Neurotoxin Brain Disorders in Asia and Beyond: Acute, Chronic, and Delayed

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Learning Objectives

- Several botanicals used for food harbor natural neurotoxins.
- Neurotoxins may be intrinsic to, or contaminate, the botanical.
- Nutritional state dictates the presence or absence of toxic response.
- Neurotoxic effects may present in the short-term or long-term.
- Neurodegeneration may appear clinically years or decades post-exposure.

Acute Immature-Litchi-Associated Encephalitis (Vietnam, Bangladesh, India)

Toxic Hypoglycemic Syndrome mistaken for JEV or pesticide toxicity

Malnourished, hungry children pick-up and eat Immature fruit.

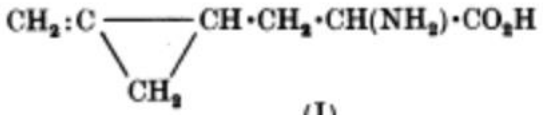
SX: Seizures, sweating, vomiting coma and, death or recovery.

TX: intravenous Dextrose in ER + correction of electrolyte imbalances

LITCHI
Litchie sinesis

RAMBUTAN
Nephelium lappaceum

I. Hypoglycin A



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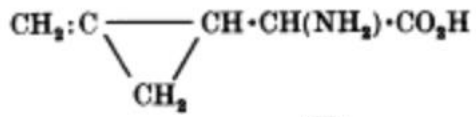


(II)

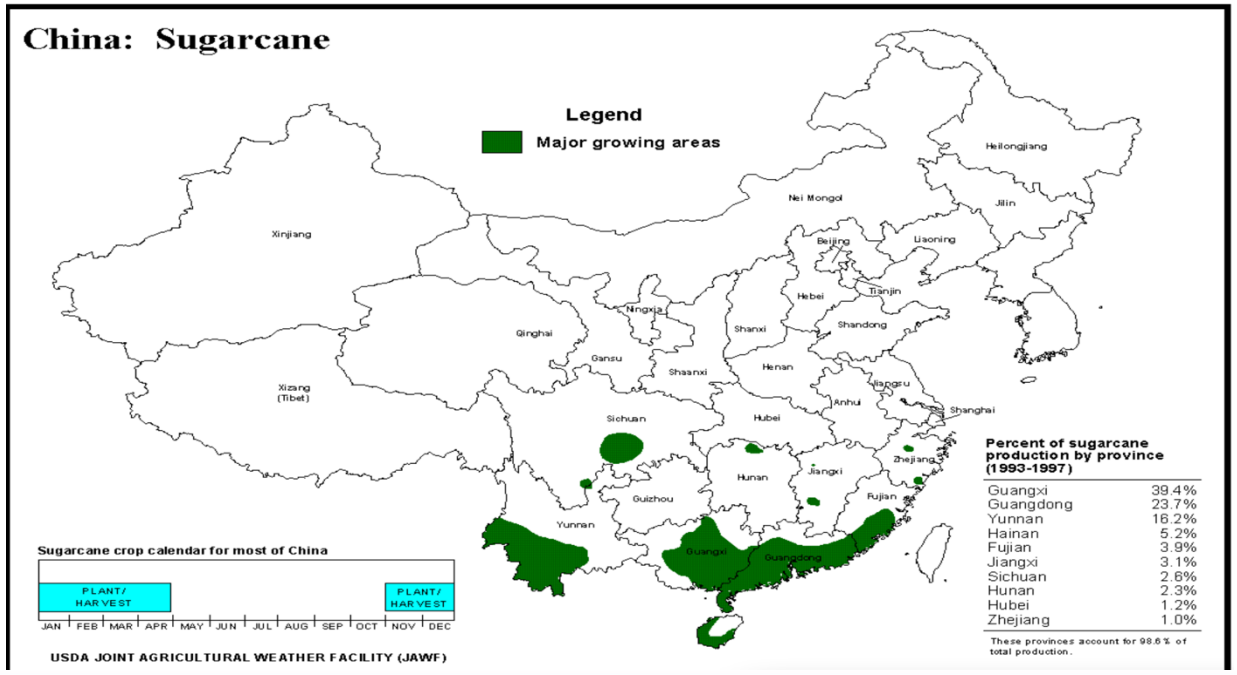
II. Lower homolog of hypoglycin A

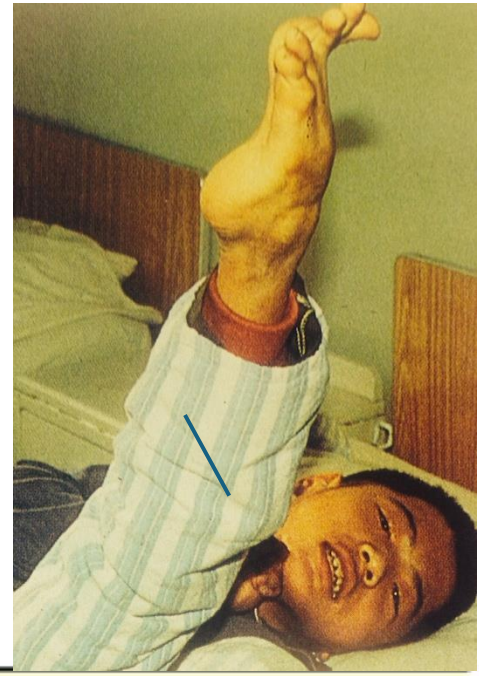
ACKEE
Blighia sapida

ACKEE and SALTFISH

Toxic Hypoglycemic Syndrome, or Jamaican Vomiting Sickness, has long been known in the Caribbean among children and adults who consume Immature ackee fruit, which is used widely in the national dish of Jamaica.

