknown, it is possible that stimulant use is an important etiological factor in some individuals.

**Importance of Screening for PH**

Considering or making a diagnosis of PAH in these patients can be difficult because their use of—and compliance with—health care is often sporadic. Moreover, they have many other issues that could complicate the evaluation of signs and symptoms of PAH. Because it appears that methamphetamine use is a risk for PAH, it is important to ascertain the patient’s level of physical activity, changes in activity, and, associated symptoms. In addition, unexplained peripheral edema or an increased P2 (pulmonic valve closure) on auscultation should prompt further investigation. Doppler echocardiography is a useful screening tool; unfortunately, its accuracy is not sufficient to establish the diagnosis definitively (>30% false positive rate). Likewise, an elevated serum BNP (brain natriuretic peptide) or NT-proBNP should raise the possibility of either right or left ventricular pressure overload, but is also not definitive. Right heart catheterization remains the only definitive diagnostic test and is essential for excluding left ventricular dysfunction or significant left-sided valvular disease.

**Treatment of Methamphetamine Use-Associated PH**

Specific treatment for this form of PAH is not well-established because of the small number of reported cases; however, it is reasonable to assume that individuals with this form of PAH would respond in a similar fashion to other forms of PAH. It is clear that further studies are needed in this area to establish the true prevalence, to determine the potential etiology and to determine optimal treatment.
About the Pulmonary Hypertension Association

The mission of the Pulmonary Hypertension Association is to find ways to prevent and cure pulmonary hypertension, and to provide hope for the pulmonary hypertension community through support, education, advocacy and awareness. PHA's members stand as part of a community that is fighting back against this terrible illness.

Under the leadership of the Scientific Leadership Council (SLC), a group of approximately 30 global leaders in the field of pulmonary hypertension, PHA proactively facilitates the development of new knowledge about pulmonary hypertension, develops educational resources for medical and public audiences and advocates to raise awareness about pulmonary hypertension. PHA's professional membership bodies enhance the care and support of PH patients by enabling interaction among PH colleagues and providing opportunities for professional advancement. Just a few of the many benefits of membership available to clinicians and researchers include listing your practice in the Find A Doctor section of PHA's website, discounted registration fees for PHA's International PH Conference and Scientific Sessions and a free subscription to an online email group, offering peer-to-peer education and information sharing. To learn more about membership, visit www.PHAssociation.org/MedicalProfessionals/PHANetworks.

PHA's Medical Education fund was founded in 2009 and provides ongoing educational information on PAH by nationally recognized and experienced medical leadership. The fund currently supports three professional education initiatives: PHA Online University, 30-City Program and Preceptorship Program, and one for patients, PHA on the Road. To learn more and get involved today, visit www.PHAssociation.org/MedicalEducationFund.

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Harrison W. Farber, MD
Boston University School of Medicine, Boston, Ma.

Michael A. Mathier, MD, FACC
University of Pittsburgh School of Medicine, Pittsburgh, Pa.

PHA fulfills its mission through:

- Funding for research
- Quarterly medical journal Advances in Pulmonary Hypertension (www.PHAOnlineUniv.org/Journal)
- Professional membership sections:
  - PH Clinicians and Researchers (PHCR) — for physicians and doctorate-level researchers (www.PHAssociation.org/PHCR)
  - PH Resource Network — for nurses and allied health professionals (www.PHAssociation.org/PHResourceNetwork)
- PHA Online University offering free CME credits and the latest information on pulmonary hypertension (www.PHAOnlineUniv.org)
- Educational conferences and materials for medical professionals and patients
- 300+ page book Pulmonary Hypertension: A Patient’s Survival Guide
- PH patient support groups
- Quarterly newsletter Pathlight
- Advocacy and awareness campaigns
- Toll-free Patient-to Patient Helpline (1-800-748-7274)
- PHA website with PH discussion boards, email groups and online support chats (www.PHAssociation.org/ConnectOnline)

For more information on methamphetamine use, visit the Partnership for a Drug-Free America at www.drugfree.org.

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