EDITORIAL

A Triage Algorithm for Inhalational Anthrax

This issue contains a thoughtful effort to make the most of limited data on a subject of intense public concern: the diagnosis of inhalational anthrax. Soon after September 11, 2001, the United States had its first experience with bioterrorism. The attack was limited but deeply troubling because the perpetrators used the U.S. Postal Service, an accurate and reasonably quick delivery system, to disseminate anthrax spores. It is all too easy to imagine a more determined effort to spread anthrax: emergency departments filled with frightened people, some in the early stages of a deadly disease.

Hupert and colleagues address the problem of efficient, accurate triage of patients with suspected anthrax (1). In this commentary, I focus on the article's principal product: a triage algorithm for people who have symptoms of inhalational anthrax.

An algorithm is a step-by-step instruction for solving a problem (2, 3). One use of algorithms is to solve the problem of sorting patients, by diagnosis or by levels of care, as in the present case. Figure 2 in Hupert's article, also shown here, is an algorithm. The boxes are decision points, which list criteria for an action. The arrows point to the next step in the triage process—another decision point or an action to take.

The ideal diagnostic algorithm for anthrax would use proven decision criteria and give each decision point's sensitivity, specificity, and corresponding probability of anthrax (4). The first step toward this goal would be to study a large number of people with the chief symptom of "I think I may have anthrax" by obtaining a standard set of clinical data and, independently of this information, establishing definite diagnoses. Standard statistical techniques can identify the best predictors of anthrax at each point in the algorithm. A key step is verifying the probabilities by using the algorithm in an independent sample of patients.

Circumstances forced Hupert and colleagues to take a pragmatic, less satisfactory approach. They could not study a large number of people with suspected anthrax because neither the symptom nor the target condition occurred often enough to support a prospective study. The rarity of inhalational anthrax (28 reported cases since 1920) meant that they had to use the findings in individual patients in published reports. Hupert and colleagues have enhanced our knowledge of anthrax by showing the frequency of these findings, alone and in several combinations. This information rests on a solid foundation. It is the first step toward choosing the decision criteria in a triage algorithm.

The next step was more difficult. Many of the findings in anthrax occur frequently in other diseases. The measure of diagnostic discrimination is the likelihood ratio. According to Bayes theorem, the likelihood ratio is a number that indicates how much the odds of disease change when a clinical finding is present. It is the probability of the finding in patients with anthrax divided by its probability in people who do not have anthrax. The authors had the numerator for individual findings and some combinations of findings; they sought the denominator in published studies of the frequency of clinical findings in patients with influenza, influenza-like viral illness, and community-acquired pneumonia. Here is where they ran into trouble. First, they could not calculate a likelihood ratio for any of the combinations of findings. They had the numerator, but they did not have the denominator because the studies of patients with the diseases that mimic anthrax did not measure the frequency of these combinations.

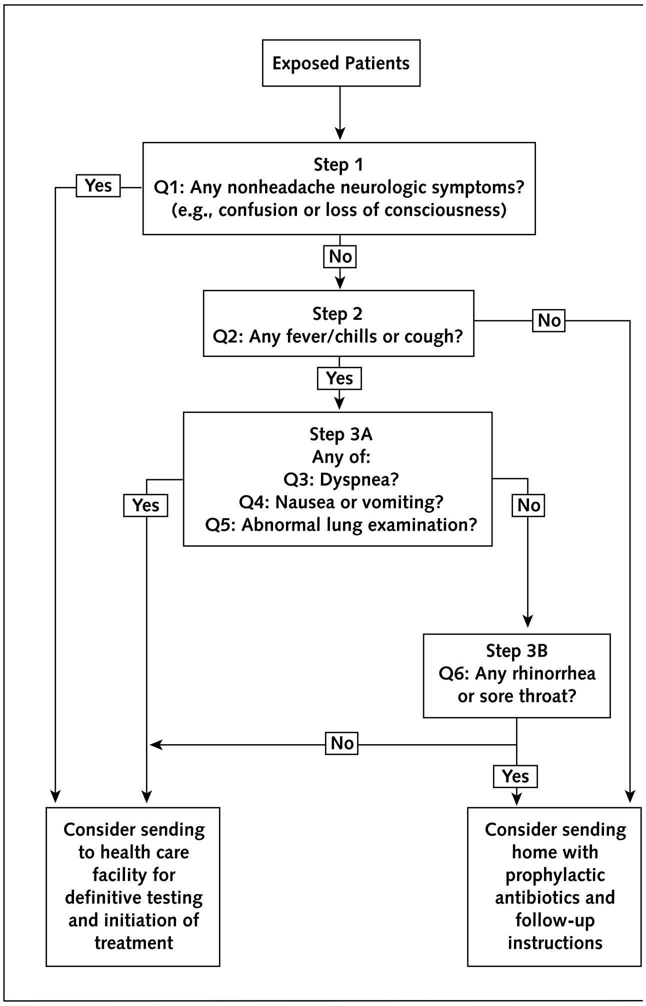
Their second problem is more arcane, and I discuss it in the Appendix (available at www.annals.org). A likelihood ratio is an approximate heuristic, usually accurate enough to be useful but inexact. Its denominator is the frequency of a clinical finding in all diseases that could be confused with anthrax. Authors of a study of people with suspected anthrax would typically divide their study sample into patients with anthrax and those with diseases that could be confused with anthrax; they would then calculate the frequency of the finding in the two groups. In fact, the group without anthrax contains people with influenza, influenza-like illness, and community-acquired pneumonia. The relative frequency of these three diseases will determine the frequency of the clinical finding in patients who do not have anthrax. The relative frequencies of influenza and influenza-like illness vary by season. Authors of articles on test performance ignore this point, thus effectively treating a mix of alternative diseases as if their relative frequencies never changed.

