Prof. Perk also pointed out that nongovernmental organizations are important to healthcare workers in promoting preventive cardiology and the European Heart Health Charter marks the start of a new era of political engagement in preventive cardiology.

The High Cost of Untreated CHD

Written by Rita Buckley

Globally, pulmonary vascular disease associated with congenital heart disease (CHD) may be the most preventable cause of pulmonary artery hypertension and related mortality and morbidity [Adatia I et al. *Chest* 2010]. Mohammed Omar Galal, MD, PhD, MBA, Prince Salman Heart Center, Riyadh, Saudi Arabia, presented an overview of advanced and combination therapies in patients with pulmonary arterial hypertension (PAH)-CHD.

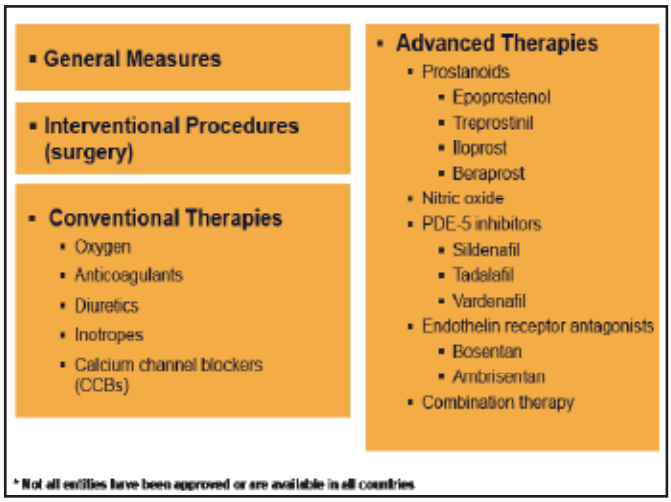
Although progress in the diagnosis and treatment of CHD has reduced the number of PAH-CHD cases in Western nations, few PAH patients in developing countries have access to treatment. Adatia et al. [*Chest* 2010] estimate that 3 million children worldwide are at risk for the development of pulmonary vascular disease due to CHD; most have a reparable heart defect, such as an isolated atrial septum, ventricular septal defect, or patent ductus arteriosus.

PAH-CHD is classified into 4 types suitable for advanced therapy. These include 1) Eisenmenger Syndrome, 2) moderate to large shunt lesions with PAH, 3) small defects with PAH, and 4) PAH after repair of CHD [Galie N et al. *Eur Heart J* 2009; Simonneau G et al. *J Am Coll Cardiol* 2009]. Eisenmenger Syndrome is the most advanced form of pulmonary vascular disease secondary to CHD [Adatia I et al. *Chest* 2010].

Treatment options in PAH range from general measures to advanced therapies (Figure 1). Conventional treatments include diuretics, anticoagulants, oxygen therapy, digoxin, and calcium channel blockers. In a randomized trial with 2 years of follow-up, Sandoval et al. [*Am J Respir Crit Care Med* 2001] found that nocturnal oxygen therapy did not modify the natural history of patients with advanced Eisenmenger Syndrome. Calcium channel blockers benefit around 10% of patients with PAH and seem to improve survival, said Prof. Galal.

According to Prof. Galal, advanced therapy should be used if there is a negative vasoreactivity test or lack of clinical improvement with calcium channel blockers. It can also be used in all groups with a NYHA functional class of II, III, or IV. However, most data on advanced care are based on studies with idiopathic PAH and PAH due to scleroderma, and the therapies are very expensive.

Figure 1. Treatment Options in PAH*.



PAH=pulmonary arterial hypertension; PDE-5=phosphodiesterase 5.

The 3 classes of advanced therapy include endothelin-1 receptor antagonists, phosphodiesterase 5 inhibitors, and prostanoids. Bosenten has been demonstrated to improve exercise capacity and stroke volume in patients without Down syndrome [Rubin LJ et al. *N Engl J Med* 2002]. In a medium-term follow-up study of adult patients with PAH associated with CHD, Duffels et al. [*Congenit Heart Dis* 2007] found that advanced treatment seemed to stabilize disease and decrease the rate of deterioration, especially in younger patients.

Based on these and other data, Prof. Galal concluded that PAH-CHD remains a serious disease leading to reduced quality of life and longevity, 4 classes of PAH-CHD justify advanced therapies, that short-term studies have confirmed the efficacy and safety of advanced/combination therapies, and long-term studies are still needed.

Greater Consistency and Protection with Newer Antiplatelet Agents

Written by Rita Buckley

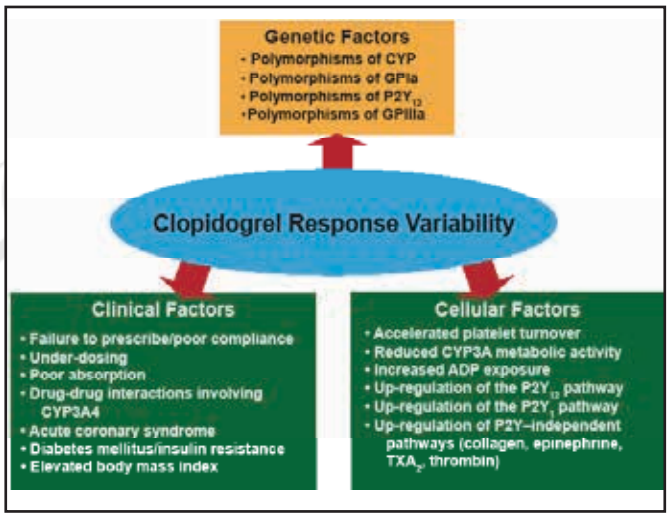
Newer antiplatelet agents offer greater consistency and protection than the current standard of care. Eyas Al-Mousa, MD, Jordan University Hospital, Amman, Jordan, discussed the latest antiplatelet therapy for percutaneous coronary intervention (PCI).

