# You asked about...

*Answers to your questions from medical experts*

**This month:**

1. **What are the facts on smallpox?**
2. **Are there risks in combining ACEIs and ARBs?**

## 1. What are the facts on smallpox?

Smallpox is associated with high fever, fatigue, myalgia, and headache. The characteristic generalized flat, red rash occurs, at first, primarily on the face and appendages, and develops into pustules in 1-2 weeks. The scabs fall off in 2-3 weeks.

**How infectious is it?**

It is very infectious with an incubation period of 2-3 weeks. It is spread by saliva and aerosol, beginning in the first week of incubation and up to the point when the scabs fall off. Smallpox equally occurs in adults and children, whereas chicken pox (varicella) is a childhood disease. There is a 30% mortality rate and no treatment is currently available, although some antiviral medications may be useful.

**Why is smallpox difficult to contain?**

The long incubation period facilitates rapid dissemination and once loose in the population, medical centres would be overwhelmed. Smallpox would be widely spread long before the first case is recognized. Response to smallpox dissemination would be delayed, especially if the attack were initiated in a smaller centre and the first cases were unrecognized. Many people would be unwittingly exposed when victims are most contagious and before the establishment of a quarantine strategy.

**What is the appropriate response?**

A "ring response" is a widening circle of quarantine around the sentinel case. The concept of a ring response would likely be ineffective with smallpox as the disease would spread far beyond any quarantined areas before it was recognized. The post-exposure immunization may be of some value. First responders (medical personnel) and key public officials should be immunized now. Polls of citizens suggest that the risk of generalized vaccinia with a death rate of 3 people/million people is less of a concern than the risk of contracting smallpox as a result of a bioterrorist attack. Hyperimmunoglobulin is being prepared from immune subjects, and a genetically engineered vaccine and an immunoglobulin are currently being developed.

**Suggested Readings**


1. Centre for Disease Control and Prevention: www.bt.cdc.gov
2. Osterholm M, Schwartz J: Living Terrors: What American Needs to Know to Survive the Coming Bioterrorist Catastrophe. Delacourte Press, New York, 2000.
3. Henderson DA, Inglesby TV, O'Toole T, ed.; 2000 Bioterrorism-Guidelines for Medical and Public Health Management. AMA, Chicago, 2000.



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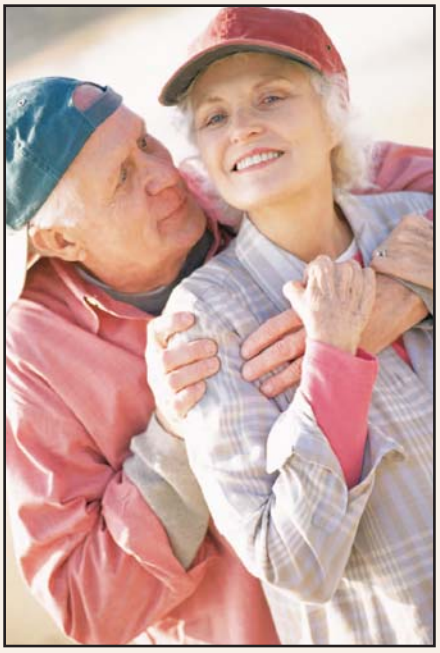
## 2. Are there risks in combining ACEIs and ARBs?

There are no good studies as yet that support the use of the combination of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blocker (ARBs) for any indication.

A couple of studies have been done in heart failure and these have shown that there is no advantage in using the combination, and there may have been harm in patients who were taking beta blockers. In this population, the benefit from further disruption of the renin-angiotensin-aldosterone axis comes from adding spironolactone or eplerenone (not yet available anywhere) to ACEIs.



**Patients with hypertension**

In the treatment of patients with hypertension, there are no adequate studies looking at this combination. I would suggest that you would get better blood pressure reduction by adding a diuretic to the ACEI or ARB, or perhaps adding spironolactone to them.

**Patients with renal disease**

In the treatment of patients with renal disease, there are no adequate studies in patients with diabetes using the combination of ACEIs and ARBs. The risk of hyperkalemia is high, and therefore I would not recommend playing with this until there are studies that have demonstrated adequate benefit to offset the risks.

There is one adequate study examining the use of ACEI/ARB combination in non-diabetic renal disease (COOPERATE study). This study did show benefit for the combination over either the ARB or ACEI. The study also showed that the ARB and ACEI had similar benefit in these patients, but it was less than the combination. Generally a recommendation to change treatment would not be made until we have another study to confirm these findings particularly since there are questions as to whether other ethnic groups would respond the same way (the COOPERATE study was done in one center in Japan), and whether other drug doses would provide a different effect.

**The verdict?**

In summary, there is no adequate data to support the use of the combination of ACEIs and ARBs for the treatment of patients, particularly patients with diabetes or renal disease, where the risks of this particular combination are high and may not be offset by the potential benefits.

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