

# US Military: Dangers of Trichothecene Mycotoxins

Learn about how common mold mycotoxins can impact health in a dire manner, per the US Military. The following refers to battlefield and agricultural conditions, but the readers will note how similar many of these symptoms are to those, very tragically, experienced in many of our mold-contaminated, damp buildings - particularly, our schools (SMH).

## Chapter 34

### TRICHOTHECENE MYCOTOXINS

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#### INTRODUCTION

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#### SUMMARY

[Dangers of trichothecene mycotoxins (found in several common school molds), some excerpts from the US Military Manual, Ch. 34](SMH):

"This family of mycotoxins causes multiorgan effects including emesis and diarrhea, weight loss, nervous disorders, cardiovascular alterations, immunodepression, hemostatic derangements, skin toxicity, decreased reproductive capacity, and bone marrow damage.<sup>4,6</sup>

...In [Ch. 34] we will concentrate on T-2 mycotoxin, a highly toxic trichothecene that, together with some closely related compounds, has been the causative agent of a number of illnesses in humans and domestic animals.<sup>1,2</sup>

The trichothecene mycotoxins are toxic to humans, other mammals, birds, fish, a variety of invertebrates, plants, and eukaryotic cells in general... Once the trichothecene mycotoxins enter the systemic circulation, regardless of the route of exposure, they affect rapidly proliferating tissues.<sup>1,2,4,6,35,42,45</sup> (Borden Institute, US Army, Chapter 34

#### TRICHOHECENE MYCOTOXINS, page 660)

T-2 Toxin: "Disease: Alimentary Toxic Aleukia; Agent: Trichothecene Mycotoxins; Producing Organisms: Fusarium & various other fungi; Entry route: Ingestion, Dermal & Inhalation; Toxic Response: Minutes to Days; Symptoms: blurred vision, hemorrhaging mucous membranes, dizziness, ataxia, tachycardia, hypothermia and hypotension; can induce DNA damage and cell death. Additional possible health effects include hemorrhagic, immunosuppressive reactions as well as nausea and vomiting".

...the primary toxic effects of the trichothecene mycotoxins is caused by their properties as potent inhibitors of protein synthesis.

Although initial investigations on the mechanism of action of the trichothecene mycotoxins suggested that the inhibition of protein synthesis as the principal mechanism of action, the above observations indicate that the effects of these toxins are much more diverse.

The lipophilic nature of these toxins suggests that they are easily absorbed through skin, gut, and pulmonary mucosa.

Mice, rats, and guinea pigs die rapidly (within 1–12 h) after exposure to high concentrations of aerosolized mycotoxin, with no apparent lung lesions or pulmonary edema.<sup>28–30</sup> This finding is in contrast to the effect of an oral dose of T-2 toxin, which causes direct damage to the intestinal mucosa.<sup>55</sup> From these data, we can conclude that the trichothecene mycotoxins very rapidly cross the pulmonary and intestinal mucosa and enter the systemic circulation to induce the toxin-related toxicoses. In contrast, trichothecene mycotoxins are only slowly absorbed through skin, especially when applied as a dust or powder.<sup>56</sup> Systemic toxicity and lethality can be produced by dermal exposure to higher concentrations of T-2 toxin, however, especially if the mycotoxin is dissolved in a penetrant such as DMSO.<sup>6</sup>

The degree of illness in an individual exposed to trichothecene mycotoxins could be affected by a

number of factors, including the nutritional status of the host, liver damage, intestinal infections, route of toxin administration, and stress. The pathological effects and clinical signs for many toxic materials can vary with the route and type (acute, single dose vs chronic, subacute doses) of exposure. For the trichothecene mycotoxins, however, a number of the toxic responses are similar, regardless of the route of exposure. As we discussed earlier in this chapter, once they enter the

systemic circulation, trichothecene mycotoxins affect rapidly proliferating tissue regardless of the route of exposure. In contrast, the symptoms and clinical signs of trichothecene intoxication can vary depending on whether the exposure is acute or chronic. Acute exposure to trichothecene mycotoxins used as biological warfare agents is the major concern for military medicine, but for continuity and historical implications, chronic intoxication will also be addressed in this chapter.

## Acute Effects

Acute oral, parenteral, dermal, or aerosol exposures to trichothecene mycotoxins produce gastric and intestinal lesions. Hematopoietic and immunosuppressive effects are radiomimetic. Central nervous system toxicity causes anorexia, lassitude, and nausea; suppression of reproductive organ function; and acute vascular effects leading to hypotension and shock. While a number of toxic effects are common to different routes of exposure, route-specific effects have been observed in animal models. Examples of local, route-specific effects include the following:

- dermal exposure: local cutaneous necrosis and inflammation<sup>6</sup>;
- oral exposure: lesions to the upper gastrointestinal tract<sup>64</sup>; and
- ocular exposure: corneal injury.<sup>6</sup>

## Dermal Exposure

Similar cutaneous irritations have been observed in numerous accidental and experimental settings:

