

## Seasonal Influenza and Cardiovascular Disease

By Daisy F. Lazarous, MD, FACC;  
Princy N. Kumar, MD,  
and William J. Oetgen, MD, MBA, FACC

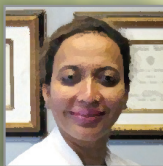
An important clinical link exists between influenza and cardiovascular disease. Recently, ACC members were reminded of this association in a letter from ACC President **David R. Holmes, Jr., MD, FACC**, and **Anne Schuchat, MD**, assistant surgeon general of the U.S. Public Health Service and director of the National Center for Immunization and Respiratory Diseases.

While no unequivocal causal relationship has been established between acute influenza infection and acute myocardial infarction, influenza is estimated to be responsible for approximately 36,000 deaths and 300,000 hospitalizations per year in the U.S. Childhood and chronic diseases, including cardiovascular disease, in adults are risk factors for poor outcomes during influenza epidemics. In 2006, the ACC and the American Heart Association (AHA), along with seven other professional associations, co-published a Science Advisory Statement which addressed the issue of influenza vaccination as a preventive strategy for patients with cardiovascular disease.<sup>1</sup>

The advisory statement and the communication from Holmes and Schuchat note that the estimated influenza vaccination rate for patients in the U.S. between 18 and 64 years of age with cardiovascular disease is between 35 percent and 40 percent. Additionally, studies of voluntary acceptance of seasonal influenza vaccine among health care workers themselves have consistently shown compliance rates of less than 50 percent.<sup>2</sup>

Among patients with chronic conditions, influenza-associated death is most common in the group with cardiovascular diseases. The exact mechanism for the association between influenza and cardiovascular events is not known; however it has been speculated that inflammation related to viral infection can lead to autoantibodies directed against low-density lipoprotein with progression of the atherosclerotic process. Alternatively, direct infection of vascular walls could stimulate local cell autoimmune responses.<sup>1</sup>

The recommendation to administer annual influenza vaccination is designed to promote secondary prevention of cardiovascular events. The strength of evidence for this recommendation is identified as Class I, Level B. The evidence is based on a randomized controlled trial (Flu Vaccination in Acute Coronary Syndromes [FLUVACS])<sup>3</sup> in which 301 hospitalized patients with coronary artery disease were randomized to receive or not to receive influenza vaccinations. At the end of one year, the relative risk of cardiovascular death in the vaccinated group was 0.25 (0.07 to 0.86) compared to the unvaccinated group, and the relative risk of the composite end point of cardiovascular death, non-fatal myocardial infarction, or severe ischemia



was 0.59 (0.30 to 0.86.) At the end of two years, similar magnitude risk reductions were noted, but because of the number of patients lost to follow-up, the statistical significance of the differences was not demonstrable.

It is important to note that there is no evidence that influenza vaccination increases the probability of cardiovascular events. In a study of more than 39,000 patients in the United Kingdom, there was no increase in the risk of myocardial infarction or stroke in vaccinated patients. In this study, the incidence rates for these acute events was lower in the vaccinated cohort at

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the measurement on day 28; however, these differences disappeared when the results were adjusted for age.<sup>1</sup>

We have outlined below steps that Holmes, Schuchat and the authors of the AHA/ACCF Scientific Advisory statement suggest to practicing cardiologists to ensure that all patients are immunized. These steps are simple, but the potential benefits for patients are great:

- Discuss with patients the importance of immunization for influenza.
- Stock and administer influenza vaccinations in the office or refer to a primary care physician's office or local pharmacy. (For patients with cardiovascular disease, only the intramuscular, inactivated type of vaccine is recommended. The live attenuated vaccine has been approved only for healthy people between the ages of 2 and 49).

- Provide patients with a "prescription" recommendation as a reminder to them to obtain an influenza vaccination (Item 22-0979, available at no charge at [www.cdc.gov/flu/freeresources/index.htm](http://www.cdc.gov/flu/freeresources/index.htm)).
- Place posters or flyers in the office to promote influenza vaccination. (Available at no charge at [www.cdc.gov/flu/freeresources/print.htm](http://www.cdc.gov/flu/freeresources/print.htm)).
- Influenza vaccine should be administered as soon as supplies become available and should be given through March of each year. (For people travelling to the Southern Hemisphere, seasonal flu vaccination is recommended as late as May).

Two additional corollary recommendations are:

- Practicing cardiologists should be immunized annually for influenza prevention for themselves and their patients.
- Cardiology practice office staff and hospital staff should likewise be immunized on an annual basis.

The Centers for Medicare and Medicaid Services (CMS) is strongly promoting the administration of influenza vaccinations to Medicare and Medicaid beneficiaries. Effective Jan. 1, all patients discharged from the hospital who are eligible for the influenza (and pneumococcal) vaccine are to be immunized prior to discharge. This is a CMS core measure and will likely be publically reported on the CMS "Hospital Compare" website.

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Lazarous is associate professor of medicine (cardiology), and Kumar is professor of medicine and chair of infectious disease at Georgetown University School of Medicine. Oetgen is clinical professor of medicine (cardiology) at Georgetown and is senior vice president of Science and Quality at the ACC.

### **References:**

1. Davis MM, Taubert K, Benin AL, Brown DW, Mensah GA, Baddour LM, Dunbar S, Krumholz HM. Influenza vaccination as secondary prevention for cardiovascular disease: a science advisory from the American Heart Association/ American College of Cardiology. *J Am Coll Cardiol*. 2006 Oct 3;48(7):1498-502.
2. Oetgen WJ, Thomas WL. First, do no harm: mandatory influenza vaccination for health care workers is a matter of patient safety. *Trustee*. 2011 Oct;64(9):39-40.
3. Gurfinkel EP, Leon de la Fuente R, Mendiz O, Mautner B. Flu vaccination in acute coronary syndromes and planned percutaneous coronary interventions (FLUVACS) Study. *Eur Heart J*. 2004 Jan;25(1):25-31.