

Cholinesterase Basics

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Goal: To provide information and resources to growers and managers.

- **Schedule Growers/Manager Breakout**

1:30- 2:00 Cholinesterase basics Patricia Boiko

2:00- 2:30 Cholinesterase monitoring rules
John Furman

2:30- 3:00 Cholinesterase testing and informed
consent/dissent John Furman

3:00- 3:15 Break- Handlers interact with growers and health
care providers

3:15- 3:35 Practicalities of the rule Dr. Todd Denny

3:35- 4:00 Grower experiences a monitoring programs

The Rule

- Employers must provide cholinesterase monitoring
 - Baseline plasma and rbc cholinesterase
 - Follow-up plasma and rbc level
 - To OP and Carbamate pesticide handlers
 - Who handle for 50 hours or more in a thirty day period for 2004, 30 hours in 2005

Medical Providers Role

- According to WAC 296-307-148 Licensed Health Care Providers must:
 - Discuss the risks and benefits of handler participation in cholinesterase monitoring
 - Obtain a signed declination if the handler chooses not to participate
 - Provide and interpret baseline and periodic testing of blood cholinesterase levels
 - Provide other written occupational health recommendations as indicated.

Cholinesterase Basics: >20% Depression From Baseline

□ Understand

□ Basic science of cholinesterase and cholinesterase inhibiting pesticides

□ Everything about monitoring

Testing methods

Responses to a positive test: Cholinesterase depression
false positives

□ Quality assurance evaluation

The Rule

- Listen for
 - Which pesticides
 - OP, carbamates
 - Which workers
 - handlers
 - What is the responsibility of growers/managers

Handler Consent

- Rule says the handler must sign a written declination statement of which a copy goes to the grower
- WHAT DOES THIS MEAN FOR YOU??

Reporting Requirements and Poisoning

☐ Pesticide-related illness

- **Reportable condition to the Washington State Department of Health (WAC 246-10)**
- **All types pesticide-related cases must be reported**
 - **Including skin, eye injuries, systemic poisonings, suicides, homicides,**
 - **Home and occupational exposures.**

Why is ChE Testing Useful?

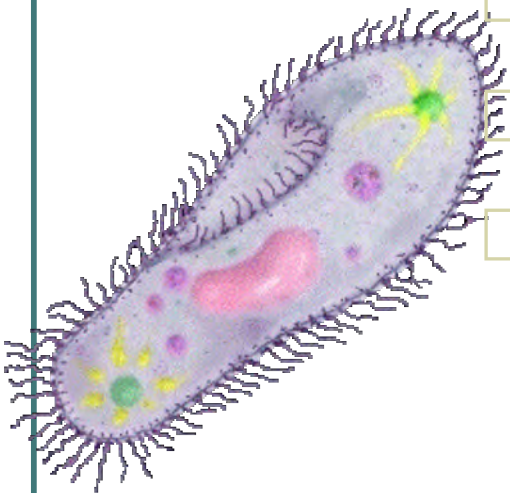
- ChE reflects the substance on its target
- Integrates exposure over time
- The test is available
- Blood tests are available
- BUT!
 - Baseline is needed
 - Good lab methods needed
 - Interpretation and timing important
 - Sample handling important

