PRACTITIONER TECH SHEET | Gliotoxin

Gliotoxin opens the doorway to fungal infection. It has been shown to be produced in vivo, contributing to the etiology of fungal infections, and is a virulence factor for the airborne pathogen Aspergillus fumigatus. Gliotoxin is highly immunosuppressive. It's the most abundant metabolite produced during hyphal growth. Many who test positive for Gliotoxin additionally have a significant yeast burden.

Fungal sulfur uptake is required for its formation, forming a disulfide bond unique to this mycotoxin. Chemical reduction of this disulfide bond contributes to its pathogenicity, often causing sulfur sensitivity in patients, not related to genetic polymorphisms but rather due to compromised metabolism.

Gliotoxin is rapidly sequestered by hepatocytes and is one of the most diverse toxins in how it affects the body.

MOLD SOURCES
Aspergillus spp., Trichoderma spp.

COLOR
Tend to be green to black, but these various species of mold can take on any color, depending on substrate

FAVORITE BUILDING MATERIAL
Flooring, carpet, textiles, wood, plywood, modified wood products, concrete

SIGNS
Fungal dermatological infections
Onychomycosis
IgG subclass 3 deficiency

SYMPTOMS
Pruritus
Mast cell reactions
Post-prandial bloating
Sweet cravings
Nausea, Constipation
Intolerance to sulfur and sulfur-containing foods
Chemical sensitivities
Fatigue
Cognitive difficulties
Headaches
Anxiousness
Frequent mood changes
Despair/suicidality
Incoordination
MS-type symptoms
Insomnia
Frequent infections
Delayed wound healing

HEALTH IMPACTS

Immunosuppressive, immunotoxic, neurotoxic, hepatotoxic, highly oxidative, genotoxic, cytotoxic, cutaneous/mucocutaneous toxic.

Apoptotic. Potent inducer of apoptotic cell death in a number of cells (immune, hepatic, neurological.)

Immunosuppressive.
- Inhibits T-cell activation and proliferation.
- Suppresses macrophage function.
- Blocks mast cell activation & degranulation, resulting in an increased total mast cells as a counter-reaction.
- Related to IgG3 subclass deficiency because of this immunoglobulin's prevalence of disulfide bonds.

Toxicity. Rapid sequestration by hepatocytes. Inhibits a number of thiol requiring enzymes via intracellular SOD/oxidization resulting in glutathione depletion.
- Monothiols: ALA, NAC, GSH
- Dithiols: DMSA, DMPS

Mitochondria. Reduces ATP via hyper-polarized membrane.

Inhibits histone methyltransferase. Implications on gene transcription, DNA repair, and methylation. Inhibition is cytotoxic to thymocytes and mast cells, and affects EBV latency.

Protein synthesis inhibition.

Neurotoxic. Penetrates and impairs the integrity of the blood-brain barrier. Capable of injuring and killing microglial cells, astrocytes, and oligodendrocytes. In vivo studies display that a non-neuronal site was able to increase neuroinflammation, therefore GI colonization and/or infection can affect CNS.

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TREATMENT OPTIONS

*Note: the doses listed are intended for when each item is used as a standalone therapy. When multiple items are combined, they often work synergistically, meaning lower doses can typically achieve similar effectiveness due to their complementary effects.

Therapeutic Diet ~
  Temporary avoidance of sulfur-containing foods ~
  ie: garlic, onions, eggs, fish, and the Brassicacea family (broccoli, kale, cauliflower, cabbage, Brussels sprouts)

Binder. Aloe long-chain polysaccharides. Antihistaminic adsorbent.

Antifungals ~ herbals or Rx-herbal combination that address:
  Systemic
  Nasal
  Topical: fungal rashes, toenails

Combine with bitters.
  Extra-oral bitter taste receptors are involved in regulating some aspects of innate immunity.
  In pts with CRS, local innate immunity deficiencies predispose to sinus mucosal bacterial colonization/infection, including deficient functioning of the extra-oral bitter taste receptor.
  Bitters. 5-10 drops on the tongue 10 minutes before meals.
  Bile acids, such as the drug ursodiol or the taurine conjugated form called TUDCA.
  Ox bile. Up to 125mg 1-2 times per day with largest meals.

Redox without harm = antioxidants (work against fungal ROS, caspases without activating Gliotoxin.)
  Mixed bioflavonoids are ideal. Every color band, and especially green (folinic acid).

Molybdenum. 250mcg qd-bid.

Resveratrol. Minimum therapeutic dose: 1000mg daily, best divided. Anti-yeast, bioflavonoid.

Turmeric. 350mg up to three times daily of liposomal turmeric.
  Begin with the lowest dose and titrate slowly. Antifungal detoxifying agent.

Quercetin. 300-600mg capsules, from 1 to 3 times daily. Reduces mast cell reactions.

Coffee enema. Induces bile secretion.

Glutathione precursors. Vit C, Vit E (tocotrienols), B-complex, Mag, Se

Zn. Use cautiously, even though a glutathione precursor.
  Assists Aspergillus in biosynthesis of gliotoxin.

Thiols. Use cautiously, and typically only once on antifungals. Replete deficiencies in the mitochondria.
  [Monothiols: ALA, NAC, GSH. Dithiols: DMSA, DMPS].
  Ex 1: NAC (cell study: “completely abolished the gliotoxin-induced caspase-3-like activity, cytotoxicity, and reactive oxygen species”)
  Ex 2: GSH study (cell study: “things that reduce the internal sulfide bond interfere with its effect on cell viability and apoptosis.”)
  ***But in vivo, may add antioxidant protection to fungi.

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