Mildewed Sugarcane Poisoning
(fungal 3-nitropropionic acid-induced putaminal necrosis)

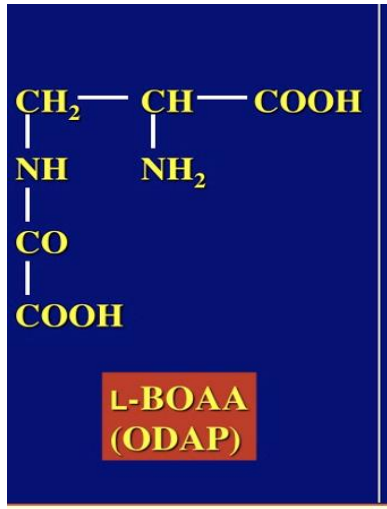


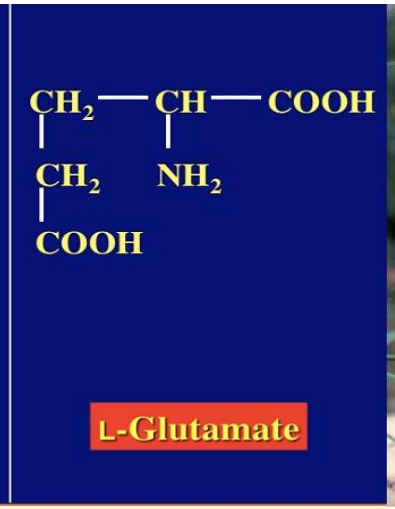


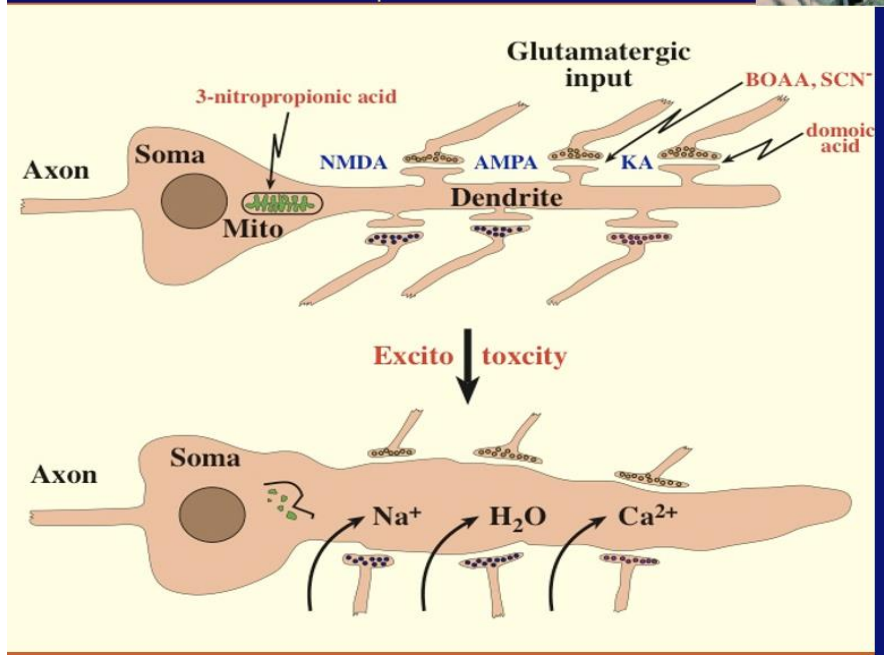
Province	Time	Poisoned cases	Severe cases	Death cases	Reference
Shandong	2003	15	15		[32]
Hubei	2003	2	2		
Shanxi	2003	3	3		
Hebei	1985-2003	27	27	1	[33]
Hebei	2004	5	1	1	[34]
Shanxi	2004	1	1		
Total		52	48	2	
TOTAL	1972-2004	861	431	46	

