



The Pathophysiology of Poisonous Plant Intoxication



ADVS 5860

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January 25, 2010



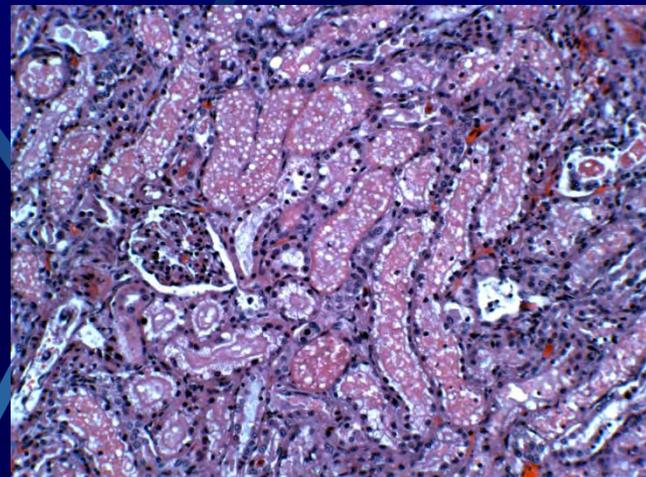


Lecture Outline

- Introduction
 - Aristolochia spp.
 - Larkspur
- Definitions
- Mechanism of Toxicity
- Specific Tissue Toxicities



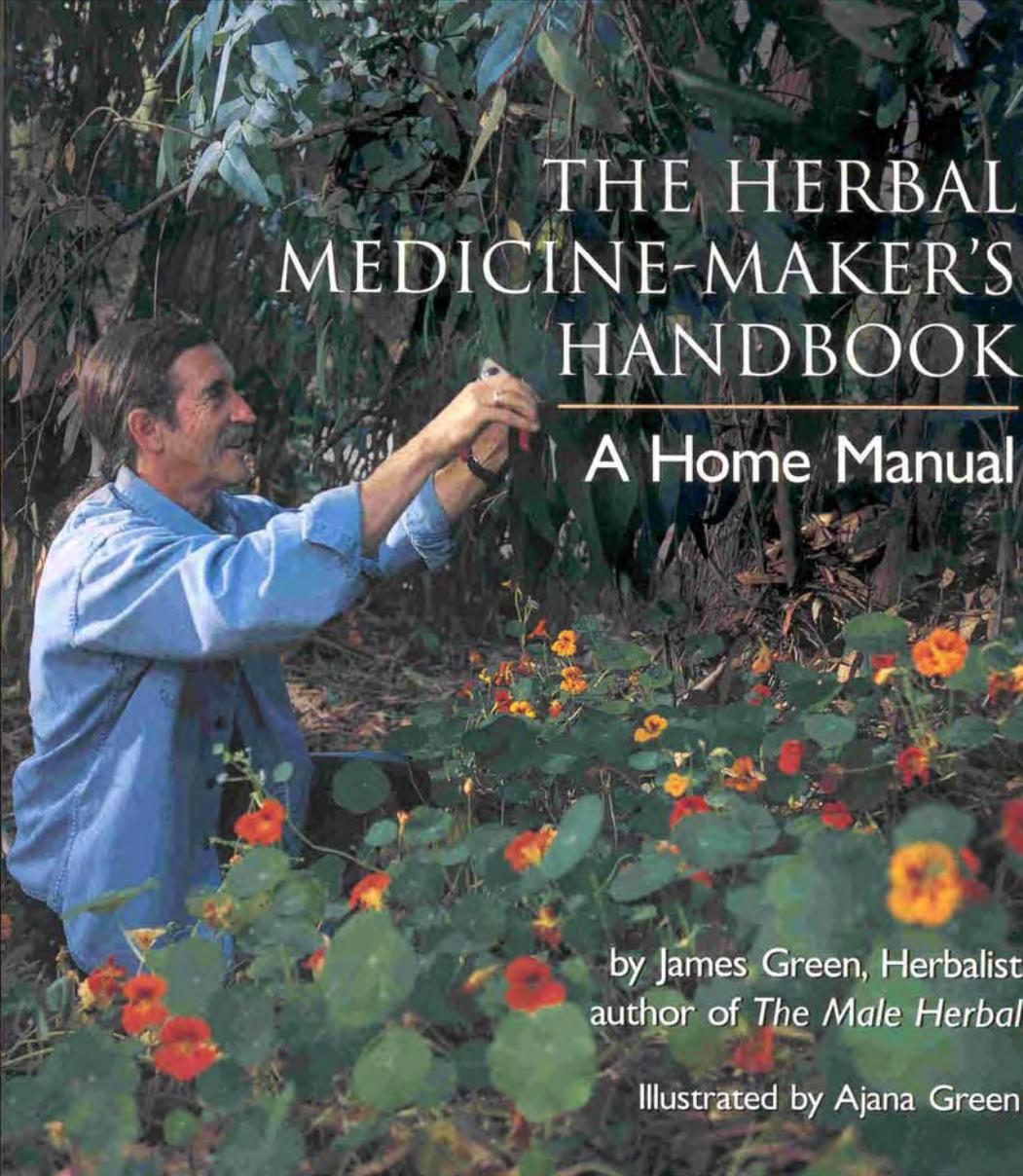
Aristolochia tomentosa



Germany 1950's

Endemic Uropathy 1980's





THE HERBAL
MEDICINE-MAKER'S
HANDBOOK

A Home Manual

by James Green, Herbalist
author of *The Male Herbal*

Illustrated by Ajana Green

\$85 Billion in 2007

Unregulated (Hatch Act)

Unproven efficacy or safety

TCM NATURE HEALTH CENTER

[-ACUPUNCTURE-](#) [-HERB-](#) [-QI-GONG-](#) [-FAO-](#) [-MORE-](#)

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- INFORMATION**
- [WHAT IS TCM](#)
- [WHAT IS CAM](#)
- [PAIN MANAGE](#)
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TRADITIONAL CHINESE MEDICINE

What is Traditional Chinese Medicine?

Traditional Chinese Medicine (TCM) is a complete medical system that has been used to diagnose, treat, and prevent illnesses for more than 2,000 years. TCM is based on a belief in *yin* and *yang*—defined as opposing energies, such as earth and heaven, winter and summer, and happiness and sadness. When *yin* and *yang* are in balance, you feel relaxed and energized. Out of balance, however, *yan* and *yang* negatively affect your health.

Practitioners also believe that there is a life force or energy in every body, known as *qi* (pronounced "chee"). In order for *yin* and *yang* to be balanced and for the body to be healthy, *qi* must be balanced and flowing freely. When there's too little or too much *qi* in one of the body's energy pathways (called meridians), or when the flow of *qi* is blocked, illness results.

The ultimate goal of TCM treatment is to balance the *yan* and *yang* in our lives by promoting the natural flow of *qi*. In an interesting analogy, often used to explain its nature, *qi* is described as the wind in a sail; we do not see the wind directly, but we are aware of its presence as it fills the sail.

What is the history of TCM?

The first writings about TCM date back to 200 B.C.E. Herbal medicine and acupuncture, including theory, practice, diagnosis, and treatment, were recorded in classical Chinese texts and refined over many centuries.

The practice of TCM stayed in Asia for centuries. Chinese immigrants had been practicing TCM in the United States since the mid-19th century, but its existence was unknown to most Americans before 1971. That year, *New York Times* reporter James Reston, who was in China covering former President Nixon's trip, had to have an emergency appendix operation. After the operation he received acupuncture for pain, and his stories about this experience with TCM fascinated the public. Since then, TCM has gone on to become a mainstream alternative medicine practiced all over the world.

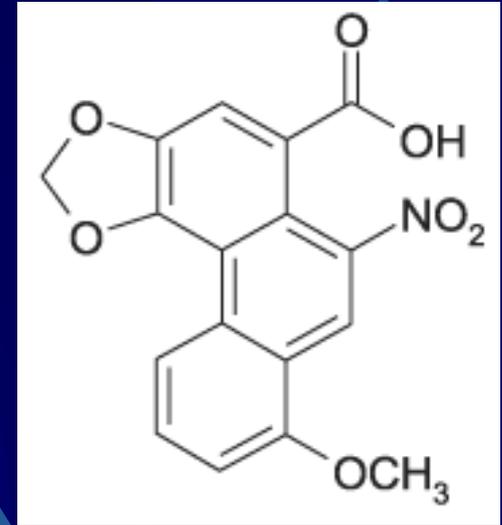
How does TCM work?

Disease (alterations in the normal flow of *qi* such that *yin* and *yang* are imbalanced) is thought to have three major causes: external or environmental factors, your internal emotions, and lifestyle factors such as diet. Through the use of its therapeutic modalities, TCM stimulates the body's own healing mechanisms. Practices used in TCM include:

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 4, Number 1, 1998, pp. 9-13
Mary Ann Liebert, Inc.

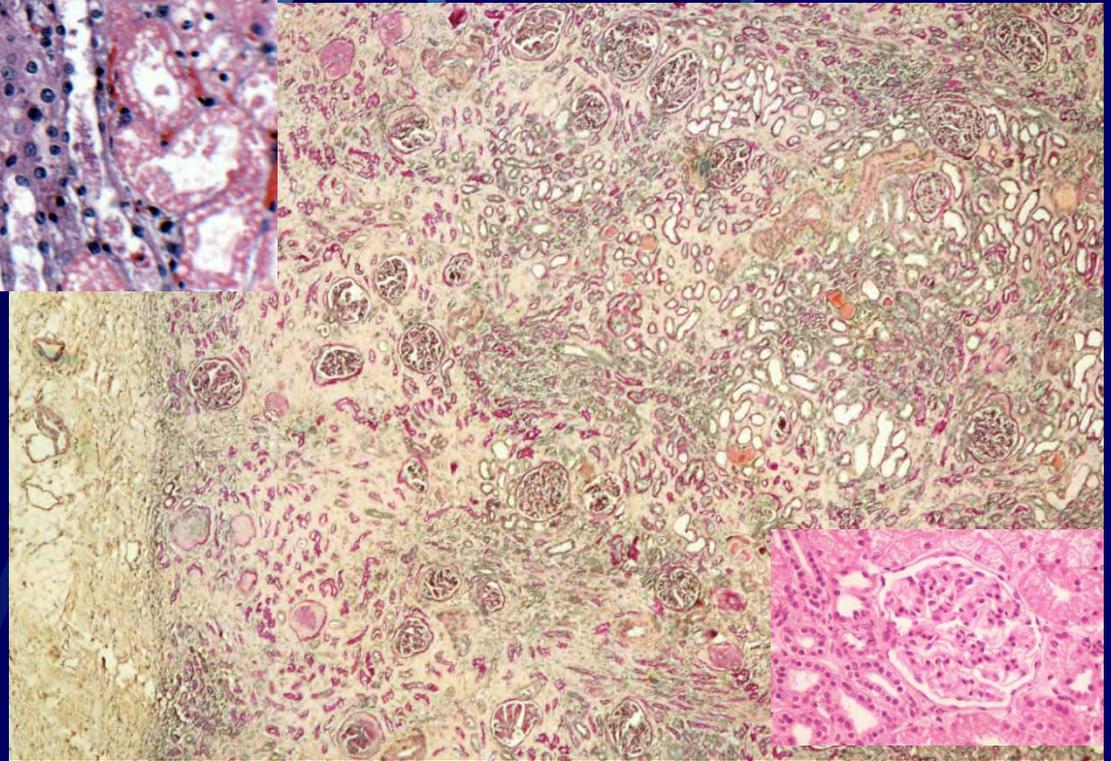
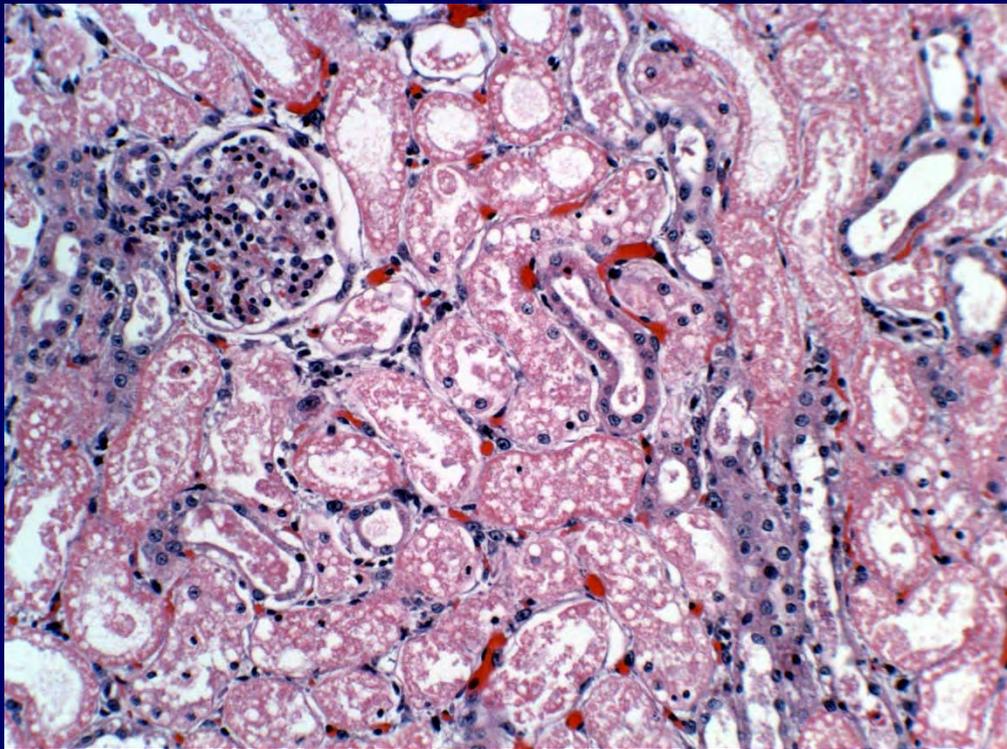
Misuse of Herbal Remedies: The Case of an Outbreak of Terminal Renal Failure in Belgium (Chinese Herbs Nephropathy)

JEAN-LOUIS VANHERWEGHEM, M.D., Ph.D.



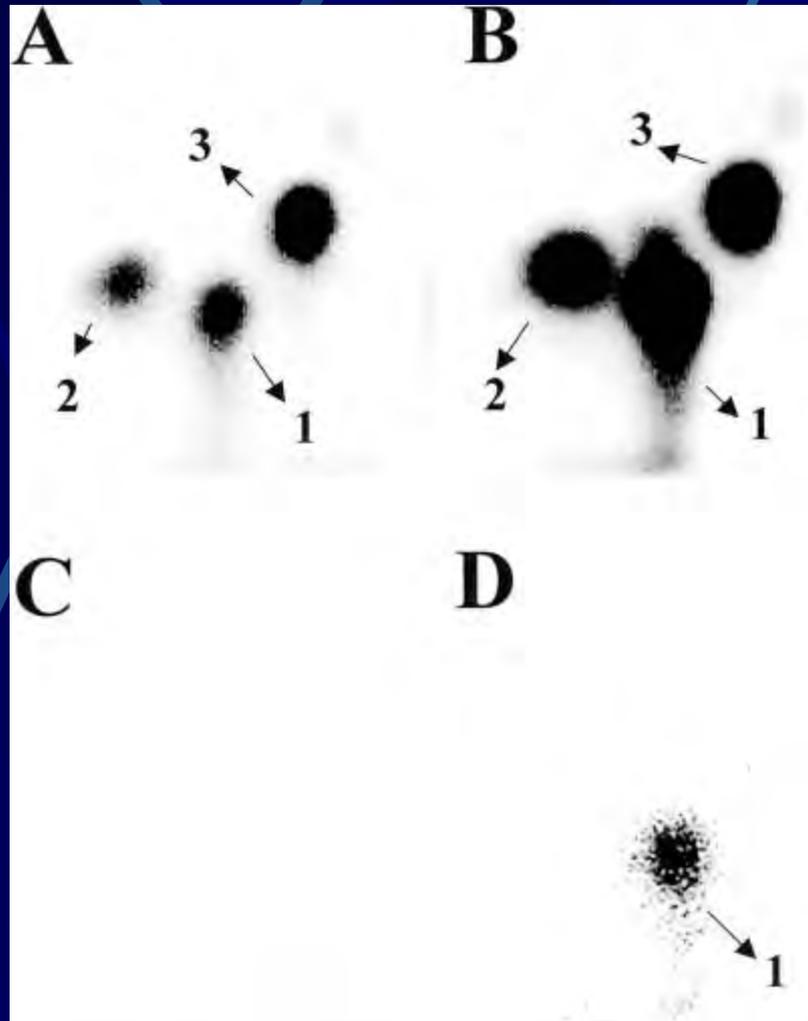
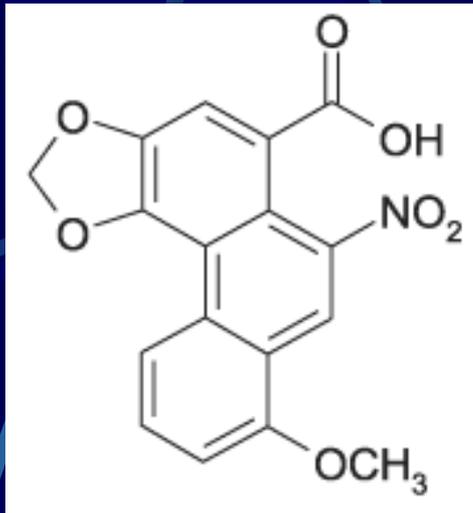
Aristolochia fanchi substituted for *Stephania tetrandra*
Chinese herb 'Mu Tong'

Weight loss herbal product





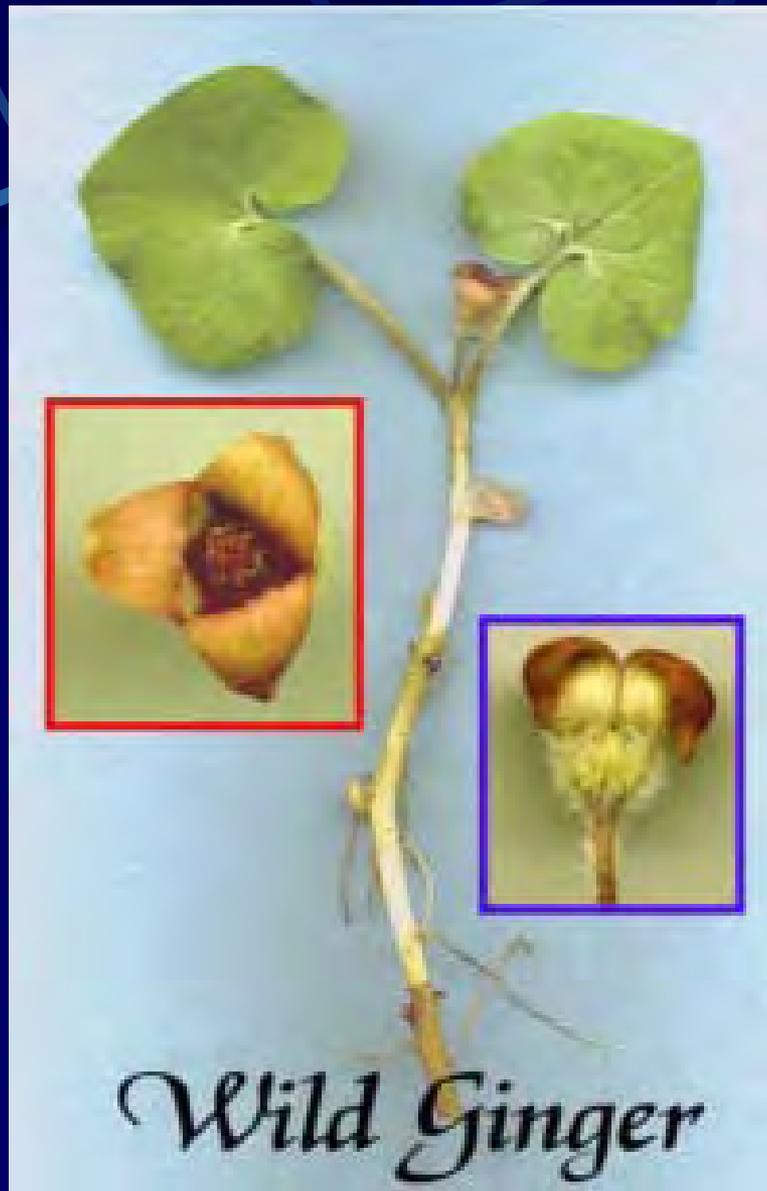
20X Incidence



Recommended it be listed as a
known human carcinogen



Dose?
Risk of exposure?



Larkspur (*Delphinium* spp.)

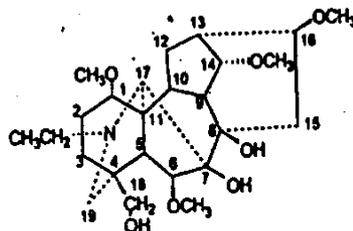




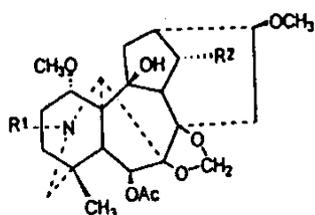
5-10% Death loss



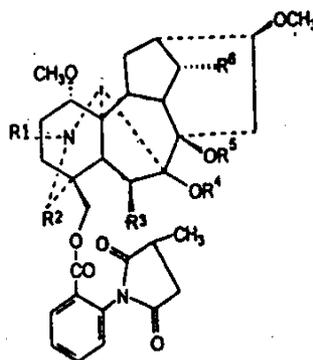
Larkspur Toxins



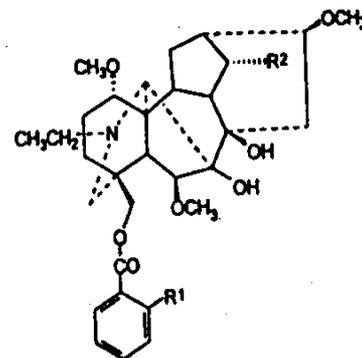
1. Lycoctonine (444 mg/kg)



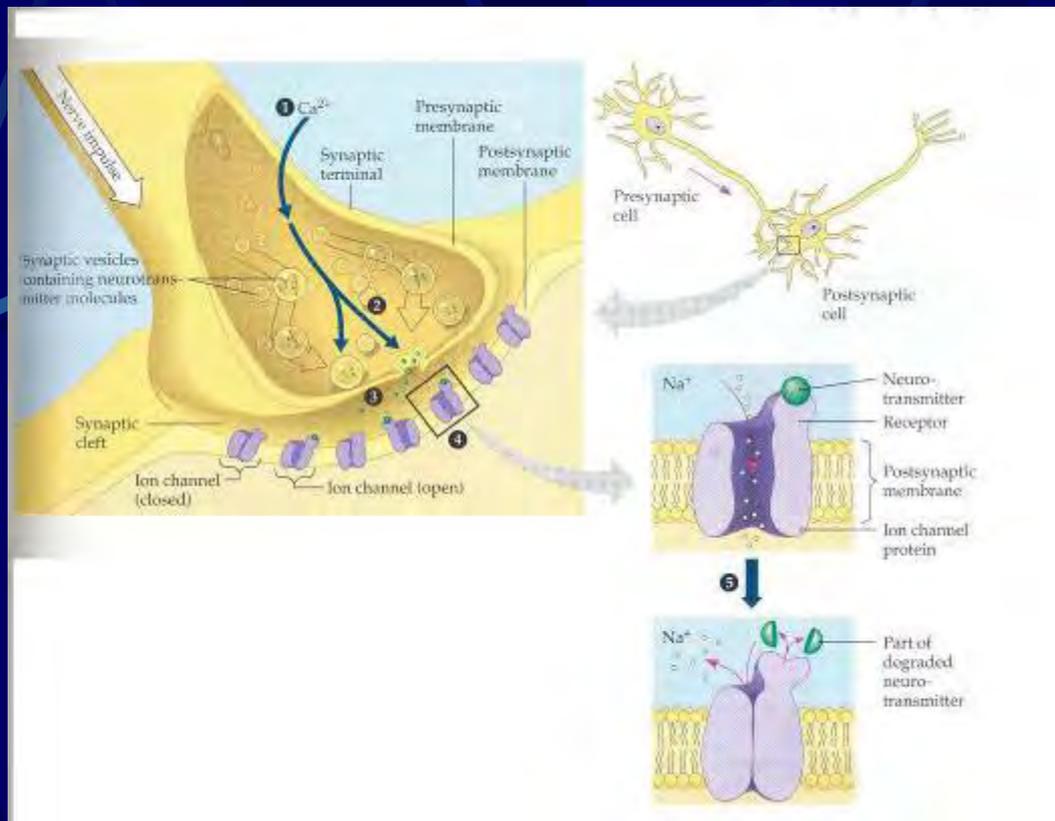
2. Deltaline (201 mg/kg)
 3. Dictyocarpine (283 mg/kg)
 4. N-Desethyl-deltaline (210 mg/kg)



5. Methilycaconitine (7.5 mg/kg)
 6. Nudicauline (2.7 mg/kg)
 7. 14-Desacetylnudicauline (4.0 mg/kg)
 8. Barbinine (= 57 mg/kg)
 9. Eliatine (9.2 mg/kg)
 10. N-Desethylmethilycaconitine (= 100 mg/kg)
 11. Zalliline (> 230 mg/kg)



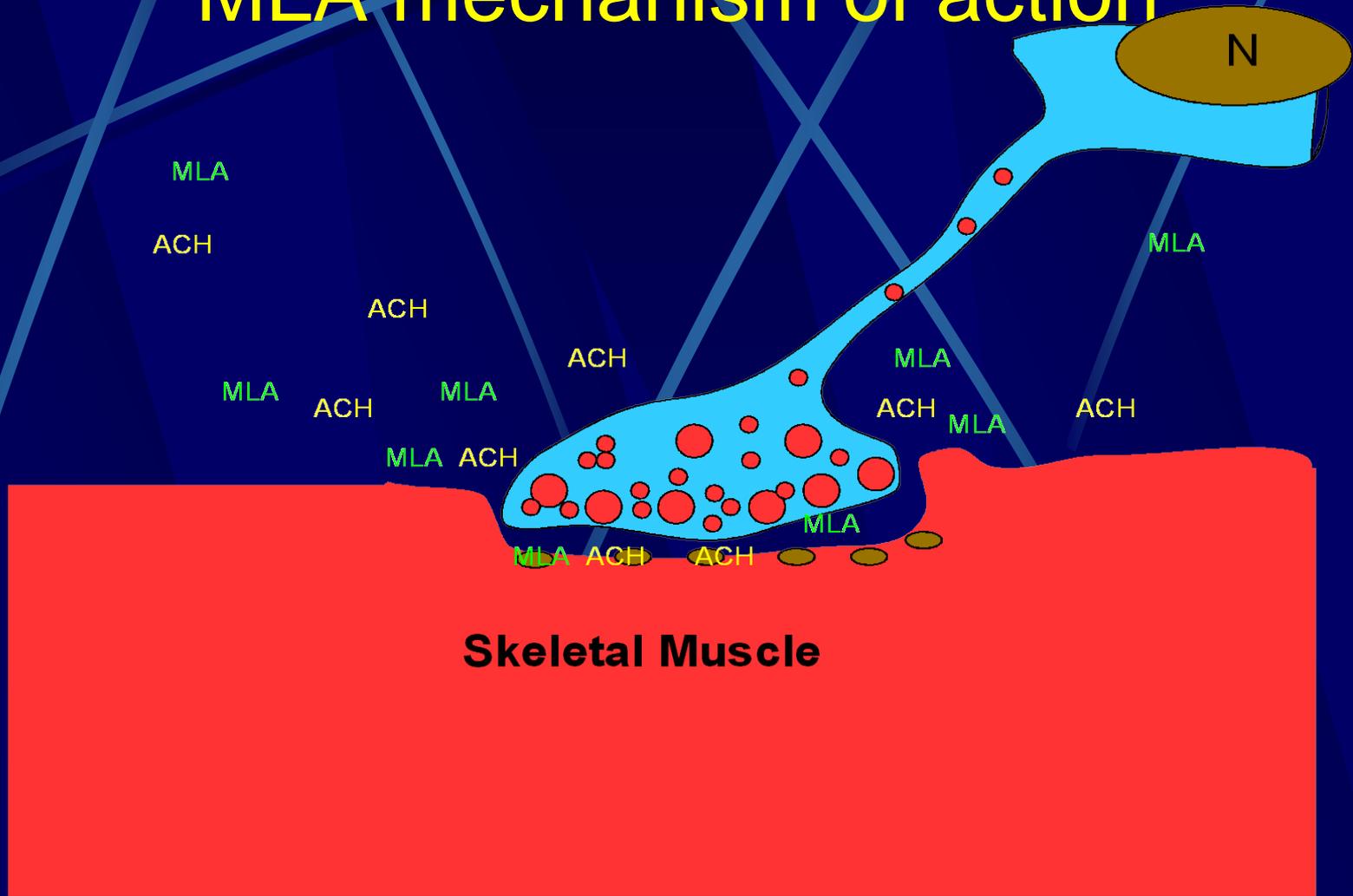
12. Anthranoylycoctonine (20.8 mg/kg)
 13. Delavaine (3.3 mg/kg)



Striated Muscle Toxins

- **Larkspur** (MLA block AchR)
- **Monkshood** (Aconitum inhibits Na channels)
- **Botulism** (cleaves synaptobrivin, syntaxin and SNAP-25 blocking cholinergic tx)
- **Tetnus** (tetanospasmin blocks glycine inhibition)
- **Cardioglycosides** (Inhibits Na/K ATPase enzyme)

MLA mechanism of action



Knowing it is poisonous is not enough.



Treatment

Select resistant animals

Medical applications

Definitions

Physiologic Response to Insult

- Molecular Response
 - No change
 - Molecular damage
 - Repairable or Permanent damage



Tissue Responses

- No Change
- Loss of function
- Inflammation
 - Rubor
 - Calor
 - Tumor
 - Dolor
 - Loss of Function
- Necrosis
- Hyperplasia
- Neoplasia



Animal Responses

- No change
- Sick- disease
- Attitude
- Appetite
- Weight
- Organ or system specific changes (Reproduction, Respiration, Cardiac Function, Hematologic Function, Immune Function, Urinary Function, Gastrointestinal Function, Musculoskeletal Function, Endocrine Function, Neurologic Function, etc)
- Death



Herd Responses

- Stocking Rate
- Economic, Emotional, and Physical Factors



Conclusions

- **There are about 10-20 tissue and animal specific responses and thousands of diseases**
- **Many diseases cause similar responses; few produce specific or pathognomonic lesions.**

Direct vs Indirect toxicity



Mechanisms of Action

- **Mechanical Injury:**
 - Various grasses- barley, foxtails etc- foreign body abscesses, stomatitis, and dermatitis
 - Cocklebur- gastric obstruction
 - Turkey mullein (*Eremocarpus setigerus*) phytobezoars and phytoconcretions
 - Oxalate crystals (Ca oxalate causing cellular damage like nephrosis)









Local irritant

- Contact dermatitis-
urushiols, *Urtica* spp.,
Stinging trees
- Stomatitis/Gastritis-
tannins, phenolic,
astringents, saponins
- Oxalates: Dumb cane
(*Dieffenbachia sequine*)
- Proteolytics- bromelain
and papain, lectins



Receptor mediated:

- AchR- Larkspur alkaloids
- Nicotinic AchR- Lupine, Tobacco, Conine
- Steroidal receptors- Veratrum
- ICA pine needles



Enzyme inhibition:

- Glycosidase inhibitors- swainsonine, calystegins, castanospermine
- Trypsin and amylase inhibitors- soybeans, peas, potatoes, barley, alfalfa
- Dicumarol- vitamin K antagonist
- Mitosis inhibition- S and prophase arrest of PA's, metaphase arrest of lupinosis
- Cholinesterase inhibitors- *Solanum* and green potatoes



Antinutritional:

- Indospecine (arginine analog) *Indospecine spicata*
- Mimosine
- Selenium toxicity-
- Anti-trypsin, anti-amylase
- Thiaminase



Direct cytotoxicity

- DNA/protein alkylation/adduct-denaturing
- Inhibit oxidative phosphorylation- Misonoxin, Cyanogenic glycosides, fluoroacetate
- Alter membrane permeability- digitalis
- Physical cellular damage- oxylates
- Alter anion or cation metabolism- Ca^{++}
- Ca chelation- phytic acid and oxalate
- Carcinogenic glycosides
- Cu and Zn storage
- Mg metabolism 3-methy-indole
- Cholestasis- Lantana, saponins
- All other tissue specific direct toxicity



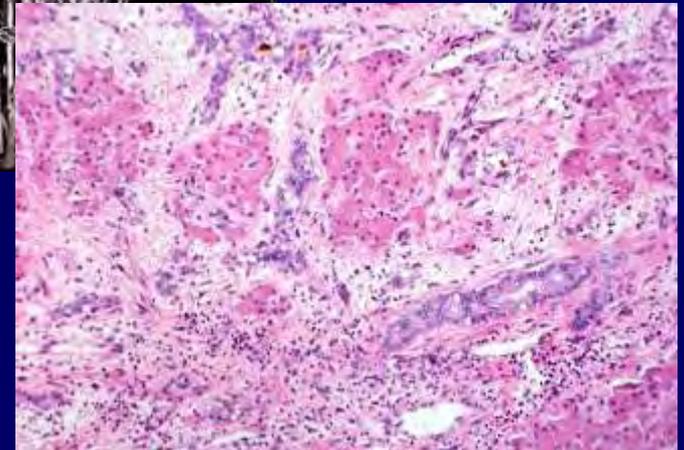
Specific Tissue Toxicity

- Neurotoxic Plants
 - 1. Locoweed
 - 2. Yellow star thistle and knapweed
 - 3. Larkspur
 - 4. Hemlocks
 - 5. Death camas
 - 6. Bracken fern
 - 7. Jimsonweed



Hepatotoxic Plants

- **Pyrrolizidine alkaloid containing plants**
- **Tetradymia and hepatogenic photosensitization vs primary photosensitization caused by St. Johns wort or spring parsley**
- **Cocklebur**
- **Alsike clover**



Nephrotoxic Plants

- Oxalate containing plants- Halogeton and greasewood
- Oak and other plants causing nephrosis



Plants with Reproductive Toxins

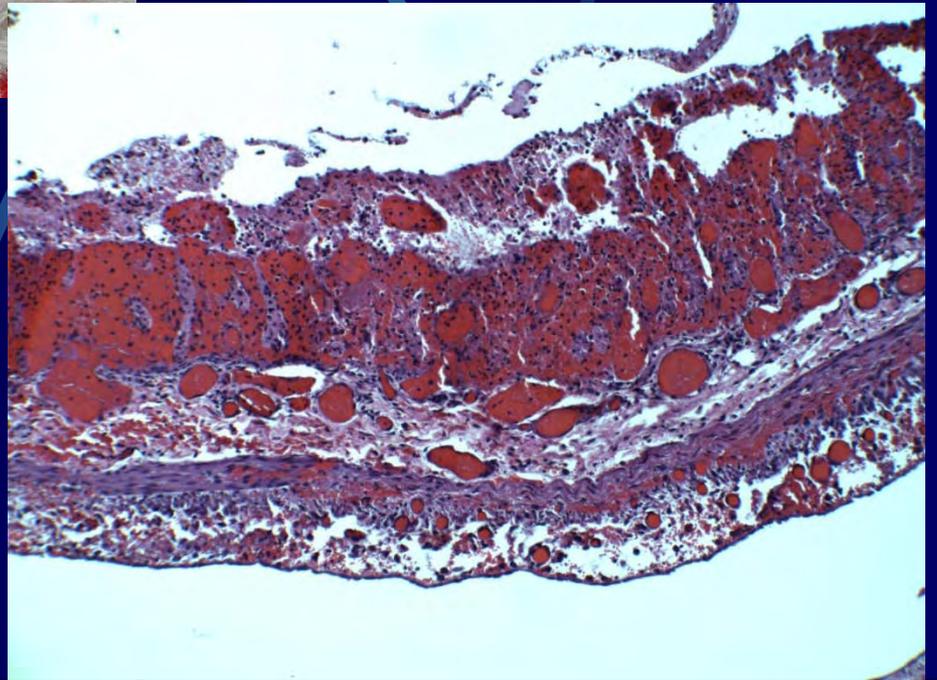
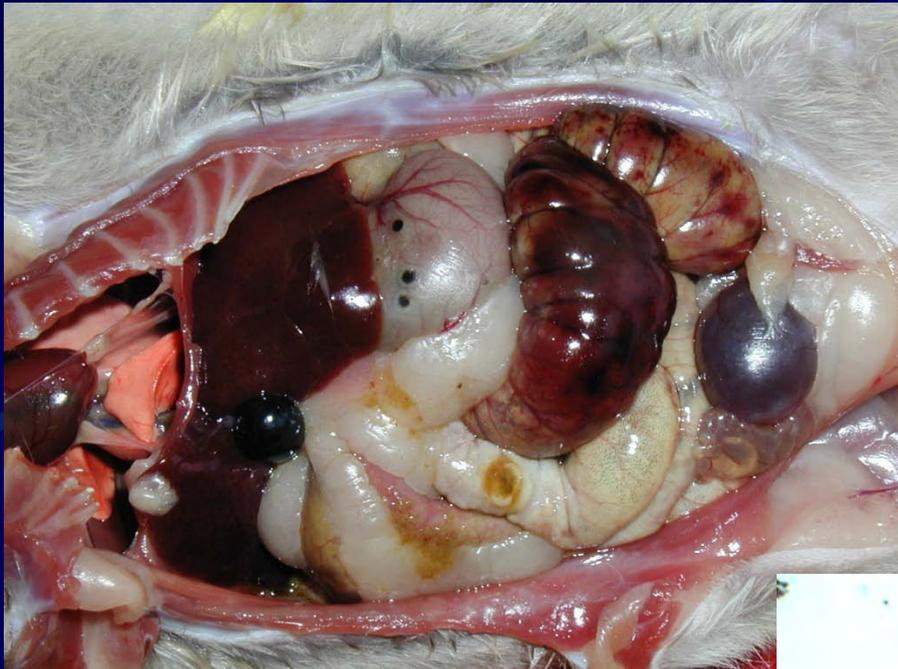
- Pinus ponderosa and broomweed
- Teratogens such as Veratrum, Lupine etc



Plants that have Gastrointestinal Toxins

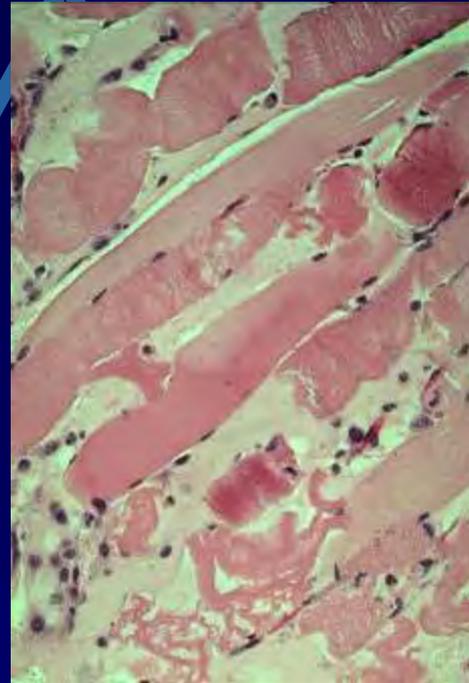
- Pineapple (bromelain), papaya (papain) proteolytic enzymes
- Enzyme inhibitors (trypsin and amylase inhibitors)
- *Dieffenbachia sequine*-dumb cane, rhubarb, halogeton, greasewood,
- oak, phenolics, tannins
- Grasses/Hay (Nitrate/Nitrite, Saponins)
- Mustards (Brassica, Raphanus, Descurania)
- Castor Bean
- Sneezeweed (Helenium)
- Nightshades





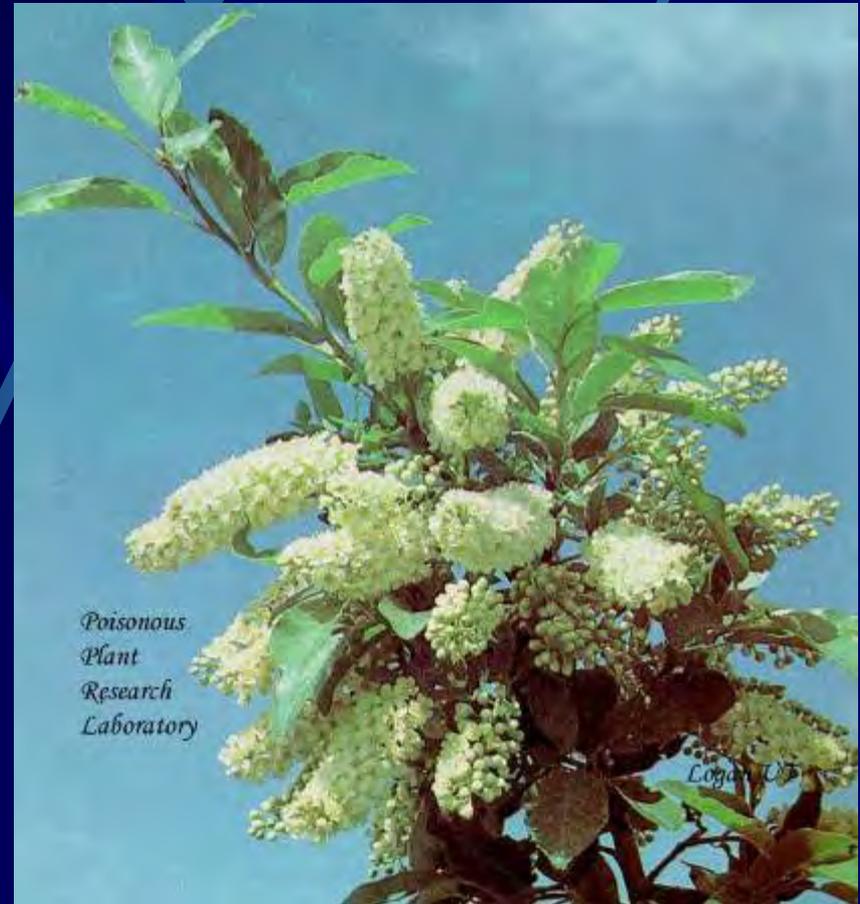
Plants that are Cardiotoxic or Myotoxic

- White snakeroot and rayless golden rod
- Oleander and milkweeds
- Thermopsis



Sudden Death without many lesions:

- Nitrates (sorghum, various grasses, oats, hay, corn, Kochia, pigweed, Russian thistle, nightshades)
- Cyanide (sorghum, larel cherry, arrow grass, chokecherry)



Reading Assignment:
**Cheeke “Natural Toxicants in Feeds,
Forages, and Poisonous Plants”
Part 1, pages 3-51**