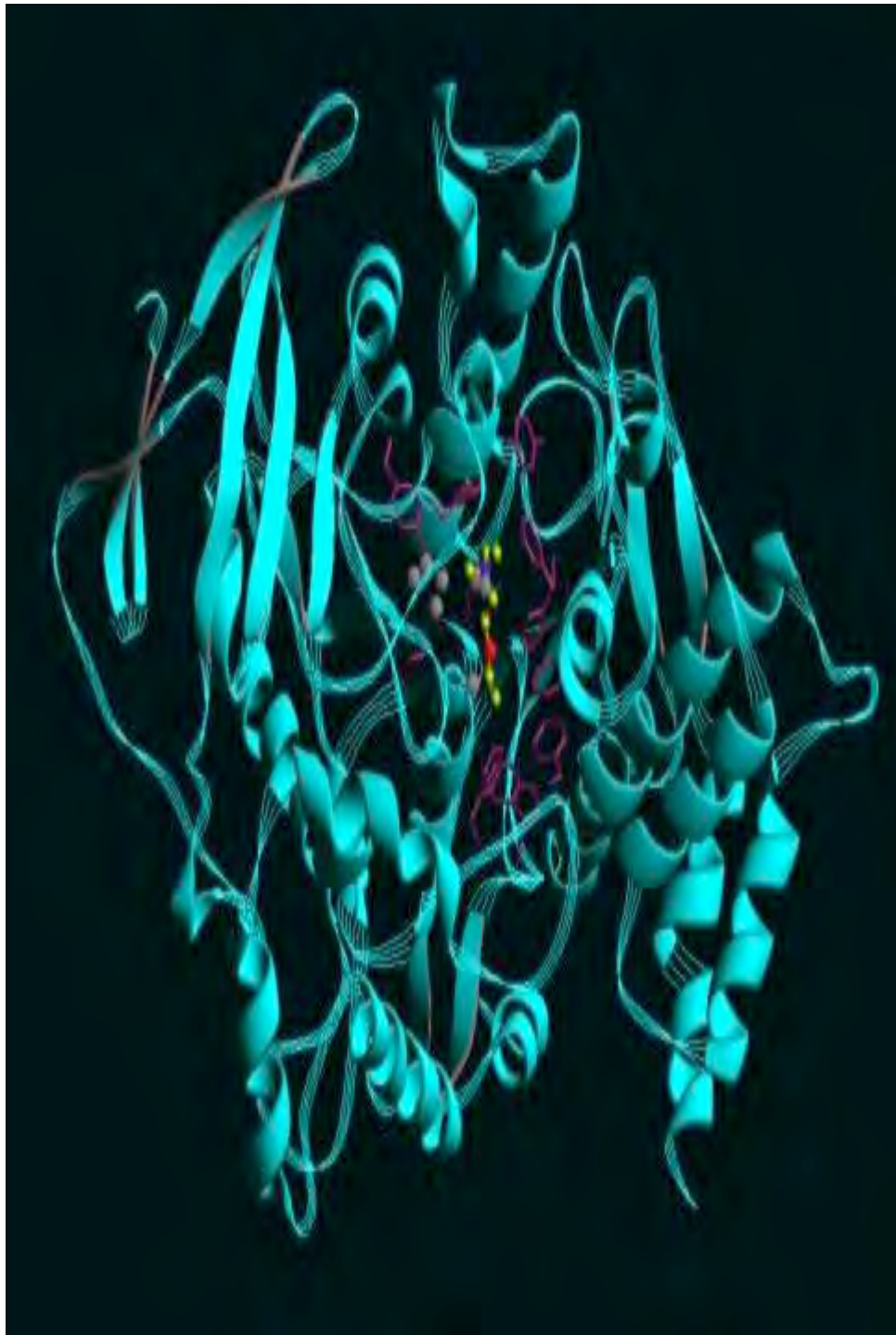
Objective

To understand the basic biology of cholinesterase and cholinesterase inhibiting pesticides.

Biology of Cholinesterase

- Present from paramecia to sapiens
- Very Fast enzyme
- Ubiquitous in the human body
- Critical for many nervous system functions





Cholinesterase Enzyme

Produced in tissues and blood

Hydrolyzes acetylcholine: A key neurotransmitter

Present in the autonomic, central and peripheral nervous systems

Two *Different Kinds of ChE enzymes*

Some behaviors in common

- **Plasma Cholinesterase**
 - Butyrylcholinesterase, pseudocholinesterase, PChE, or just cholinesterase and ChE
- **RBC Cholinesterase**
 - True cholinesterase, acetylcholinesterase, or AChE

Plasma ChE

- Floats freely in plasma
- Made by liver
- Rapid recovery from depression
- Rapid replacement by new synthesis
- Liver disease may affect levels
- Sensitive to most ChE inhibitor pesticide exposures

Red Blood Cell Cholinesterase

- Bound to red blood cells
- Made at the same time as the Rbc's
- Recovery from depression 0.8%/day
- Slower to depress, slower to recover
- Low RBC count may cause lower levels
- Identical to neuronal ChE