Hupert and colleagues do not ignore this problem, but their solution is not very satisfactory. They calculated the likelihood ratio of a finding for anthrax as against one of the alternative diagnoses. That approach does not help to calculate a probability when several diagnoses in addition to anthrax are being considered, and the finding in question occurs in all of them. Therefore, I do not have much confidence in the likelihood ratios shown in this article.

The important question is how well the authors' proposed triage algorithm discriminates between patients with anthrax and those with other diseases. The authors could not test it on a large number of patients with suspected anthrax to see how often the algorithm directed physicians to send patients with anthrax home. I evaluate the steps in their triage algorithm (**Figure**) by describing the frequency of patients who have the findings at each decision point.

Step 1: The authors discovered a finding that would triage many patients with anthrax and few other patients to hospital care: 43% of the patients with anthrax had neurologic symptoms other than headache. The reports of patients with influenza and influenza-like illness did not describe this finding. Most physicians' clinical experience

Figure. **Proposed three-tier screening protocol to identify potential early inhalational anthrax cases in the setting of a large-scale anthrax attack.**



would confirm the authors' assumption that this finding seldom occurs in these patients. So, the first step in the algorithm will probably triage nearly half of patients with anthrax and few, if any, patients without anthrax to hospital care. This decision point looks pretty solid (although because there are only 28 patients with anthrax, the 43% of them with nonheadache neurologic symptoms has a wide 95% confidence interval).

Step 2: This decision point uses fever, chills, or cough to identify patients with anthrax. The big risk is sending home a patient with inhalational anthrax who lacks all three of these findings. In the authors' data set of 28 patients with proven anthrax, 96% had one of these three findings. Therefore, the decision point would triage all but 4% of patients with anthrax to hospital care. We do not know the corresponding figures for patients with diseases that mimic inhalational anthrax. The frequency of the most common of these findings is a minimum estimate of the frequency that at least one of the three findings is present. Cough is the most common finding. It occurs in 92% of patients with influenza and 78% of patients with influenza-like illness. So, the algorithm probably triages most patients with alternative diagnoses to hospital care. Thus, while this decision point seems safe, it probably does not discriminate very well between patients with anthrax and patients with alternative diagnoses.

Step 3A: Step 3A uses the presence of dyspnea, nausea or vomiting, or abnormal lung examination to identify patients with anthrax. A patient with any one of these findings would get immediate care. Individually, these findings are common in anthrax and relatively uncommon in alternative diagnoses, so this decision point is efficient. Its safety is a concern. We do not know how often all of these findings are absent in a patient with anthrax; taken individually, they are absent in 32%, 39%, and 19%, respectively. The safety of this decision point is unknown.

Step 3B: This step applies to patients who do not have dyspnea, nausea or vomiting, or an abnormal lung examination. If they have rhinorrhea or sore throat, they go home. Sore throat occurs in 22% of all patients with anthrax, and rhinorrhea occurs in 18%; thus, the algorithm might triage a small number of patients with anthrax to home care. However, only a small number of patients with anthrax are likely to slip through earlier decision points without being triaged to hospital care. Thus, the safety of step 3B depends on the number of patients with anthrax who make it through step 3A, which is unknown.

Hupert and colleagues have used detailed case reports of individual patients to create a useful data set that gives us considerable confidence in the safety of the triage algorithm. Their analysis of alternative diagnoses is relatively weak because published studies do not report the frequency of combinations of findings that they found useful. As a result, we do not know the efficiency of triage; possibly, the algorithm would triage most patients with alternative diagnoses to hospital care. We do not know how the probability of anthrax at any decision point changes as the overall prevalence of anthrax changes in persons seen in emergency departments. We would be closer to these goals if authors of articles on the manifestations of influenza and influenza-like illness measured the frequency of the combinations of findings in the triage algorithm. If a bioterrorist attack occurs in the meantime, we have a triage algorithm that seems safe but is probably inefficient.

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