

# Treatment of Amatoxin Poisoning: 20 year retrospective Analysis

- Enjalbert F, Rapior S, Nouguiet-Soule J, Guillon S, Amouroux N, Cabot C.
- J tox Clin Tox 2002 40(6):715-767

Presented by;

Michael Beuhler, MD, FACMT

Medical Director, Carolinas Poison Center

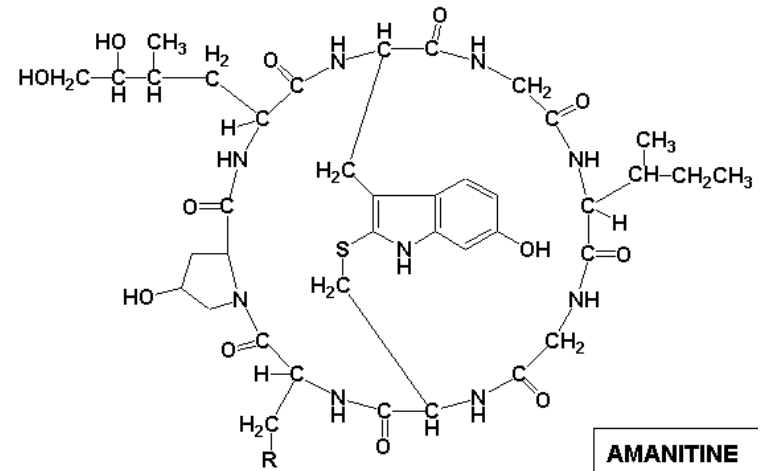


# Introduction

- Amanita Poisoning Review:
  - Incubation stage
  - Gastrointestinal phase
    - Vomiting, diarrhea, abdominal pain
  - Hepatotoxic phase
    - Hepatic damage with progressive coagulopathy
  - Hepatorenal syndrome
    - Hemorrhages, seizures, renal injury, fulminant hepatic failure (and probably death)



# Introduction



- Toxin responsible are amanitins ( $\alpha, \beta, \gamma$ )
- Bicyclic peptides bridged by sulfur atom
- Use the transport system for biliary acids to reach the liver
- Inhibits RNA polymerase II
  - This prevents transcription
  - So no new mRNA
  - Protein synthesis is limited



# Review Of Therapies (selected)

## ■ Silymarin Complex

- **Silybin** major compound
- Animal studies have shown treatment benefit
- Competes for  $\alpha$ -amanitin cellular uptake by the bile salt transport systems of the hepatocyte membrane
- Radical scavenger
- Anti inflammatory effects
- Stimulates liver cell metabolism and growth.
- Side effects: nausea, headaches, pruritus, urticaria



# Methods

- A review of cases in literature of human amanita mushroom poisonings from North America and European countries from the last 20 yrs.
- 2108 cases included with 32 liver transplants
  - Herculean effort shows in pages of tables....
- Most frequent implicated mushrooms were *A. phalloides*, *bisporigera*, *magnivelaris*, *ocreata*, *verna* and *virosa*



# Statistical analysis

- Cases were separated into 11 modes of care
  - Supportive care only
  - Detoxication\* (oral, extra-corporeal)
  - Benzylpenicillin (PCN)
  - N-acetyl cysteine (NAC)
  - Silybin
  - Silybin/PCN, PCN/antioxidant, PCN/steroid, PCN/thioctic acid
  - PCN/( $X_1 + X_2 + \dots$ )+Silybin, PCN/( $X_1 + X_2 + \dots$ )-Silybin
- Detoxication procedures were ignored for assignment of the various modes.



# Analysis

- Rates of drug therapy use:
  - Benzylpenicillin (86.5%),
  - Silybin (38.2%)
  - Steroids (27.6%)
  - Thiocctic acid (27.1%)
  - NAC (11.8%)



# Analysis

- Overall survival was 89.7%
- Mortality rates broken into: transplant included (LTi), and transplant excluded (LTe)
  - LTi counted Liver transplants as mortalities
  - LTe removed Liver transplants from numerator and denominator
- The highest mortality rate was in the supportive measures only group (47.3%).
- Detoxication had a mortality rate of 10.4%
  - Not statistically different than the pooled drug treatment groups.



# Analysis

- The lowest mortality rates were seen in (no difference between them)
  - Silybin\*
  - NAC
  - Silybin/PCN\*
  - PCN/( $X_1 + X_2 + \dots$ )+Silybin
- Unless grouped with Silybin, PCN did not demonstrate any benefit.

\*Significantly different than detoxication only group **only** for LTe



# Discussion

- Although no adjustments were made for multiple comparisons, co-morbidities, treatment location, age, detoxication therapies, conclusions made were:
  - Benzylpenicillin (PCN) did not demonstrate any treatment benefit.
  - Silybin is beneficial in decreasing mortality
  - NAC is beneficial in decreasing mortality



# Take home points

- Overall survival was 89.7%
- The lowest mortality rates were seen in the silybin groups and the NAC monotherapy group
- “..Silymarin [*Silybin*], and...NAC play a crucial role in the recovery of amatoxin-poisoned patients.”
- “Clinical data.....do not show benzylpenicillin [*PCN*] to be an effective drug”

