

VACCINATION AND HEART DISEASE

Infections have long been suspected in playing a role in the pathogenesis of atherosclerosis. The epidemiology of coronary artery disease indirectly supports these hypotheses. Rates of myocardial infarction (MI) and cardiac death rise in the winter, as well as after influenza epidemics. Retrospective case-control studies have found that flu vaccinations seem to protect against ischemic cardiovascular events, MI, and stroke, as well as against influenza itself. Most recently, the use of macrolide antibiotics to eradicate chlamydia infections in small randomized controlled trials proved to be positive at preventing recurrent cardiovascular events. However, much larger trials turned out to be negative.

Now, an Argentinean pilot study, recently reported in *Circulation*, offers prospective, multicentre, randomized clinical evidence that suppressing viral activity does lower the risk of ischemic events in patients with established atherosclerotic disease. Fifty-eight per cent fewer major thrombotic end points were experienced by post-MI patients who received an immunization against influenza than those who did not.

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Table 2

Primary end points in post-MI patients at 6-month followup

End point	Vaccine group	Control group	Relative risk	p value
Death	2	8	0.25	0.05
Reinfarction	4	4	1.00	-
Rehospitalization for PTCA or CABG	4	12	0.33	0.03
Any of above	10	24	0.42	0.008

n=100
p=probability

PTCA=percutaneous transluminal coronary angioplasty
CABG=coronary artery bypass grafting

Simple methodology, provocative result

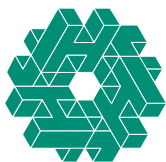
The Flu Vaccination Acute Coronary Syndromes (FLUVACS) study enrolled 200 MI patients with a new MI (within 72 hours of presentation) and randomized 100 of them to receive the vaccine. The other 100 were controls. Immunization was by single injection of trivalent vaccine. The trial took place during the winter of 2001, and followup was at one and six months by telephone (Table 1).

The sample size did not permit a high degree of confidence for any single end point. The trial was only single-blinded, as no serology was done. Neither the efficacy of the vaccine, nor viral activity, nor any hypothesized mechanism of action was investigated.

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We have no information about whether the patients in both groups actually got the flu or not and whether there was any relationship between potential viral infections and cardiovascular events. Followup was for only six months.

A look at the evidence

Although the vaccine trial in MI patients constituted the larger part of the FLU-VACS study, there was also a second, concomitant trial of the flu vaccine in patients undergoing planned coronary artery stenting. One hundred patients scheduled for stenting were enrolled, 51 were randomized to receive the vaccine prior to the procedure, and 50 similar patients were followed as controls. Baseline data showed only slight differences between the two groups. Followup was at one and six months by telephone (Table 2).

There have been three other studies that also suggested that the influenza vaccination may reduce the risk of cardiovascular events. There was a study which was a population-based case-controlled study showing that vaccination was associated with a reduced risk of cardiac arrest.¹ In another study looking at patients with acute coronary syndromes vaccination was also associated with a reduced risk of recurrent MI.² Finally, in a recent French population-based case-controlled study, influenza vaccination was associated with a reduced risk of brain infarction, and an odds ratio of 0.42.

Physician's perspective

The results of these two trials are provocative. Although one of two randomized controlled trials were positive, the totality of information available is extremely small. We have been fooled many times by pilot data. The observational data also provided should only be considered hypothesis generating. As the authors point out, large-scale randomized con-

Table 2

Primary end points in post-stenting patients at 6-month followup


End point	Vaccine group	Control group	p value
Death	1	4	NS
Myocardial infarction	4	4	NS
Rehospitalization for PTCA or CABG	3	3	NS
Any of above	8	11	NS

n=50 NS=not seen CABG=coronary artery bypass grafting
n=51 p=probability PTCA=percutaneous transluminal coronary angioplasty

trolled trials are needed to confirm whether vaccination with influenza or other vaccines are truly vascular protective. Most recently in Ontario, widespread influenza vaccinations have been recommended to prevent overcrowding of emergency rooms and decrease morbidity and mortality from flu. Polio eradication has been a tremendous medical success through vaccination. Most physicians in my generation can only imagine the pain and suffering caused by polio and how a simple strategy of vaccination proved to be so effective.

The current take-home message is to vaccinate appropriately whenever possible. For patients with cardiovascular disease, this would include:

- yearly influenza immunization, and
- pneumococcal vaccination.

Finally, we all await the results of future trials on the potential of vaccination to eradicate vascular disease and other potential modalities. 

References

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2. Naghavi M, Barlas Z, Siadaty S, et al: Association of Influenza Vaccination and Reduced Risk of Recurrent Myocardial Infarction. *Circulation* 2000; 102:(25)3039-45.
3. Lavallée P, Perchaud V, Gautier-Bertrand, et al: Association between Influenza Vaccination and Reduced Risk of Brain Infarction. *Stroke* 2002; 33(4):513-8.