



Drug Monitor

Smallpox Protection: Will One Shot Do?

Smallpox was eradicated from the world in 1977 and vaccination programs were subsequently discontinued. If the disease were to reemerge today, experts say the current vaccinia virus vaccine stockpile would not be enough for a mass inoculation program. But some epidemiologic studies have suggested that the past inoculation standard—every five years for people with repeated smallpox exposure—may not be necessary. Researchers from the National Institutes of Health (NIH), Baltimore, MD investigated the question of whether one shot is enough.

The researchers identified all participants from the Baltimore Longitudinal Study of Aging (a study of normative aging in which, beginning in 1958, participants' fasting serum samples have been collected and stored every one to five years) who had a known history of smallpox infection ($n = 8$) or documented smallpox vaccination ($n = 209$). They also included 29 control participants who had no history of smallpox infection or vaccination. The vaccinated participants had been vaccinated one or more times as many as 88 years before the NIH study. Stored serum samples were available from various follow-up points.

The researchers found that the vaccinated participants maintained antivaccinia immunoglobulin G and neutralizing antibody titers above three natural logs "indefinitely." In 97% of participants, the researchers found no reduction in vaccinia-specific antibody titers over the follow-up period. Those who had survived smallpox infection retained antivaccinia antibody titers similar to those in vaccinated partici-

pants. Multiple vaccinations appeared to produce only marginally—although statistically significantly—higher titers than single vaccination.

As their data suggest a single vaccination elicits functional antibody that remains stable over a person's lifetime, the researchers say limited supplies of vaccine could be applied to those who have never been vaccinated.

Source: *Am J Med.* 2008;121(12):1058–1064. doi:10.1016/j.amjmed.2008.08.019.

Missing the Target with Beta-blockers

National guidelines recommend that providers treat patients with current or previous symptoms of heart failure (HF) and reduced left ventricular ejection fraction with beta-blockers that have been shown through major clinical trials to be effective, such as carvedilol and metoprolol succinate. They also advise providers to make every effort to achieve the target doses of the beta-blockers shown to be effective in those trials, while considering patient tolerance. But results of a study of patients with HF reveals a substantial "titration gap."

To gather real-world evidence, investigators analyzed data from a pre-specified subset of the 48,612 patients hospitalized with HF who were enrolled in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) trial. This subset included 5,791 patients who had 60- to 90-day follow-up data collected from 91 hospitals across the United States. Of these patients, the investigators identified 2,373 with documented left ventricular systolic dysfunction who, based on no documented contraindications or intoler-

ance to beta-blockers, were eligible for this therapy at discharge.

They found that 1,537 patients were receiving beta-blockers prior to hospital admission—1,350 (88%) of whom had this therapy continued at discharge. Of the 187 patients who had prior beta-blocker therapy withdrawn, 79 had no documented contraindication or intolerance. Another 632 patients (27% of the 2,373 eligible for beta-blockers) had this therapy newly started at discharge, and 303 (13%) were not treated.

The researchers also found that the mean total daily dose for each beta-blocker prescribed to patients before admission was less than half the recommended target dose, with infrequent up- or down-titration during the hospitalization. More than two thirds of patients had no change in their beta-blocker doses in the first 60 to 90 days after discharge. At follow-up, only 18% of patients taking carvedilol and 8% of those taking metoprolol succinate were being treated with the recommended target doses.

The researchers point out that, since the method of titrating up to a patient-tolerated limit has been the only strategy used in major clinical trials, beta-blocker doses below the current "evidence-based" levels have not been evaluated. Also, reasons for patients' beta-blocker dosing changes were not available for analysis.

Source: *Am J Cardiol.* 2008;102(11):1524–1529. doi:10.1016/j.amjcard.2008.07.045.

Are Perioperative Medications Useful for Elderly Patients?

Elderly patients undergoing major surgery have a high risk of cardiac com-

plications, mainly because of their age and comorbidities. Do perioperative medications help, or is the age factor overwhelming? Researchers from Erasmus Medical Centre, Rotterdam and Leiden University Medical Centre, Leiden, both in the Netherlands, conducted a study of 1,693 patients aged 65 and older who had major non-cardiac vascular surgery—and found both short- and long-term benefits for perioperative medications.

In their observational cohort study, researchers preoperatively screened patients presenting to Erasmus Medical Centre from January 1990 to January 2004 for cardiac risk factors and use of certain cardiac medications. The mean (SD) age of the cohort was 73 (5) years and the mean (SD) number of cardiac risk factors was 1.7 (0.8). Patients taking statins (16%) were more likely to have had hypercholesterolemia and coronary artery disease, those tak-

ing angiotensin converting enzyme (ACE) inhibitors (24%) were more likely to have had a history of heart failure, those taking beta-blockers (26%) were more likely to have had hypertension or coronary artery disease, those taking calcium channel blockers (27%) were more likely to have had hypertension, and those taking aspirin (32%) were more likely to have had coronary artery disease or cerebrovascular disease.

During a median follow-up of 8.2 years, 619 patients died—137 (8%) in the hospital. Cardiac disease accounted for nearly half of the deaths. Perioperative use of beta-blockers, statins, and aspirin was significantly associated with a 68%, 65%, and 47% lower risk of hospital mortality, respectively. Moreover, perioperative beta-blockers, aspirin, statins, and ACE inhibitors were significantly associated with a lower risk of long-term death (39%, 35%, 35%, and 26%, respectively).

The researchers found that the number of cardiac risk factors increased with age and that age and number of cardiac risk factors were each significantly associated with increased mortality. No significant interaction between age and medication use was found—although overall mortality risk declined in a gradient from the youngest to the oldest patients among those taking statins. The researchers concluded that very elderly patients, in particular, may benefit from perioperative use of statins. ●

Source: *Arch Gerontol Geriatr.* 2009;48(1):116–120. doi:10.1016/j.archger.2007.11.003.