► The Autonomic Nervous System

What Cholinesterase Does: Physiologically

Autonomic Nervous System

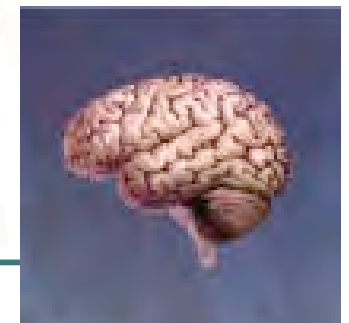
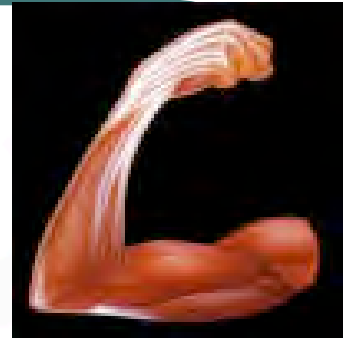
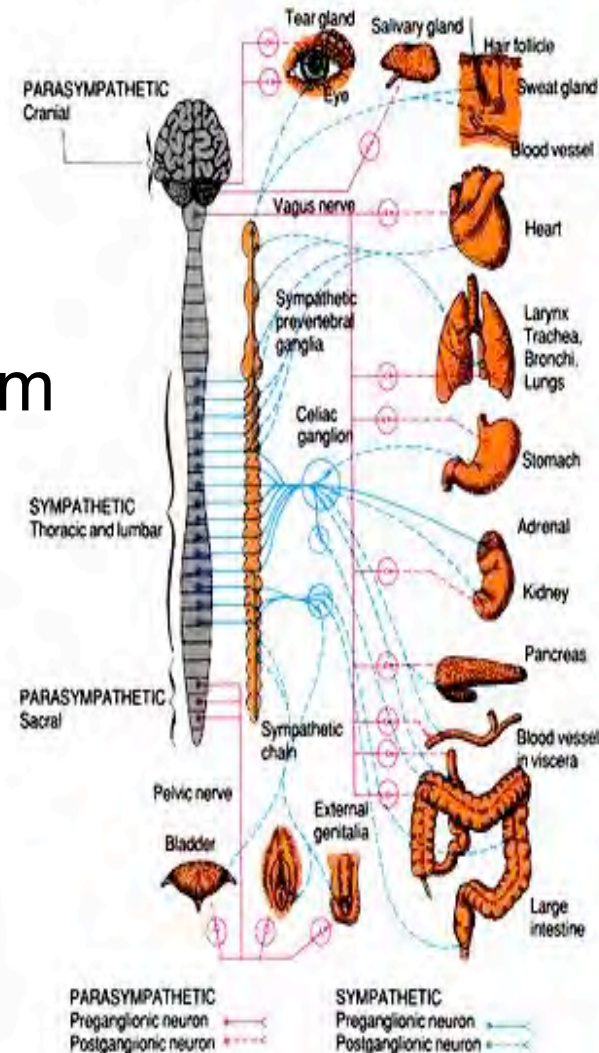
- Parasympathetic
- Presynaptic Sympathetic

PNS

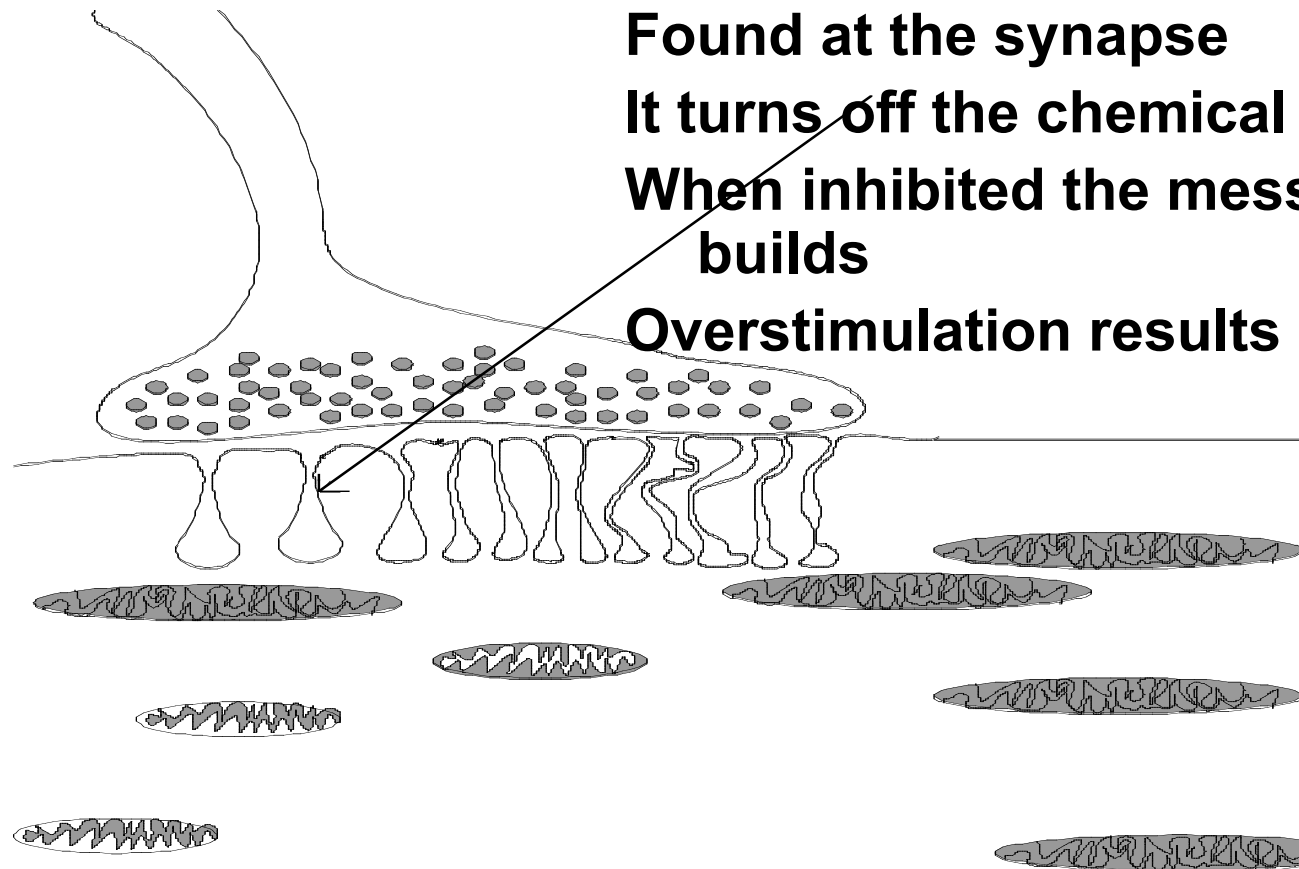
- Skeletal muscle

CNS

- Memory & others



Cholinesterase



Found at the synapse

It turns off the chemical messenger

**When inhibited the messenger
builds**

Overstimulation results

Pesticides That Inhibit Cholinesterase

□ Organophosphates

- Inhibit irreversibly
- “aging of complex”
- ChE must be replaced by the body

□ Carbamates

- Inhibit temporarily
- No “aging”
- Reversal is rapid and level related
- ChE reactivates and is ready to go

Toxicity of ChE Inhibitors

Mild cases:

tiredness, weakness, dizziness, nausea and blurred vision

Moderate cases:

headache, sweating, tearing, drooling, vomiting, tunnel vision, and twitching

Severe cases:

abdominal cramps, urinating, diarrhea, muscular tremors, staggering gait, pinpoint pupils, hypotension (abnormally low blood pressure), slow heartbeat, breathing difficulty, and possibly death

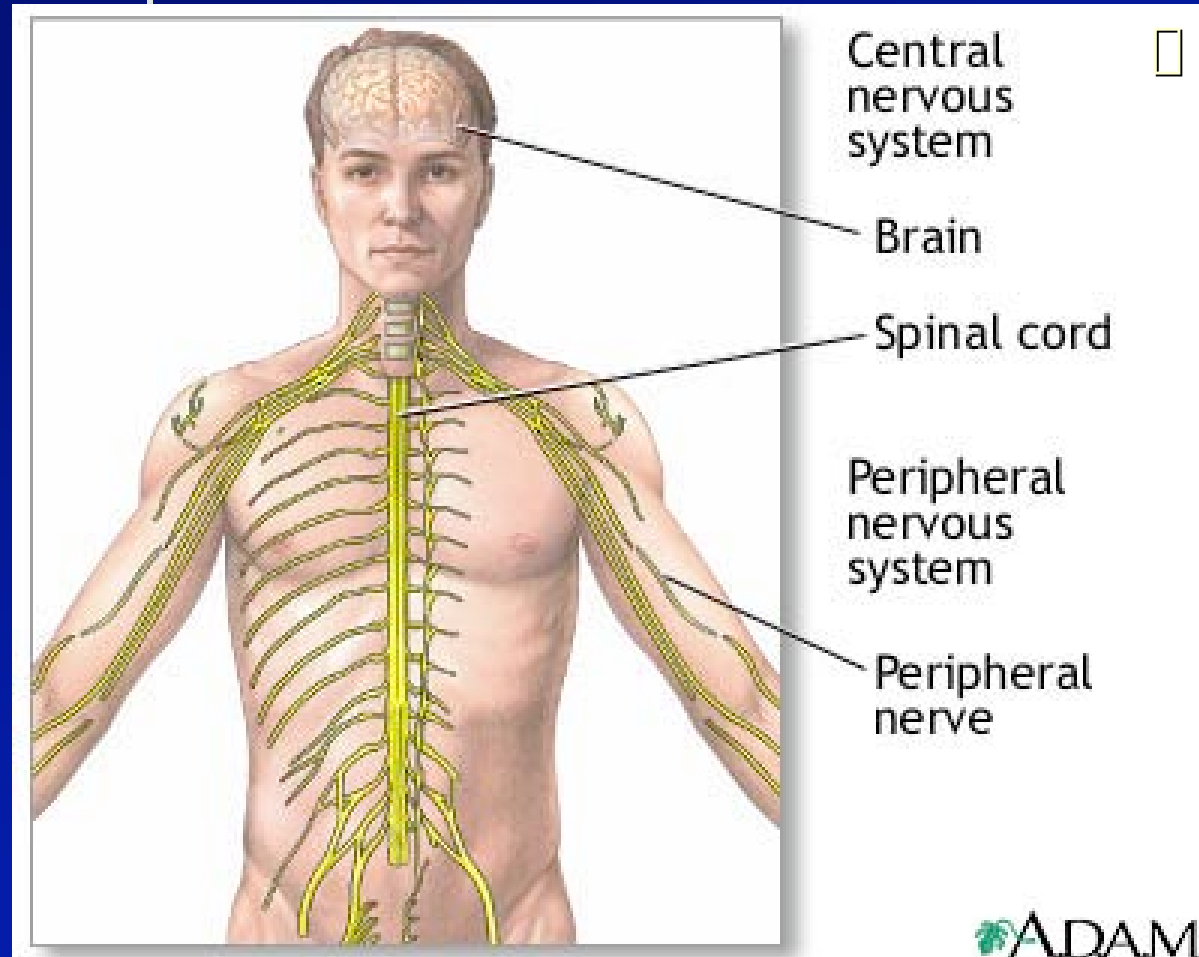
Exttoxnet <http://ace.ace.orst.edu/info/exttoxnet/>

Cholinesterase Basics

Insecticides

- Most insecticides affect the nervous system of animals (insects and humans)
- DOSE is the primary factor as to why insects are most susceptible, but with increased doses (exposure) humans are susceptible

Nervous System Review



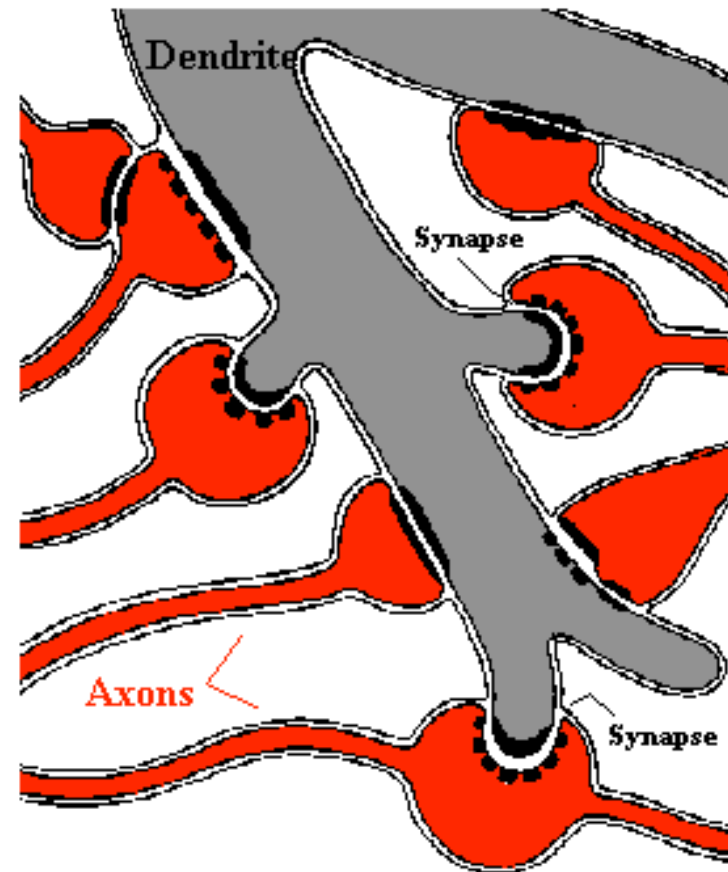
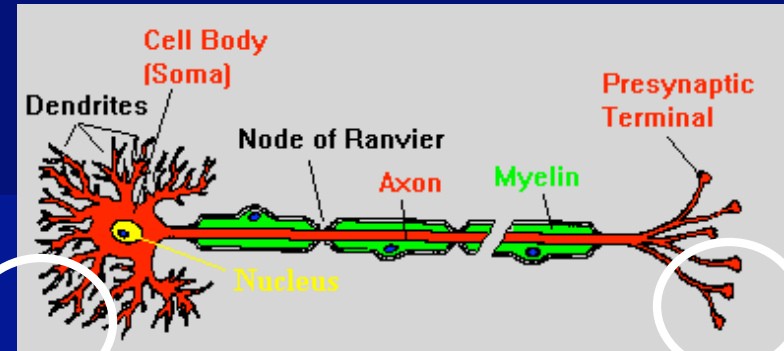
Peripheral Nervous System (input/output)

- Nerve to nerve transmission
- Nerve to muscle transmission
- Nerve to organ transmission

□ Nerve Cells (neurons)

- Cell body
- Dendrite - receives the message
- Axon - sends the message
- Synapse - chemical transmitter released, cleansing enzyme shuts off transmission

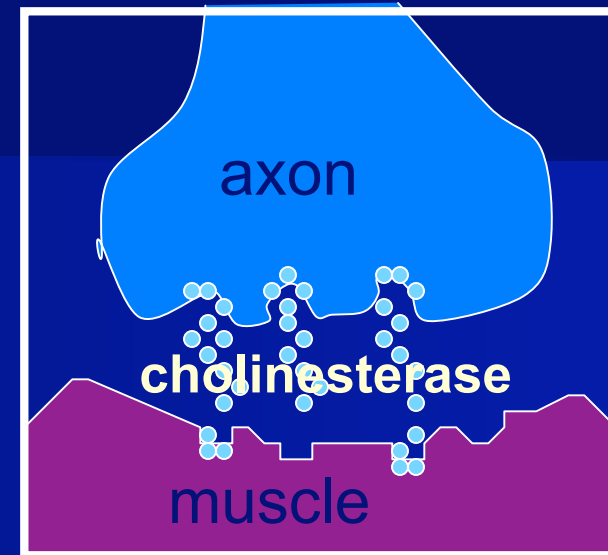
□ Sensory stimulation evokes a motor



□ Neural Transmission

- Axon to dendrite
- Axon to muscle
- Synapse

- chemical transmitter = acetylcholine
- cleansing enzyme = cholinesterase



Cholinesterase stops the continual transmission. Nerves then are back to normal resting state, awaiting next stimulation

Monitoring Cholinesterase

- Baseline in off season (30-day exposure free)
- Red blood cell
 - drop 30% or more from baseline
- Plasma
 - drop 40% or more from baseline
- You can return to handling when levels return to within 20% of baseline

Exposure to Organophosphate and Carbamate Insecticides

- These two classes of insecticides actually TRAP the cholinesterase (cholinesterase inhibition)
- Once inhibited, there is NO free cholinesterase enzyme to cleanse the synapse
- Thus, acetylcholine (transmitter) continually stimulates the nerves, muscles, glands
- Muscles and glands remain overexcited (this is poisoning).
- Poisoning can be mild, moderate, severe, or deadly.

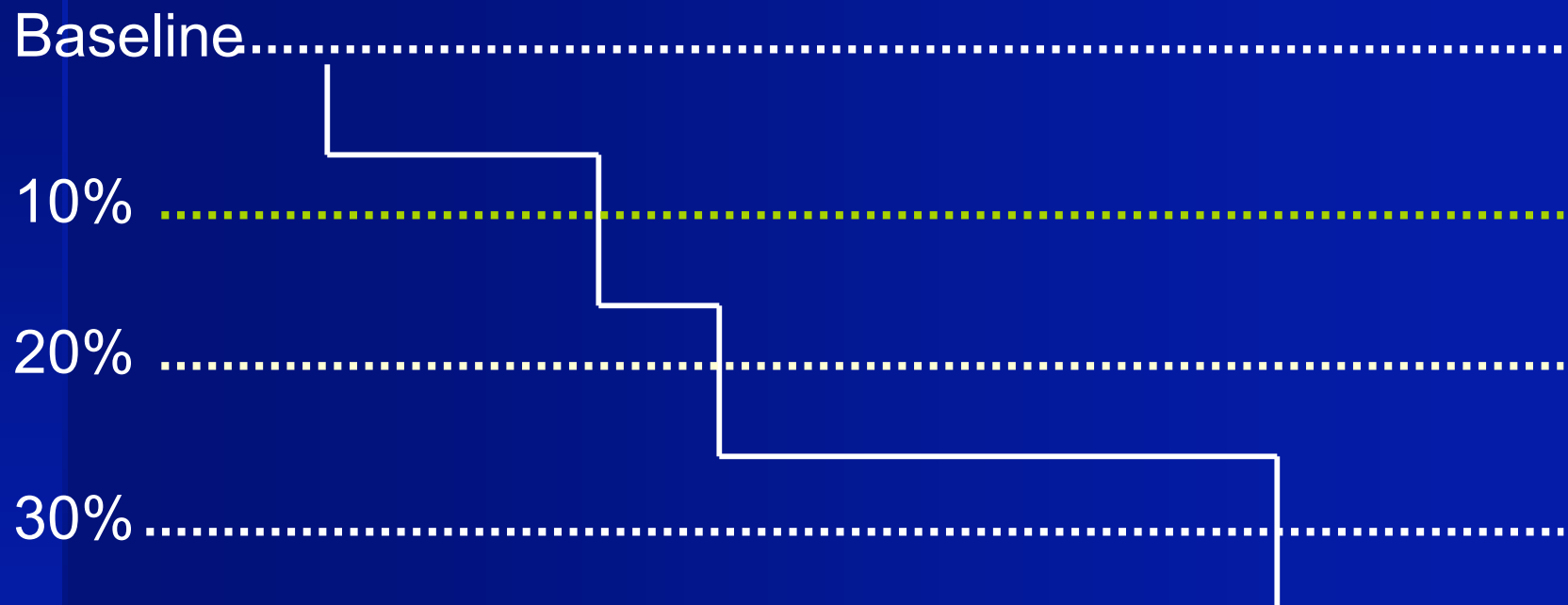
Symptoms from Over-Stimulation (insecticide poisoning)

- Too much neural transmitter
- Not enough cholinesterase (50% decreased)
- Headache, dizzy, nauseous, diarrhea
- Muscle aches, clumsy, cramps, out of breath
- Pin point pupils, blurred vision
- Convulsions, coma
- Death

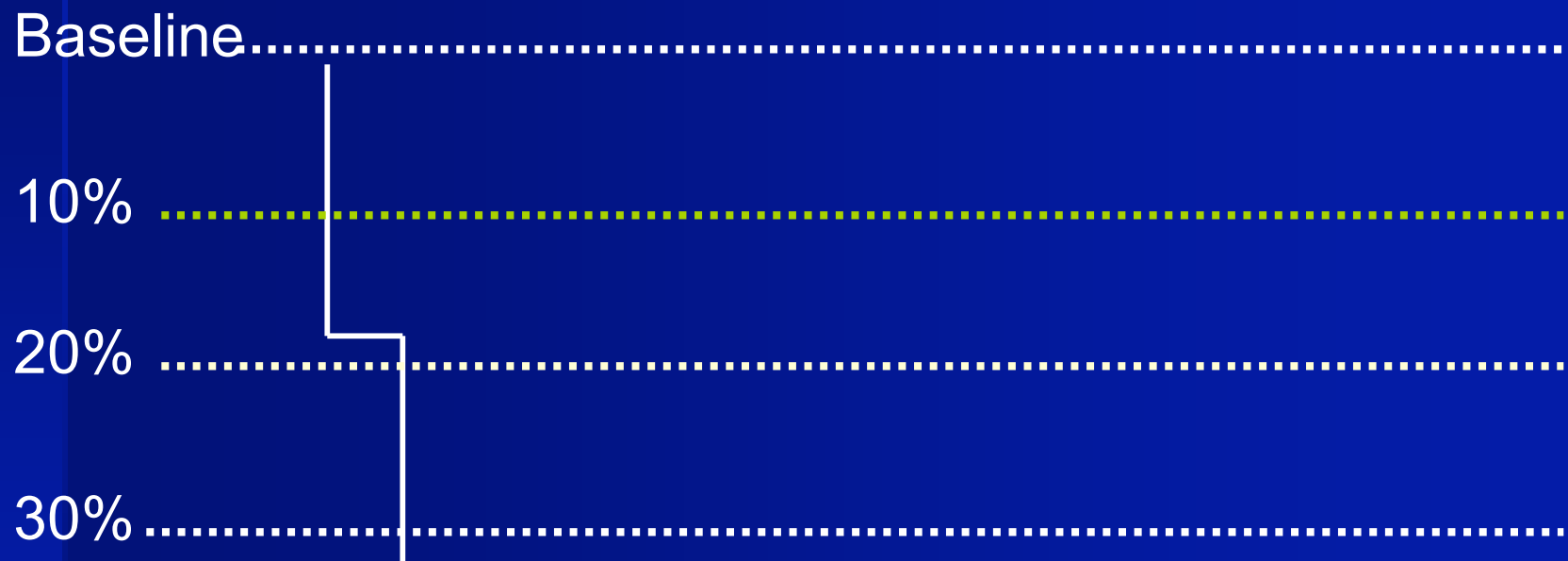
Function of Cholinesterase

- An enzyme that is critical for “cleaning out” the synapse and stopping the ongoing transmission of neural messages to muscles and glands.
- Cholinesterase is found in the blood system and nervous system (“equally”), so measuring levels in the blood is a great indicator of the bodies’ supply of cholinesterase in nerves.

Examples of Exposure



Examples of Exposure



Examples of Exposure



Body Builds Cholinesterase

- Your body continually makes more cholinesterase enzyme (Liver and bone marrow)
- Keep exposure low so that you do not deplete your body's reserves of cholinesterase to a harmful level, especially organophosphates
- The body does not recognize the depletion, and only builds so much a day (1% per day for red blood cells)
- It may take a month or two for your body to build back to a safe level

HAZARD

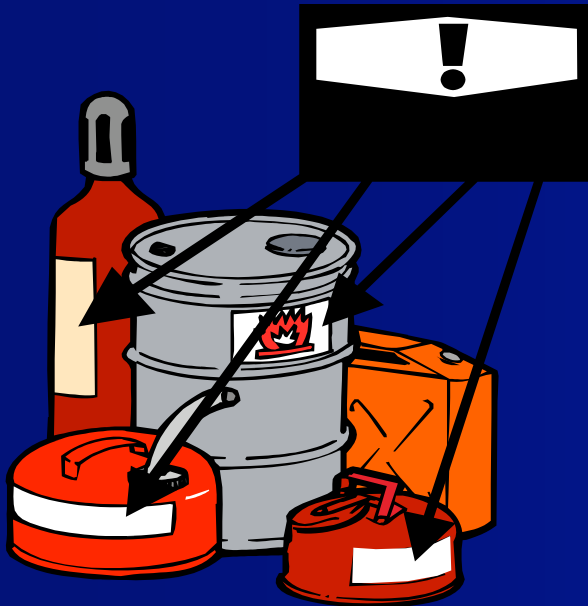
- Amount of exposure needed to cause harm
- Levels are predetermined
- Risk of pesticide use and symptoms vary
 - Frequency of exposure
 - Concentration of the pesticide
- Toxicity can be cumulative
 - Rate of depletion, rate of generation

Factors that may produce a low baseline

- Genetic Trait
- Liver disease
- Certain medications



Preventive measures



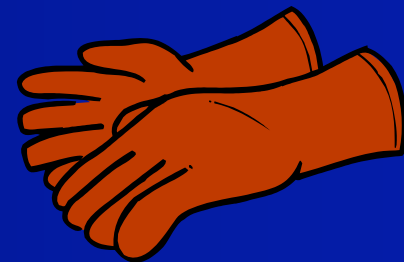
- Become familiar with pesticides used
- Save labels!
- Wear appropriate equipment

- Clothing should provide an effective barrier to pesticide sprays and dusts!
- Respirators should be chemical specific



Hand protection

- Use unlined rubber or plastic gloves
- Never wear leather!
- Not too tight
- Not too big
- Wear on the outside of the sleeve
- Wash gloves after use
- Dispose of old gloves



Foot protection

- ❑ Wear Neoprene or nitrile boots
- ❑ Do not wear leather
- ❑ Wear pant legs outside of boots



Closed Systems

- Used closed systems. When using closed systems, you do not add those hours handling to the total exposure period prior to testing.

Questions

