Man-on-Horseback, *Tricholoma equestre* (=*T. flavovirens*): "The mushroom toxicity literature is littered with poor or questionable information. Rarely is it challenged once a mushroom is declared toxic it is difficult to change its designation."

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aving recently completed a mycophagy survey with almost ▶ 500 respondents from around the USA, I was struck by the number of people who occasionally eat "Manon-Horseback" despite fifteen years of warnings from many of the amateur mycological societies and clubs to avoid this mushroom. No adverse effects from eating this mushroom were reported by any of the participants in our survey. Even that font of all knowledge, Wikipedia, has declared this mushroom toxic. This followed a publication about the possible toxicity of Tricholoma equestre in the New England Journal of Medicine (Bedry et al., 2001).

The discordance between how people were behaving and "official" recommendations began my reflecting on a number of issues, including science, publication and peer review, liability, and critical thinking.

"Ladies and gentleman, you are embarking on a career in medicine. Our role is to teach you what we know. At least 50% will prove to be wrong. Your problem is that you don't know which 50% that is." So began my education in the healthy skepticism that has informed my career. As a contributor to the medical literature as well as an editor, the fallibility of the scientific medical enterprise was always close to the surface. Peer review, the system used to validate a scientific study is a very imperfect mechanism.

Being published in a "prestigious" medical journal provoked much commentary in the lay press with dramatic headlines like "The Muscle Destroying Mushroom." The French investigators described twelve individuals who suffered muscle damage (rhabdomyolysis) after eating large quantities of *T. equestre* over a three-day period. Supposedly they excluded the many other causes that can produce identical symptoms, including exercise, drugs, infections, cold, alcohol, endocrine disorders, etc.

The report was intriguing, but raised numerous questions not addressed in the manuscript such as: incomplete clinical histories including, exertion, dietary and drug details of each patient. They should have included the quantity of mushroom material actually eaten, the mode of preparation, who identified the mushrooms, and any alcohol ingestion. The fate of "control" subjects was never reported, since it is most unlikely that others did not eat a similar quantity of mushrooms. Eating alone is not common practice in France, and presumably friends or family shared these meals. How many other

individuals ate the same mushrooms and in what quantity, and did all who ate the mushrooms develop symptoms? What were the heavy metal concentrations in the mushrooms? Could the mushrooms have been contaminated with pesticides, solvents etc? Did these patients have any genetic predisposition to muscle disease? How was this possibility investigated? Is this isolated to one region of the country and not reported from elsewhere? Is there a geographic / environmental / habitat/mycorrhizal / seasonal difference in the putative toxin production? Is the *T. equestre* in France the same species as *T. flavovirens* in the USA as is claimed? In short, the report raised far more questions than answers.

The initial experimental data was also fraught with problems. The quantity administered to a few mice equated to a total of 6.6 pounds of mushrooms ingested over three days by a 150-pound human—a prodigious and unrealistic quantity. Administration of the mushroom powder itself produced a bare twofold rise in the muscle CPK enzyme, a less than convincing increase. Moreover, to claim a dose dependent effect when only three groups of three mice was tested stretches statistics to its outer limits. The remainder of the initial experimental data was equally problematic, since highly concentrated extracts were employed. Later experiments have not clarified the picture.

This report was followed by a few similar cases from Poland (Chodorowski et al., 2002; Chodorowski et al., 2003; Chodorowski et al., 2004; Chodorowski et al., 2005; Chwaluk, 2013; Sein Anand and Chwaluk, 2010). Every couple of years there are claims that the putative toxins have been identified (Nieminen et al., 2008). There have been no further reported occurrences from France, although it is likely that people still eat this mushroom. To confuse the issue even further, a recent publication about *Tricholoma terreum*, which has never been shown to cause any issues in humans, was claimed to have some unusual toxin in an experimental model producing rhabdomyolysis and also affecting cardiac muscle (Xia et al., 2015). Other than the genus name, there was no reason to relate this to Manon-Horseback, and yet that is exactly what the authors and science journalists managed to do. Guilt by association—a wild speculation.

Why has there not been a single report of muscle damage from eating this mushroom (*T. equestre*) in the USA? There are many possible reasons:

- 1. What is called *T. flavovirens* is not the same species as *T. equestre* in Europe.
- 2. American mycophagists do not find or eat the same quantity as Europeans.
- 3. The toxins are not produced in any of our ecosystems and habitats.
- 4. The original report was specious, with the symptoms due to other factors, e.g. the presence of a statin medication (Chodorowski et al., 2005)
- Personal, unique factors such as genetics / metabolism / immune system etc. are critical predisposing requirements.
- 6. Physicians have failed to recognize the association.
- 7. Physicians have not taken the necessary effort to document and publish any occurrence.

This muscle damage story is somewhat analogous to another rare problem reported from the eastern Mediterranean region known as corturnism. Every few years some who eat quail (*Coturnix coturnix*) develop severe rhabdomyolysis. Nobody knows why (Aparicio et al., 1999; Giannopoulus et al., 2003; Korkmaz et al., 2008; Papadimitiriou et al., 1996; Tsironi et al., 2004). Investigations have failed to determine a mechanism. Could Man-on-Horseback be the mushroom equivalent?

The mushroom toxicity literature is littered with poor or questionable information. Rarely is it challenged. Once a mushroom is declared toxic it is difficult to change its designation. And this is where attorneys and our litigious society supersedes science. Almost every mushroom club and publication feels obligated to adopt the prudent approach of declaring this mushroom at least of questionable edibility, if not frankly toxic. France and Poland no longer permit the commercial sale of *Tricholoma equestre* (Peintner et al., 2013). However the ambivalence towards this fungus persists, as evidenced by this statement from a Spanish mycological society: "the existing controversy regarding its potential toxicity, it is our duty not to recommend its consumption or at least consume with caution, although we continue eating it without a hitch."

So what is the bottom line? Only time will tell if this observation belongs in the true column, or becomes relegated to a rare, not well understood, event. The book is not closed on this, so keep watching and listening. There is still much to learn. In the meantime, if you do feel obligated to eat this mushroom, avoid gluttony if faced with an unlikely surfeit of *Tricholoma flavovirens* and don't eat them at every meal. Live by the words of Marcus Cicero: "never go to excess, but let moderation be your guide."

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