- Individuals who were exposed to hay or hay dust contaminated with trichothecene-producing molds developed severe cutaneous

irritations.<sup>38</sup>

- In working up large batches of fungal cultures

from trichothecene-producing organisms,

laboratory personnel suffered facial

inflammation followed by desquamation of

the skin and considerable local irritation.<sup>65</sup>

- When trichothecene mycotoxins of relatively

low toxicity (crotocin and trichotecin)

were applied to the volar surface of

human forearm or to the human head, reddening

and irritation occurred within a few

hours of exposure, and was followed by

inflammation or scrubbing that healed in

1 to 2 weeks.<sup>66</sup>

- The hands of two laboratory workers were

exposed to crude ethyl acetate extracts containing

T-2 toxin (approximately 200  $\frac{1}{4}$ g/

mL) when the extract accidentally got inside

their plastic gloves.<sup>66</sup> Even though the

workers thoroughly washed their hands

with a mild detergent within 2 minutes after

contact, they experienced severe cutaneous

irritations.

These observations provide evidence that when

human skin is exposed in vivo to small amounts of

trichothecene mycotoxins, severe cutaneous irritations

develop and can last 1 to 2 weeks after acute

exposure.

A number of animal models have been used

to assess local and systemic toxicity and lethality

from skin exposure to trichothecenes.<sup>6</sup> In a dermal

study that used a mouse model, necrosis in the skin

was present by 6 hours after dermal application.

## Respiratory Exposure

Victims of yellow rain reported a variety of upper respiratory signs and symptoms.<sup>7,27</sup> The major subdivisions of the respiratory tract that were affected include the nose (itching, pain, rhinorrhea, and epistaxis); the throat (sore/pain, aphonia, and voice change); and the tracheobronchial tree (cough, hemoptysis, dyspnea, and deep chest pain or pressure or both). Agricultural workers who were exposed to hay or hay dust contaminated with trichothecene mycotoxins developed similar signs and symptoms of upper respiratory injury. The descriptions of the yellow rain attacks in Southeast Asia (ie, the droplets, heavy mist, vapor), suggest that the aerosols were larger than 1 to 4  $\frac{1}{2}$   $\mu$ m—the particle size required for deposition in the alveoli. Thus, respiratory tract exposure from the larger particle aerosols would involve mycotoxin deposition in the upper respiratory and tracheobronchial region, followed by secondary gastrointestinal tract exposure after clearance from the lungs.

The symptoms of vomiting, diarrhea, melena, abdominal pain, and acute gastroenteritis with hematemesis<sup>7</sup> could be related to ingestion of toxin that was deposited in the upper respiratory tract and tracheobronchial region.

In humans, many of the acute enteral effects (from either yellow

rain or contaminated hay and dust particles) of the trichothecene mycotoxins are probably the result of secondary ingestion of toxins that originally were deposited in the respiratory tract by large-particle aerosol.

### Chronic Toxicity

Chronic exposure to subacute doses of trichothecene mycotoxins is not thought to be an effect of biological warfare. This type of exposure, however, was responsible for ATA toxicosis in humans and mycotoxicosis in domestic animals. In addition, chronic toxicity has been iatrogenically induced when repeated subacute doses of a trichothecene mycotoxin were administered intravenously to cancer patients as a chemotherapy for colon adenocarcinoma.

### DIAGNOSIS (battlefield)

The early signs and symptoms of an

aerosol exposure to trichothecene mycotoxins would depend on particle size and toxin concentration. For a large-particle aerosol (particles > 10  $\mu\text{m}$ , found in mist, fog, and dust; similar to that used in Southeast Asia), the signs and symptoms would include rhinorrhea, sore throat, blurred vision, vomiting, diarrhea, skin irritation (burning and itching), and dyspnea. Early (0–8 h) signs and symptoms from a deep-respiratory aerosol exposure (from aerosol particles in the 1- to 4- $\mu\text{m}$  range) have not been fully evaluated but could include vomiting, diarrhea, skin irritation, and blurred vision.

Later signs and symptoms (8–24 h) would probably

be similar (except for the degree of skin rash and blisters) for both large-particle and deeprespiratory aerosol exposure to trichothecene mycotoxins. They could include continued nausea and vomiting, diarrhea, burning erythema, skin rash and blisters, confusion, ataxia, chills, fever, hypotension, and bleeding.

[http://www.bordeninstitute.army.mil/published\\_volumes/chemBio/Ch34.pdf](http://www.bordeninstitute.army.mil/published_volumes/chemBio/Ch34.pdf) (Borden Institute, Textbooks of Military Medicine, Medical Aspects of Chemical and Biological Warfare, TRICHOTHECENE MYCOTOXINS, Ch. 34. Click here for a .pdf of this document.

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Satratoxin H: "Description: Mycotoxin; Fungus: Stachybotrys chartarum; this family of mycotoxins has a very high cytotoxicity" [toxicity to cells] (Aerotech P&K, Biological Warfare Agents, Microbial Toxins).