Would you be able to diagnose the first case of Ebola in a febrile patient who has no travel history and presents to an ED during flu season? Could you distinguish the lesion of cutaneous anthrax early in a bioterrorist attack from that of a brown recluse spider bite? Could you recognize the initial signs of botulism compared to those of stroke, myasthenia gravis, or Bell’s palsy?

In the 1940s, University of Maryland Professor Theodore Woodward advised his medical house staff that “when you hear hoofbeats, think of horses, not zebras.” Though directed at internists who are also trained to think of rare or esoteric illnesses in their patients’ differential diagnoses, the zebra aphorism is also applicable in a variety of medical settings including the emergency department and ED triage. In a busy ED, ruling out zebras every time hoofbeats are heard would waste an enormous amount of diagnostic resources while causing extensive delays in caring for all who come to the ED.

On the other hand, focusing exclusively on the most common or obvious explanations for patients’ presenting complaints risks missing serious, potentially fatal illnesses at a time when lifesaving interventions may still be possible. Even worse, not considering unexpected or atypical illnesses in patients when they first present may result in exposing others to danger and potential health care disasters. For example, a patient who has meningococcal meningitis requires prompt diagnosis, effective treatment, and isolation, along with the identification, evaluation, and prophylactic treatment of everyone who came into close contact with the patient.

Sometimes the first patient or “index” case presenting to an ED is a victim of a source of illness that may also affect many others. Common sources include food and drink, drugs and poisons, and the air we breathe. It is more difficult to identify the true source of a patient’s illness that may affect many when there are other plausible explanations and when nonspecific ED treatments such as fluids, oxygen, antipyretics, and pain meds alleviate the presenting signs and symptoms allowing the patient to be discharged home with follow-up care.

This time of year, I am reminded of a young restaurant kitchen worker who several decades ago had been brought to the ED after being found unconscious on the floor of a restaurant men’s room. The ED “drug screen” revealed the presence of several drugs of abuse, and after a few hours of IV hydration, nasal O₂, and “psych clearance,” the patient was discharged home. The next day, a middle-aged male customer of the restaurant was found dead on the floor of the same men’s room. Only then was carbon monoxide poisoning from a faulty heater identified as the true cause of both illnesses. This time of year, too, home cooking and food preparation for the holidays may become sources of serious foodborne bacterial, viral, and parasitic illnesses affecting large numbers of people.

Determining when hoofbeats are caused by a horse and when they are caused by a zebra is one of the most difficult challenges of emergency medicine.