Antiplatelet therapy is the cornerstone of treatment for patients who have acute coronary syndromes (ACS) and/or are undergoing PCI [Angiolillo DJ et al. *J Am Coll Cardiol* 2007].

In the last 2 decades, dual antiplatelet therapy with clopidogrel and acetylsalicylic acid has become the standard of care for patients with ACS .

However, clopidogrel has drawbacks that include delayed therapeutic effect, significant interindividual variability of platelet aggregation inhibition or reduced action on thrombocytes due to interaction with other drugs or genetic polymorphisms. Although aspirin enhances the effects of clopidogrel, numerous *in vitro* studies have still verified that individual responsiveness to clopidogrel is not uniform in all patients and varies in response to genetic, clinical, and cellular factors (Figure 1) [Angiolillo DJ et al. *J Am Coll Cardiol* 2007].

Figure 1. Clopidogrel Response Variability.



ADP=adenosine diphosphate; CYP=cytochrome P450; GP=glycoprotein.
Reprinted from *Am J Cardiol*, Vol 101/4, Angiolillo DJ et al. Functional effects of high clopidogrel maintenance dosing in patients with inadequate platelet inhibition on standard dose treatment, 440-5, Copyright 2008, with permission from Elsevier.

Prasugrel, which represents the third generation of thienopyridines, inhibits platelet aggregation by irreversibly blocking the adenosine diphosphate P2Y12 receptor. In a randomized trial that compared prasugrel and clopidogrel loading doses (LDs) on rate of onset, magnitude, and consistency of platelet inhibition, Brandt et al. [*Am Heart J* 2007] found that a 60-mg LD of prasugrel resulted in more rapid ($p<0.001$), potent ($p<0.001$), and consistent ($p<0.01$) inhibition of platelet function than a 300-mg LD of clopidogrel. In the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction [TRITON-TIMI] 38, treatment with prasugrel compared with clopidogrel resulted in a significantly lower rate of ischemic events (HR, 0.81; 95% CI, 0.73 to 0.90; $p<0.001$) [Wiviott S et al. *N Engl J Med* 2007].

Ticagrelor is an oral, reversible, direct-acting inhibitor of the adenosine diphosphate receptor P2Y12 that has a more rapid onset and more pronounced platelet inhibition than clopidogrel [Wallentin L et al. *N Engl J Med* 2009]. The Platelet Inhibition and Patient Outcomes [PLATO] trial demonstrated that treatment with ticagrelor versus clopidogrel in a broad population of patients with ACS substantially reduced the primary composite endpoint of death, myocardial infarction, or stroke by 16% (95% CI, 8 to 21), as well as the rates of all-cause death and death from vascular causes [Wallentin L et al. *N Engl J Med* 2009].

According to Prof. Al-Mousa, 1000 ACS patients using ticagrelor versus clopidogrel for 12 months resulted in 14 fewer deaths, 11 fewer myocardial infarctions, and 7 fewer cases with stent thrombosis, with no increase in bleedings requiring transfusion. "Platelets are the principal effectors of hemostasis and key mediators in the pathogenesis of thrombosis. With clopidogrel, a wide response variability may exist and a substantial percentage of patients can exhibit nonresponsiveness," he explained.

GSA Holds Promise for Treatment of Hypertrophic Obstructive Cardiomyopathy

Written by Rita Buckley

Cyanoacrylates are the main liquid adhesives used in the vascular system and have an important role in managing vascular abnormalities, especially arteriovenous malformations [Pollack JS, White RI, Jr. *J Vasc Interv Radiol* 2001]. Ali Oto, MD, Hacettepe University, Ankara, Turkey, discussed the use of glue septal ablation (GSA) treatment for hypertrophic obstructive cardiomyopathy (HOCM).

HOCM is characterized by asymmetric myocardial hypertrophy that is most pronounced in the interventricular septum and is responsible for the dynamic obstruction of the left ventricular outflow tract (LVOT) [Fifer MA et al. *Circulation* 2008]. Prof. Oto explained that LVOT obstruction is due to the hypertrophied septum and mitral regurgitation.

Alcohol septal ablation (ASA) for HOCM is a less invasive alternative to surgical myectomy to reduce the LVOT gradient in patients resistant to drug therapy [Alam M et al. *Eur Heart J* 2009]. A recent assessment of the technique found that a significant decrease in mean peak gradient ($p<0.0001$) in the LVOT was associated with a decrease in LV mass ($p=0.0006$) and with regression of LV hypertrophy outside the scar after ASA [Timmer SA et al. *Am J Physiol* 2011.

According to Prof. Oto, limitations of the ASA led him and his colleagues to publish their first-in-man GSA case in an HOCM patient with extensive collaterals to the posterior