Acute Vasodilator Testing:

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In patients with idiopathic and hereditary pulmonary arterial hypertension (IPAH and HPAH) acute vasodilator testing during right heart catheterization (RHC) is strongly recommended based on current guidelines.

In these patients, acute vasodilator testing may identify patients who might respond favorably to calcium channel blockers (CCB). While patients with a sustained long term response to CCB therapy are rare, ~ 6-8%,¹ a positive response predicts a better clinical outcome and prognosis.² Thus, in patients with IPAH and HPAH the acute vasodilator test is still recommended during the initial hemodynamic evaluation in the catheterization (cath) lab. In patients with other associated PAH etiology the testing is up to the discretion of the physician. But, of note, anorexigen-associated PAH patients also demonstrate vasoreactivity with a long-term response to CCB.³ If patients are already on a pulmonary vasodilator therapy, repeat vasodilator testing may guide care but is not necessarily standard of care.⁴,⁵

Potential risks/contraindication:

- In patients deemed too ill (e.g. NYHA/WHO functional class IV or with low cardiac output, CI < 2.0 L/min/m², during initial hemodynamic assessment) the vasodilator test may be deferred.

- In patients with baseline bradycardia, or risk of bradycardia (infiltrative connective tissue disease) IV adenosine should probably be avoided.

- In patients who are judged to have a high risk of pulmonary venous hypertension (e.g. congestive heart failure, elevated PCW/LVED pressure during the cardiac cath, pulmonary veno-occlusive disease) the vasodilator testing may be deferred.

Methodology:

During a RHC, acute pulmonary vasodilator testing may be performed to assess the ability of the pulmonary arteries to relax acutely in response to medications such as IV epoprostenol, IV adenosine, or inhaled nitric oxide. The following measurements are usually done pre medication and at the final titrated dose of vasodilator: mean right atrial pressure, mean pulmonary artery pressure (PAP), cardiac output, wedge pressure, PA saturation, and a systemic oxygen saturation.

Medications used for acute vasodilator testing include inhaled nitric oxide, intravenous epoprostenol, and intravenous adenosine. Appropriate medication dose and interval is necessary to ensure a reliable and reproducible vasodilatory test. The goal of dose titration
of the vasodilator drug being used is to achieve hemodynamic effects at the minimum necessary dose and not necessarily reach the maximum dose; at excessive doses patients may experience untoward side effects such as severe headaches, dizziness, breathlessness, and nausea/vomiting. Testing with nitroglycerin is contra-indicated.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Doses</th>
<th>Interval</th>
<th>References</th>
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<tbody>
<tr>
<td>Inhaled nitric oxide</td>
<td>20 or 40 ppm</td>
<td>for 5 minutes or until a positive response is seen</td>
<td>Pepke-Zaba J, et al., Lancet 1991;338:1173-1174.</td>
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<td>IV epoprostenol</td>
<td>2 to 12 ng/kg/min</td>
<td>2 ng/kg/min every 15 minutes</td>
<td>Rubin et al., Circulation 1982;66:334-338.</td>
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<tr>
<td>IV adenosine</td>
<td>50 to 250 mcg/kg/min</td>
<td>50 mcg/kg/min every 2 minutes</td>
<td>Morgan et al., Circulation 1991;84:1145-1149.</td>
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**Interpretation/Positive test:** The 2009 ACC/AHA and 2015 ESC/ERS guidelines define a positive study based on a reduction in the mean pulmonary artery pressure of at least 10 mmHg to an absolute mean PA pressure of less than 40 mm Hg with a stable or improved cardiac output. Patients should have normal oxygen saturation prior to starting inhaled nitric oxide so that one can assess the true response on pulmonary vascular tone and not response to improved oxygenation.

**Considerations in Children with PH:** As in adults, AVT in children is undertaken to assess the response of the pulmonary vascular bed to pulmonary specific vasodilators. Similarly, the current practice in children with IPAH or familial PAH (isolated PVHD) is to use AVT to define the likelihood of response to long-term treatment with CCB therapy and for prognosis. There are 2 definitions of responders to AVT in IPAH or isolated PHVD, including 1) a decrease in mPAP of at least 10 mmHg to below 40 mmHg with a normal or increased increase in cardiac output; and 2) a decrease in mean PAP ≥ 20% and increase or no change in CI and decrease or no change in PVR:SVR. AVT in children with PH associated with congenital heart disease (CHD) is undertaken to assess if the PVR will decrease sufficiently for surgical repair to be undertaken in borderline cases. In general, positive AVT for borderline cases with post tricuspid shunts is defined as decreases in PVRI to < 6-8 WU/m^2 or PVR:SVR <0.3. However, AVT is only one measure used to define operability and the whole clinical picture, the age of the patient and the type of lesion need to be taken into
AVT may be studied with iNO (20–80 ppm), 100% oxygen, inhaled or intravenous PGI2 analogues, intravenous adenosine or sildenafil.

References: