Pesticides
January 2, 2004

Part 2
Pyrethrins and Pyrethroids

I. Introduction

A. Description
   • Pyrethrin based products are the most common household insecticides on the market today.
   • Terminology
     - “Pyrethrum” refers to the dried and powdered flower heads of Chrysanthemum cineriaefolium
     - Pyrethrum extract is the product of solvent extraction of the flower heads
     - “Pyrethrins” refers to the active components of pyrethrum extract
     - “Pyrethroid” refers to synthesized pyrethrins
     - Piperonyl butoxide is a synergist which limits the metabolism of pyrethrins in insects increasing effectiveness

B. Substances
   General:
   • Brand names of household products include Black Flag and Raid insecticides.
   • These compounds are also found in various flea treatments for pets (spot treatments e.g. Sargent’s Pretect for Dogs)
   • Many pyrethrin based products are formulated in petroleum distillate bases
   • Permethrin, a synthetic pyrethroid, is available as a 1% pediculocide solution

I. Pyrethrins
   - Chemically composed of esters of pyrethric acid and chrysanthemic acid and 3 keto alcohols
   - the three esters of chrysanthemic acid are pyrethrin I, cinerolone I and jasmolin I. The three esters of pyrethric acid are pyrethrin II, cinerolone II and jasmolin II.
   - often formulated with piperonyl butoxide
   - very unstable in light
   - not as commonly used compared to pyrethroids
   - Half life: a few days
   - Minimal skin absorption seen in studies
2. Pyrethroids
   - synthesized pyrethrins
   - 2 subgroups
     a. Non Photostable: e.g. tetramethrin, resmethrin, allethrin, butethrin, dimethrin, bioresmethrin, prothrin, proparthrin
     b. Photostable (had an alpha-cyano group added to them to stabilize) e.g. lambdocyhalothrin, cyfluthrin, cypermethrin, deltamethrin, fenfluthrin, cyphenothrin
        Note: permethrin is a pyrethroid in this group which does not carry a alpha-cyano group
   - Half life: 2-4 weeks for light stable products
   - Rapidly broken down in soil with half-life of about 4 weeks
   - Less toxic to mammals, in general, when compared to pyrethrins
   - Minimal skin absorption seen in studies

II. Pharmacology
   - In general, pyrethoids/pyrethrins are poorly absorbed dermally. Less than 2% of permethrin has been shown to be absorbed in human studies.
   - In mammals, permethrin is rapidly detoxified via liver enzymes. Plasma levels following application of topical 5% cream were below detectable limits in human studies.
   - Pyrethrins are metabolized and excreted faster than they can be absorbed making tissue storage unlikely

III. Mechanism of Toxicity
   - Pyrethroids and pyrethrins interact with sodium channels in peripheral and central nerve cells to prolong the increase in permeability during the action potential excitatory phase of impulse transmission resulting in failure of the cell to depolarize.
   - In humans, rapid cleavage of the acid/alcohol ester along with oxidation to nontoxic metabolites limits toxicity.
   - Piperonyl butoxide is a hepatic enzyme inducer in mammals but has a low order of toxicity in humans.

IV. Range of Toxicity
   - Pyrethrins are one of the least toxic group of insecticides currently marketed.
   - Oral LD50s in rats are several hundred or thousand mg/kg making mammalian toxicity low
   - Minimum lethal dose in humans has not been established
   - Seizures were reported in an adult who ingested 30 ml of a 2.5% deltamethrin based product
   - There have been reports of hypersensitivity reactions associated with use of these chemicals. These can occur with minimal exposure.
   - Systemic effects have been reported with prolonged heavy dermal exposure.
V. Adverse Effects

A. Dermal
   1. Pyrethrum
      • Chief effect is dermatitis
      • Pyrethrins are not known to cause skin sensitization
   2. Pyrethroids
      • Not known to cause hypersensitivities, not considered irritants.
        However, certain formulations upon testing have been shown to cause
        these problems after repeated exposure.
      • Exposure can result in paraesthesias
        - Symptoms: numbness, tingling, itching, warmth
        - Time to onset: may be up to 4-6 hours after exposure
        - Duration: up to 24 hours
        - Symptoms can be exacerbated by warm water and sweating.

B. HEENT
   • Irritation and redness may occur.

C. GI
   • Nausea, vomiting and abdominal cramping may be seen.

D. Neurological
   • Headache, weakness, lethargy, dizziness,
   • Fasciculations, coma and seizures may occur in severe toxicity.

E. Respiratory
   • Rhinitis, sneezing, cough, shortness of breath, wheezing and chest pain
     have been reported.
   • Anaphylactoid reactions, asthma-like in nature, have been documented
     in sensitive individuals.
     - One study indicated that 50% of individuals sensitive to ragweed
       exhibited cross-sensitivity to pyrethrum

VI. Decontamination

A. Ingestion
   • Syrup of ipecac is contraindicated due to expected symptoms of
     vomiting upon ingestion and potential rapid onset of seizures and
     hypotension. Products carried in petroleum distillates create an
     aspiration risk.
   • Gastric lavage may be utilized in large ingestions. A cuffed ET tube
     should be used due aspiration risk secondary to emesis.
   • Activated charcoal may be used and is probably the preferred method
     of treatment although limited data is available on its efficacy.
B. Dermal
   • Wash exposed areas well with mild soap and water to prevent further exposure.

C. Inhalation
   • Move patient to fresh air.
   • Monitor for respiratory distress.
   • If any signs of respiratory distress, the patient should be immediately transferred to a health care facility.

D. Ocular
   • Remove contacts if present
   • Flush eyes with room temperature water for 15 minutes
   • Allow eye to heal over next hour.
   • If symptoms persist beyond an hour or if any visual abnormalities ensue, refer the patient to a physician.

VII. Treatment

A. Antidotes
   • There is no antidote available

B. Treatment of specific symptoms
   1. Anaphylactoid reactions
      a. Epinephrine
         • Adult- 0.3-0.5 ml of 1:1000 solution
         • Children: 0.01 ml/kg of 1:1000 solution
         • Can repeat dosing q 20-30-minutes
      b. Diphenhydramine (for mild cases where urticaria presents)
         • Adult: 50 mg IV then 25-50 q 4-6 hours
         • Children: 2 mg/kg IV
   2. Seizures
      a. Diazepam
         • Adults: 5-10 mg every 5 minutes as needed
         • Children: 0.2-0.5mg/kg every 5 minutes as needed.
      b. Lorazepam
         • Adults: 2-4mg every 5 minutes as needed may be as an alternative to diazepam.
         • Children: 0.1 mg/kg IV, may repeat second dose of 0.05 mg/kg in 10-15 minutes
      c. Phenobarbital
         • Adult: 300-800 mg IV initially followed by120-240mg/dose at 20 minute intervals until seizures controlled or a total of 1-2 grams
         • Children: 10-20 mg/kg, may give additional doses of 5 mg/kg/dose q 15-30 minutes until seizures controlled or a total of 40 mg/kg.
   3. Hypotension
- A fluid challenge of 0.9% Normal saline or D5-1/2NS should be tried first.
- Dopamine: start at 2ug/kg/min and titrated as needed.
- Norepinephrine: start at 0.1-0.2 mcg/kg/min titrated as needed.

4. Parasthesias
- Vitamin E: Rub into affected area as needed for relief.

VIII. Labs and Monitoring

In cases of severe anaphylactoid reactions or symptomatic patients monitor the following:
- Electrolytes
- EKG. vitals
- Urine myoglobin and CK if seizures present

References