People living with HIV have long had enough to worry about common opportunistic infections and HIV-related conditions. There are, however, a number of less well-known illnesses for which HIV is a risk factor.

One such illness is called PH, short for pulmonary hypertension. Though hypertension (high blood pressure throughout the circulatory system) is a common illness in many people, PH is a relatively rare condition. It is distinguished by high blood pressure in the pulmonary artery, the main blood vessel that carries blood from the lungs to the right chamber of the heart. It is typically a progressive disease that ends in death if left untreated.

The general cause of this increased blood pressure is a thickening or constriction of the pulmonary artery and the smaller blood vessels in the lungs that branch out from it. In a person with PH, the branches begin to close off as the blood vessels thicken, starting with the smallest vessels first.

This in turn produces less oxygenated blood and the body becomes starved for oxygen. This causes the right chamber of the heart to work furiously, trying to force more blood through the lungs to get more oxygen. The artery is not designed for such high pressure and the muscle soon stretches and eventually leads to heart failure and perhaps death.

What are the symptoms?
Symptoms of early disease are often not present. However, they can include shortness of breath, dizziness, fatigue, swollen ankles, poor lung capacity and sudden fainting or loss of consciousness due to inadequate intake of oxygen for the brain. The process begins slowly and most people have the disease for a few years before getting a correct diagnosis because the early symptoms are similar to those of many other diseases.

The diagnosis is made differentially — by ruling out other causes. The disease is progressive for 2 reasons. (1) The underlying cause remains present despite treatment; and (2) the rising blood pressure in the lungs continues to increase an already rising amount of damage to the pulmonary artery.

One prominent specialist has likened PH to “a slow death by drowning.” The progressive inability of the lungs to supply oxygen can greatly restrict a person’s activity and lead to isolation. Although a person with PH might feel fine while sitting, getting up out of a chair or taking a short walk can trigger shortness of breath, dizziness or even blackout. Without treatment, many people become housebound and in need of oxygen tanks and masks.

PH must be diagnosed by an experienced cardiologist, pulmonologist or a PH specialist. A similar level of experience is needed to treat the disease.

PH and its connection to HIV
No one knows for certain what the mechanism or link is that connects PH with HIV infection. Certain inflammatory immune chemicals, which are common in people with HIV, are suspected as one of its causes. HIV has been shown to be an independent risk factor for PH as well as chronic hepatitis B and C. But these explain only a small portion of the cases of PH among HIV-positive people. Given the silent nature of PH, we’re likely still in the learning stages about PH and do not yet have a full picture of who gets it and why.

The risk of PH is several thousand times greater for HIV-positive people than the general population. Two stud-
ies concluded that the rate of PH in people with HIV is about 1 in 200, as compared to about 2 cases per million in HIV-negative people. It’s likely that PH has been somewhat under-reported over the years, and so its true picture is not yet fully understood. An HIV-positive Project Inform board member was diagnosed with PH. Her struggle led to this publication’s effort to better inform the community about this illness.

How is pulmonary hypertension treated?

In 2001, the drug, Treacleer (bosentan) was approved by the FDA. This tiny pill is taken twice a day. Though it’s easy to take, bosentan doesn’t work in every case and may not be able to treat advanced disease. However, for those who can use it, it’s a godsend compared to the earlier drug that’s given by IV. Bosentan appears to at least halt disease progression within 30 days in most people and improves oxygen flow in many. Fortunately, its mechanism of action is believed to be the most relevant mechanism for HIV-associated PH.

People using certain HIV drugs, specifically ritonavir, need to be careful when using bosentan because of possible drug interactions. These have not yet been tested, but it seems likely that ritonavir could increase the blood levels of bosentan, leading to an increased risk of liver-related side effects. Although studies combining bosentan with epoprostenol have not yet begun, there’s interest in pursuing this because of their different mechanisms of action.

Before bosentan became available, the only treatment for PH was a drug called Flolan (epoprostenol). It usually works quite well, reversing most symptoms for a considerable period. But it comes at a high price in terms of side effects, quality of life and cost. The drug must be given through a surgically implanted IV 24 hours per day. People must carry a continuous infusion pump for the rest of their lives. Having an IV line carries risks of severe and life-threatening infections like sepsis. The drug is not a cure and works only as long as it’s used. It’s extremely expensive, given that it’s an “orphan drug” — one used for a relatively rare disease that affects less than 200,000 people each year.

Final thoughts

Project Inform encountered a slightly bumpy road in pursuing access to bosentan for HIV-positive people. Well before the drug was approved, it was available on an expanded access basis to people with PH, using the regulatory mechanisms fought for and won by AIDS activists in earlier years. But the expanded access program excluded HIV-positive people, on the grounds that the new drug had not yet been tested in people with HIV. They had also been excluded from the studies used to license the drug. Concerns about interaction with HIV drugs continued.
Project Inform, which has played a fundamental role in creating earlier access programs for drugs, responded with a ferocious burst of activity. Through appearances at an FDA Advisory committee, pressure and support from the FDA, and hastily called meetings with company officials and clinical investigators, the ban on access for HIV-positive people was lifted just 10 days after we first became aware of it.

Recent research
A study presented at the 2008 CROI revealed a surprisingly high rate of PH in about 100 people. Everyone was on potent HIV therapy and had been living with HIV on average for 11 years. In all cases, their PH was mild and without visible symptoms. More sensitive testing was done to identify which participants had signs of PH.

The most notable result was a 5.5% rate of PH in this group. The results also showed that in addition to HIV being a risk factor for PH, 3 other factors also increased its risk: injection drug use, excessive alcohol and smoking. CD4s, viral loads, cardiac risk factors, use of protease inhibitors or high risk for AIDS were not related to PH in this study.

These results point to perhaps a higher rate of PH than previously known in people with HIV. They also suggest that more study needs to be done to more clearly define who is at risk for developing more severe PH and to discover tests to help predict these risks.