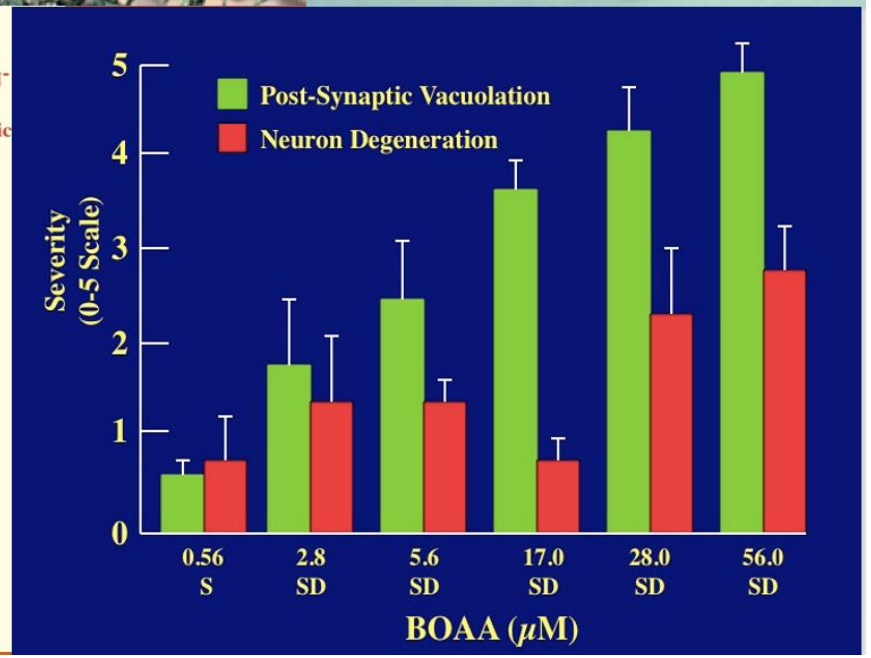
Grass Pea (*Lathyrus sativus)* and Lathyrism

(Ethiopia, Afghanistan, Indian Subcontinent, China previously)









Lathyrism is an irreversible upper motor neuron disease caused by food dependency on Grass Pea, a protein-rich legume that resists flood and drought. Forty years of research has been invested in developing safe strains of Grass Pea (by genetically reducing the seed content of the neurotoxin L-BOAA [1]) because its environmental tolerance + protein content make it an invaluable crop for a globally warming world.

1. Dellino et al.,
Food Frontiers 0:1–16, 2025.

Cassava (*Manihot esculenta*)and Cassavism (Thailand*, India (Kerala)**, Sub-Saharan Africa***)

Consumption of cassava that has been insufficiently processed to remove cyanogenic glucosides can trigger dizziness, headache, muscle weakness, confusion, seizures, and death from cyanide poisoning*. Food dependence on poorly processed cassava is associated with an ataxic myeloneuropathy** and irreversible spastic paraparesis*** or *konzo* (cassavism), an upper motor neuron disorder to which children and women of childbearing age are especially susceptible.

CASSAVA – MANIOC
YUCA - MANDIOCA
(*Manihot esculenta*)

- Tropics/subtropics
- Food staple for 500m
- Sweet and bitter types
- Some protein in leaves

- Roots are a valuable carbohydrate source but have potential neurotoxicity from cyanogenic glycosides.

- Provides food security

1. Nzwalo and Cliff, *PLoS Negl Trop Dis*. 28:e1051, 2011.

False Morel : *Gyromitra esculenta*
(China*, Korea**, Malaysia, Singapore, Thailand)

Ingestion causes acute onset of seizures 2-8 hours after eating. The principal toxin gyromitrin is metabolized in the consumer to monomethylhydrazine, which inhibits pyridoxyl 5'-phosphate, vital cofactor for GABA-dependent glutamic acid decarboxylase. Reduced brain GABA results in excessive glutamate excitation.

Repeated consumption with or without acute intoxication has been associated with Amyotrophic Lateral Sclerosis 5-20 years after food use in the French Alps (Lagrange et al., *J. Neurol. Sci.* 427: 117558, 2021 and *eNeurologicalSci*. 35:100502, 2024).

*Li et al. Mushroom Poisoning Outbreaks - China, 2020. *China CDC Wkly* 3:41-45, 2021.
**Cho et al. *Korean Journal of Mycology* 49: 363, 2021. www.kjmycology.or.kr/4903-09/

Cycad Seed (*Cycas* spp.) and ALS/PDC (Guam, Japan (Kii Hanto & Ryukyu Isles), India (Odisha)




Traditional food and medicinal use of cycad seed (Sago Palm) has been strongly associated with the former very high incidence of Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia Complex among the Chamoru people of Guam and Japanese residents of Kii Peninsula, Honshu Island, respectively. Attendant sub-clinical pigmentary retinopathy and cerebellar ectopia arose from developmental (second-trimester) exposure to cycasin. Transgenerational cycad food use resulted in familial as well as sporadic cases [1].

In India, "*a household survey of 10 villages by the authors revealed that 33% of* Cycas sphaerica *flour-eating adult population of Odisha suffers from neurodegenerative disorders*" [2].

1. Spencer et al., *J Neurol Sci*. ;419:117185, 2020.

2. Bal et al. *Toxicon* 238:107566, 2024.

Take-home Lessons

- Acute neurotoxic illness from ingestion of certain botanicals is most commonly found among impoverished, undernourished communities.

- Chronic/delayed neurotoxic illness often results from prolonged use of incompletely detoxified certain plant and fungal materials.

- Identification of etiology requires detailed investigation of patients' lifetime exposomes, young-onset and conjugal cases, and clusters of disease.

- Neurology and public health can work together to educate consumers and prevent botanical neurotoxin disorders, thereby promoting Brain Health.

감사합니다

gamsahamnida