

Recognition, Management, and Reporting of Pesticide Illness

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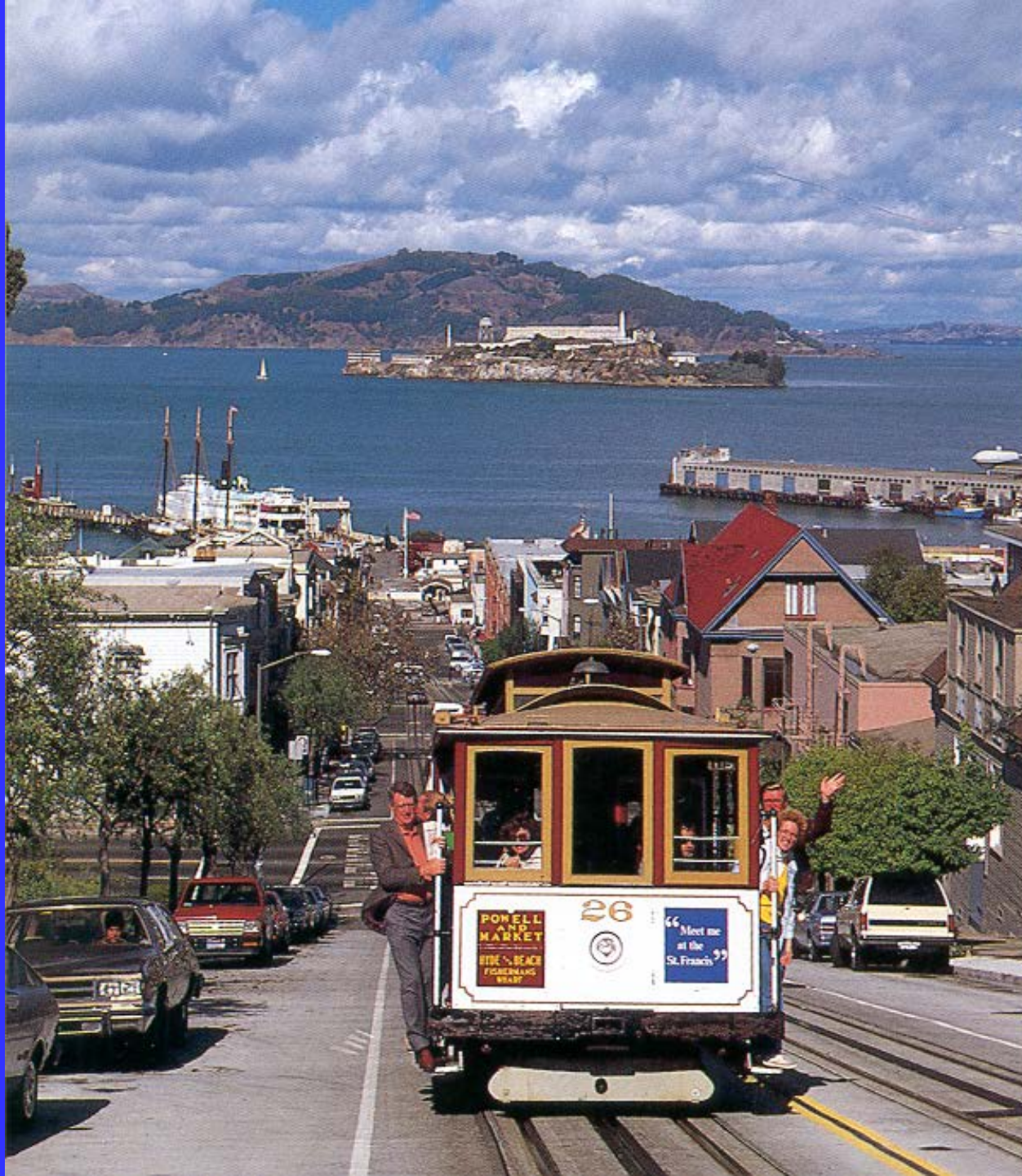
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**NOTICE OF PESTICIDE
APPLICATION**

Ordinance no. 274-97

Pesticide Name(s): Roundup Pro
Active Ingredient: Glyphosate
Target Pest: Grass and weeds
Area to be Treated: Reforestation plot
Date / Time of Application: Jan -9-17 / 7:00 - 10:00am
Signal Word: CAUTION
EPA Number: 524-475
Re-entry Period: Treated areas will be safe to re-enter
once sprays have dried
For information Call: Mike Hegarhorst 753-7042

San Francisco Recreation and Park Department
Integrated Pest Management (415) 753-0242

Application made as scheduled Application postponed to _____



ssment

Pesticide Usage in 2016

- California (58 counties)
 - 208,972,917 lbs. of pesticide active ingredients applied (mainly agricultural use)
 - Fresno, Kern, and Tulare counties applied the most per county
 - 687,123,130 lbs. of pesticide active ingredients sold in 2014.
 - This includes agricultural use pesticides as well as sanitizers and anti-microbials



Definition of Pesticide

“Any substance, or mixture of substances which is intended to be used for defoliating plants, regulating plant growth, or for preventing, destroying, or mitigating any pest,..., which may infest or be detrimental to vegetation, man, animal, or households, or be present in any agricultural or nonagricultural environment whatsoever.

(California Food and Ag code)



Definition of Pest

“Any of the following that is, or liable to become, dangerous or detrimental to the agricultural or nonagricultural environment of the state:

- (a) Any insect, predatory animal, rodent, nematode, or weed;
- (b) Any form of terrestrial, aquatic, or aerial plant or animal, virus, fungus, bacteria, or other microorganism (except viruses, fungi, bacteria, or other organism on or in living man or other living animals);
- (c) Anything that the director, by regulation, declares to be a pest.”

(California Food and Ag code)



Pesticide Illness Reporting



Reporting Requirement

California Code of Law, Health and Safety Code Section 105200

- **Who** - *“Any physician or surgeon who knows, or has reasonable cause to believe...”*
- **What** - *“...that a person is suffering from pesticide poisoning or any disease or condition caused by a pesticide...”*
- **To whom** - *“...shall promptly report that fact to the local health officer...”*
- **How** – *“...by telephone...”*
- **When** – *“...within 24 hours...”*



Reporting Requirement

California Code of Law, Health and Safety Code Section 105200

- **For the case of a worker** - “...and by a copy of the report required pursuant to subdivision (a) of Section 6409 of the Labor Code within seven days...”
- **Failure to comply** - “...shall be liable for a civil penalty of two hundred and fifty dollars...”
- **Not first aid** - “In no case shall the treatment administered for pesticide poisoning or a condition suspected as pesticide poisoning be deemed to be first aid treatment.”

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Reporting Pesticide Illnesses

Physicians must report pesticide illnesses using one of these methods:

1. Call or fax local health officer. Numbers to call for each county found at: www.cdph.ca.gov/Programs/CCLHO/Pages/CCLHOHealthOfficerDirectory.aspx
2. Call the California Poison Control Center at:
 - a. For general public: (800) 222-1222
 - b. For health care providers: (800) 411-8080
3. Report it on the Confidential Morbidity Report, available at: www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdph110b.pdf
4. In many counties physicians can report electronically using CalREDIE, the California Reportable Disease Information Exchange at: www.cdph.ca.gov/Programs/CID/DCDC/Pages/CalREDIE-HELP.aspx

There are additional requirements for reporting work related cases of pesticide illnesses



Reporting a Work Related Case of Pesticide Illness

For a work related case of pesticide illness:

- A. Report the case using a method listed on the previous slide
- B. Send the Doctor's First Report to:
 - i. Employer or insurer within 5 days of first visit
 - ii. Local health officer within 7 days
 - iii. Div. of Labor Statistics and Research of Dept. of Industrial Relations



**Title 17, California Code of Regulations (CCR), §2500, §2593, §2641–2643, and §2800–2812
Reportable Diseases and Conditions***

§2500. REPORTING TO THE LOCAL HEALTH AUTHORITY.

- **§2500(b)** It shall be the duty of every health care provider, knowing or in attendance on a case or suspected case of any of the diseases or conditions listed below, to report to the local health officer for the jurisdiction where the patient resides. Where no health care provider is in attendance, any individual having knowledge of a person who is suspected to be suffering from one of the diseases or conditions listed below may make such a report to the local health officer for the jurisdiction where the patient resides.
- **§2500(c)** The administrator of each health facility, clinic or other setting where more than one health care provider may know of a case, a suspected case or an outbreak of disease within the facility shall establish and be responsible for administrative procedures to assure that reports are made to the local health officer.
- **§2500(a)(14)** "Health care provider" means a physician and surgeon, a veterinarian, a podiatrist, a nurse practitioner, a physician assistant, a registered nurse, a nurse midwife, a school nurse, an infection control practitioner, a medical examiner, a coroner, or a dentist.

URGENCY REPORTING REQUIREMENTS (17 CCR §2500 (h) (i))

- ♦ = Report immediately by telephone (designated by a ♦ in regulations).
- † = Report immediately by telephone when two or more cases or suspected cases of foodborne disease from separate households are suspected to have the same source of illness (designated by a † in regulations).
- FAX ☒ = Report by FAX, telephone, or mail within one working day of identification (designated by a + in regulations).
- = All other diseases/conditions should be reported by FAX, telephone, or mail within seven calendar days of identification.

REPORTABLE COMMUNICABLE DISEASES §2500(j)(1), §2641–2643

<p>Acquired Immune Deficiency Syndrome (AIDS) (HIV infection only: see "Human Immunodeficiency Virus")</p> <p>FAX ☒ Amebiasis</p> <p>FAX ☒ Anisakiasis</p> <p>♦ Anthrax</p> <p>FAX ☒ Babesiosis</p> <p>♦ Botulism (Infant, Foodborne, Wound)</p> <p>♦ Brucellosis</p> <p>FAX ☒ Campylobacteriosis</p> <p>Chancroid</p> <p>Chlamydial Infections</p> <p>♦ Cholera</p> <p>♦ Ciguatera Fish Poisoning</p> <p>Coccidioidomycosis</p> <p>FAX ☒ Colorado Tick Fever</p> <p>FAX ☒ Conjunctivitis, Acute Infectious of the Newborn, Specify Etiology</p> <p>FAX ☒ Cryptosporidiosis</p> <p>Cysticercosis</p> <p>♦ Dengue</p> <p>♦ Diarrhea of the Newborn, Outbreaks</p> <p>♦ Diphtheria</p> <p>♦ Domoic Acid Poisoning (Amnesic Shellfish Poisoning)</p> <p>Echinococcosis (Hydatid Disease)</p> <p>Ehrlichiosis</p> <p>FAX ☒ Encephalitis, Specify Etiology: Viral, Bacterial, Fungal, Parasitic</p> <p>♦ <i>Escherichia coli</i> O157:H7 Infection</p> <p>† FAX ☒ Foodborne Disease</p> <p>Giardiasis</p> <p>Gonococcal Infections</p> <p>FAX ☒ <i>Haemophilus influenzae</i> Invasive Disease</p> <p>♦ Hantavirus Infections</p> <p>♦ Hemolytic Uremic Syndrome</p> <p>Hepatitis, Viral</p> <p>FAX ☒ Hepatitis A</p> <p>Hepatitis B (specify acute case or chronic)</p> <p>Hepatitis C (specify acute case or chronic)</p> <p>Hepatitis D (Delta)</p> <p>Hepatitis, other, acute</p> <p>Human Immunodeficiency Virus (HIV) (§2641–2643): reporting is NON-NAME (see www.dhs.ca.gov/aids)</p> <p>Kawasaki Syndrome (Mucocutaneous Lymph Node Syndrome)</p> <p>Legionellosis</p> <p>Leprosy (Hansen Disease)</p> <p>Leptospirosis</p> <p>FAX ☒ Listeriosis</p> <p>Lyme Disease</p> <p>FAX ☒ Lymphocytic Choriomeningitis</p> <p>FAX ☒ Malaria</p> <p>FAX ☒ Measles (Rubeola)</p> <p>FAX ☒ Meningitis, Specify Etiology: Viral, Bacterial, Fungal, Parasitic</p> <p>Meningococcal Infections</p> <p>♦ Mumps</p> <p>Non-Gonococcal Urethritis (Excluding Laboratory Confirmed Chlamydial Infections)</p>	<p>♦ Paralytic Shellfish Poisoning</p> <p>Pelvic Inflammatory Disease (PID)</p> <p>FAX ☒ Pertussis (Whooping Cough)</p> <p>♦ Plague, Human or Animal</p> <p>FAX ☒ Poliomyelitis, Paralytic</p> <p>FAX ☒ Psittacosis</p> <p>FAX ☒ Q Fever</p> <p>♦ Rabies, Human or Animal</p> <p>FAX ☒ Relapsing Fever</p> <p>Reye Syndrome</p> <p>Rheumatic Fever, Acute</p> <p>Rocky Mountain Spotted Fever</p> <p>Rubella (German Measles)</p> <p>Rubella Syndrome, Congenital</p> <p>FAX ☒ Salmonellosis (Other than Typhoid Fever)</p> <p>♦ Scombroid Fish Poisoning</p> <p>♦ Severe Acute Respiratory Syndrome (SARS)</p> <p>FAX ☒ Shigellosis</p> <p>♦ Smallpox (Variola)</p> <p>FAX ☒ Streptococcal Infections (Outbreaks of Any Type and Individual Cases in Food Handlers and Dairy Workers Only)</p> <p>FAX ☒ Swimmer's Itch (Schistosomal Dermatitis)</p> <p>FAX ☒ Syphilis</p> <p>Tetanus</p> <p>Toxic Shock Syndrome</p> <p>Toxoplasmosis</p> <p>FAX ☒ Trichinosis</p> <p>FAX ☒ Tuberculosis</p> <p>♦ Tularemia</p> <p>FAX ☒ Typhoid Fever, Cases and Carriers</p> <p>Typhus Fever</p> <p>♦ Varicella (deaths only)</p> <p>FAX ☒ <i>Vibrio</i> Infections</p> <p>♦ Viral Hemorrhagic Fevers (e.g., Crimean-Congo, Ebola, Lassa and Marburg viruses)</p> <p>FAX ☒ Water-associated Disease</p> <p>FAX ☒ West Nile Virus (WNV) Infection</p> <p>♦ Yellow Fever</p> <p>FAX ☒ Yersiniosis</p> <p>♦ OCCURRENCE of ANY UNUSUAL DISEASE</p> <p>♦ OUTBREAKS of ANY DISEASE (Including diseases not listed in §2500). Specify if institutional and/or open community.</p>
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REPORTABLE NONCOMMUNICABLE DISEASES AND CONDITIONS §2800–2812 and §2593(b)

Disorders Characterized by Losses of Consciousness
Cancer (except (1) basal and squamous skin cancer unless occurring on genitalia, and (2) carcinoma in-situ and CIN III of the cervix)
Pesticide-related illness or injury (known or suspected cases)**

LOCALLY REPORTABLE DISEASES (If Applicable):

* This form is designed for health care providers to report those diseases mandated by Title 17, California Code of Regulations (CCR). Failure to report is a misdemeanor (Health and Safety Code §120295) and is a citable offense under the Medical Board of California's Citation and Fine Program (Title 16, CCR, §1364.10).
** Failure to report is a citable offense and subject to civil penalty (§250) (Health and Safety Code §105200).



Why Report Pesticide Illness

- Can serve as an early warning system
- Can get state agencies to assist
- Establishes history and trends in poisonings
- Helps identify problem pesticides
- Assists State in writing pesticide regulations
- Assists State in health based investigations
- Requirement of California Code of Law Health and Safety Code



Why Physicians Don't Report Pesticide Illness

- People won't see a physician (esp. if non work related)
- M.D.'s may not recognize pesticide illness
- M.D.'s unaware of reporting requirement or how to report
- Confusion over what is a pesticide
- “Cumbersome reporting process”
- Forms burdened with questions that can't be answered
- Doubt on when to report
- M.D.'s overburdened with paperwork
- Concern about patient confidentiality
- Loss of capture of California workers who seek medical treatment in Mexico



Pesticide Illness Surveillance Program

(Department of Pesticide Regulation)

Number of Pesticide Illness Reports

Year	Total	Associated with Pesticide		
		Total	Agric	Non-Agric
2011	1473	1067	239	816
2012	1418	992	245	741
2013	1718	1128	435	685
2014	1685	1073	265	798
2015	1757	1187	397	787

Which pesticide usually generates the most reports?



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Pesticide Illness Surveillance Program of 2015

- Occupational cases
 - 573 of 1187 reports associated with pesticides
 - Fieldworkers (206), applicators (110), mixer/loaders (38), routine indoor (24)
- Non-occupational cases
 - 609 of 1187 reports associated with pesticides
- 5 cases could not be determined



Pesticide Illness Surveillance Program of 2015

- 26 hospitalizations
 - 12 for ingestions
 - 9 intentional ingestions to cause “self harm”
- 2 deaths reported definitely associated with pesticides
 - A pool maintenance tech consolidating containers of muriatic acid in an unventilated garage
 - A 34 y.o. male with hx. of mental illness reentered a tented house being fumigated with sulfuryl fluoride



Pesticide Illness Surveillance Program of 2015

- 225 cases associated with pesticides involved children (less than 18 y. o.). Almost all were non-occupational. 4 cases due to agricultural use pesticides.
 - 5 involved hospitalizations
 - None resulted from “self harm” attempts
 - 44 (20%) exposed by ingestion
 - 33 less than 6 years old
 - 28 probably due to improperly stored pesticides
- 53 cases were exposed at school when a pesticide drifted from a nearby service establishment



Diagnosing Pesticide Related Illness



Case Example 1.0

- An 18 y.o. patient comes into your office complaining of a headache, dizziness, not feeling well, weakness, and slight nausea of a few hours duration.
- Can you make a diagnosis just from this information?



What Is Most Important to Make a Diagnose of a Pesticide Related Illness?

- A) **History**
- B) Physical exam
- C) **History**
- D) Lab tests
- E) **History**



Case Example 1.1

The patient states that everyone in his family has been sick with the same symptoms. It started with his younger sister who is now well, then his mother who is getting better, then his father who is home ill with these symptoms, and now him. The family's M.D. told his father that he had a "flu bug."



Case Example 1.2

The patient states that his headache is severe and his neck is very stiff. He feels feverish and has noted a rash on his neck and chest. He mentions that he spent the weekend at a friend's apartment who attends Cal. Also staying there that weekend was a woman from the basketball team who has since been hospitalized for some kind of "infection of the spine".



Case Example 1.3

The patient states that this morning he was waiting at one of his company's vanpool pickup spots for the van that took him to work today. This spot was near an orchard that was being dusted by a plane. Some of the cloud of the spray drifted over the van and him. He felt some droplets from this cloud hit his face and he probably breathed in some of the spray.



Case Example 1.4

2 other workers from the same company come in to see you with the same symptoms. Each states he/she was at the same vanpool pickup spot waiting for the van as the previous patient. None of these patients felt any droplets hit their faces but they all saw the cloud go over them and they remember it had an odor.



Case Example 1.5

Another patient from the same company comes in with some of the same symptoms. She states she was on the same van as the 3 previous patients. This patient boarded the van 2 pickup stops before the previous patients did. She thinks that a couple of the windows of the van were open but did not feel any droplets and did not smell any unusual odors.



Case Example 1.6

Later in the afternoon, 5 other workers from the same company come in with the same symptoms. They were not on the van and did not work in the same work area as the 4 previous patients but they heard about what happened and were worried. These 4 did not know the other 4 patients (who were sent home earlier) nor anyone else who took that van to work.



Case Example 1.7

- Going back to Case Example 1.1, where the whole family had a “flu-like illness”
 - What if this family lived across the street from an agricultural field?
 - What if a member of this family worked as a pesticide applicator?



Case Example 1.7

- Could this family's illnesses be due to a pesticide applied on the agricultural field?
 - Could the family have been exposed to applied pesticides and not know it?
- Could this family actually have the “flu”?
- Could this family have a known exposure to pesticides but actually have the “flu”?
- Could there be other causes of this family's illnesses?



Diagnosis

- Most important in the HISTORY is:
 - **Exposure History**. Ask in detail.
 - What was the toxin?
 - What was the exposure?
 - Enough to cause the signs & symptoms?
 - » Consistent with the known effects?
 - Was the protective equipment working?
 - When was the exposure and when did the signs and symptoms occur?



Other Questions in Occupational Medicine History

- Does occupation involve an exposure to a toxin?
- Exactly, what are the job duties (not just the job title)?
- Do other co-workers have the same symptoms?
 - Are the symptoms related to anything at work?
 - Are the symptoms worse at work and improved when off work or on vacation?
- Are there exposure to other chemicals (at work or home with hobbies)?
- List past occupations and exposures
- (Consider a visit to the worksite)



“The Quick Survey”

1. What kind of work do you do?
2. Do you think your health problems are related to your work?
3. Are your symptoms better or worse when you're at home or at work?
4. Are you now or have you previously been exposed to dusts, fumes, chemicals, radiation, or loud noise?

(Newman LS)



Diagnosis

1. History
2. Physical findings
3. Lab tests (if there are any)
4. Response to therapy (if there is a specific therapy)



Important Points for Diagnosis

- The **EXPOSURE HISTORY** is the most important information the physician needs to make the correct diagnosis
- Pesticide related Illnesses can commonly resemble other illnesses
- Pesticide illnesses can be difficult to diagnose
- **For most pesticide poisonings, there are no diagnostic tests or specific therapies**



Accuracy of Diagnosis

- Lamminpaa and Riihimaki
 - Study of a case series of serious acute pesticide poisonings (79)
 - Less than 50% of the cases were correctly diagnosed
- Zweiner et al
 - 37 children, 1 month to 11 years old, with serious organophosphate poisonings
 - Only 20% of cases (4 of 20) transferred from other ER's were correctly diagnosed



Sources of Information

- Safety Data Sheet (formerly MSDS)
- Pesticide label
- Employers
- Agricultural commissioner
- California Poison Control Center
 - a. General public: (800) 222-1222
 - b. Health care providers: (800) 411-8080



Sources of Information

- California Department of Public Health
 - Occupational Health Branch (800) 970-6680
 - <http://www.dhs.ca.gov/ohb/contact.htm>
- California Department of Pesticide Regulation
 - Worker Health and Safety Branch (916) 445-4222
 - www.cdpr.ca.gov
- California Office of Environmental Health Hazard Assessment
 - (510) 622-3170
 - www.oehha.ca.gov



Sources of Information

- Recognition and Management of Pesticide Poisonings, 6th Edition by the U.S. EPA
 - <http://www2.epa.gov/pesticide-worker-safety/recognition-and-management-pesticide-poisonings>
 - 5th Edition available in Spanish
- U.S. Environmental Protection Agency, Region 9 Office
 - Phone: (415) 744-1500
 - www.epa.gov/pesticides
- National Pesticide Information Center
 - Phone: (800) 858-7378
 - <http://npic.orst.edu/>



Classification of Pesticides

Target

- Insecticides: insects
- Herbicides: weeds
- Fungicides: fungi
- Rodenticides: rodents
- Acaricides: mites
- Nematicides: worms
- Antimicrobials: microbes

Chemical Groups

- Organophosphates
- N-methyl carbamates
- Pyrethroids
- Neonicotinoids
- Organochlorines



Organophosphate and N-methyl Carbamate Pesticide Related Illness

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Cholinesterase Inhibiting Pesticides

- Cause more serious illness than any other class of pesticides
 - Historically, were 30-36% of all reports
 - 26% in 2008
- A test that can aid the diagnosis and an antidote are available for poisonings due to them



Case Example

23 farm workers went into a cauliflower field in Salinas Valley 6 hrs. after mevinphos and phosphamidon were applied. A 72 hr. restricted entry interval was required. 2 hrs. later, a few noticed onset of blurred vision and eye irritation. Shortly, some developed dizziness, weakness, disorientation, headache, nausea, and vomiting. Several had cramps of arms, legs, and stomach. 2 collapsed with bradycardia, increased salivation, miosis, and muscle fasciculations. 16 sought treatment and 5 were hospitalized. The sickest ones were treated with IV atropine and pralidoxime.

15 received weekly followup of their RBC cholinesterase.
(Midtling et al.)

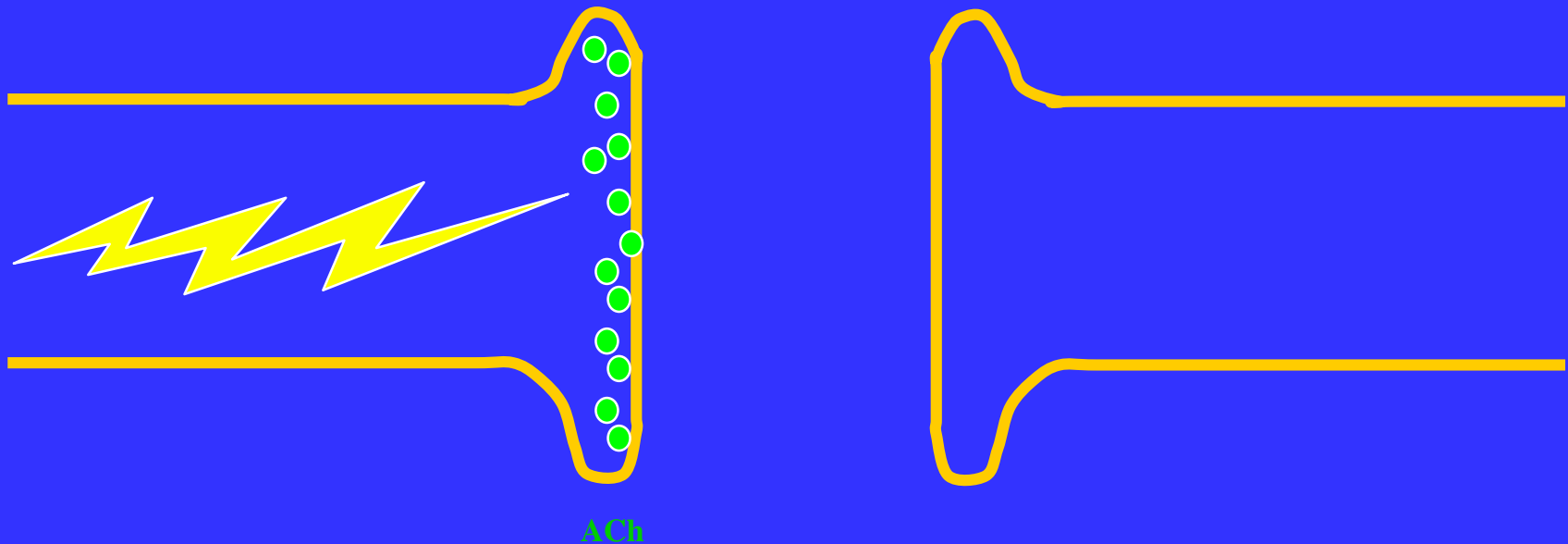


Pathophysiology of Cholinesterase Inhibition

- Acetylcholine is a neurotransmitter
 - Enzyme, **acetylcholinesterase**, hydrolyzes acetylcholine to choline and acetic acid
- OP and carbamates covalently bind to acetylcholinesterase at the binding site for acetylcholine rendering the enzyme inactive
 - Leads to accumulation of acetylcholine at the synapses and continuous or overstimulation of the receptors
 - Signs and symptoms depend on which sites are stimulated



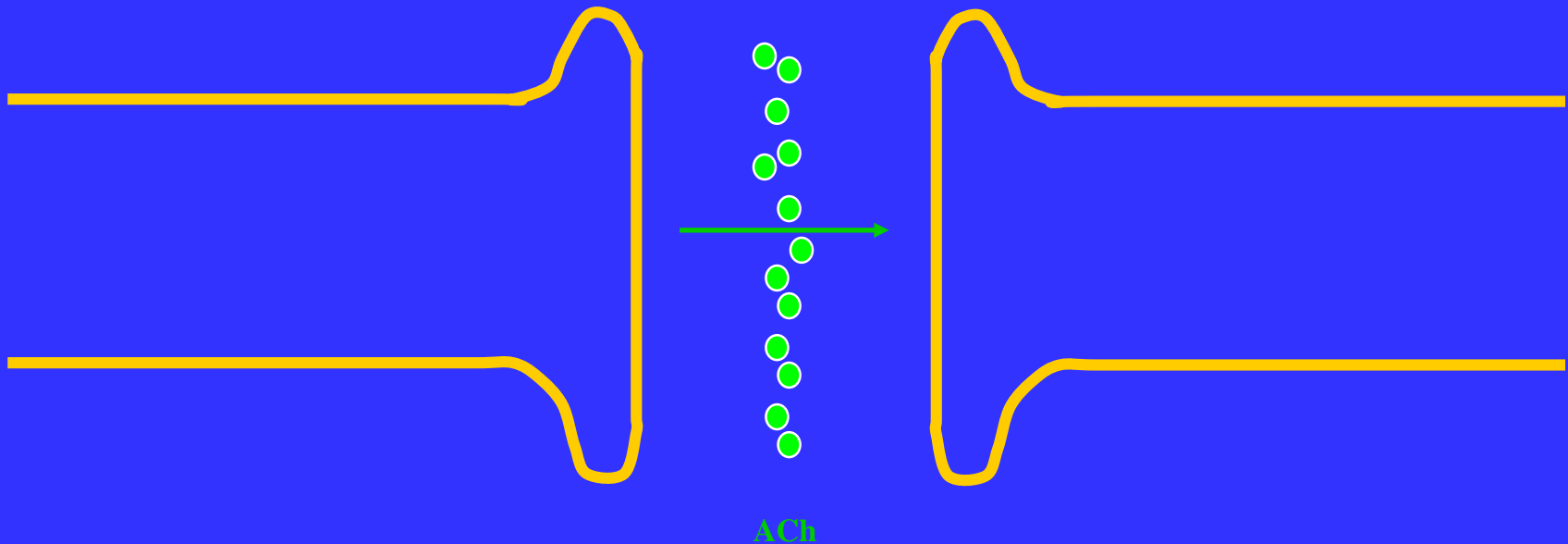
Nerve Transmission: Nerve to Nerve



(Slide from US Army Medical Research Institute of Chemical Defense)



Nerve Transmission: Nerve to Nerve

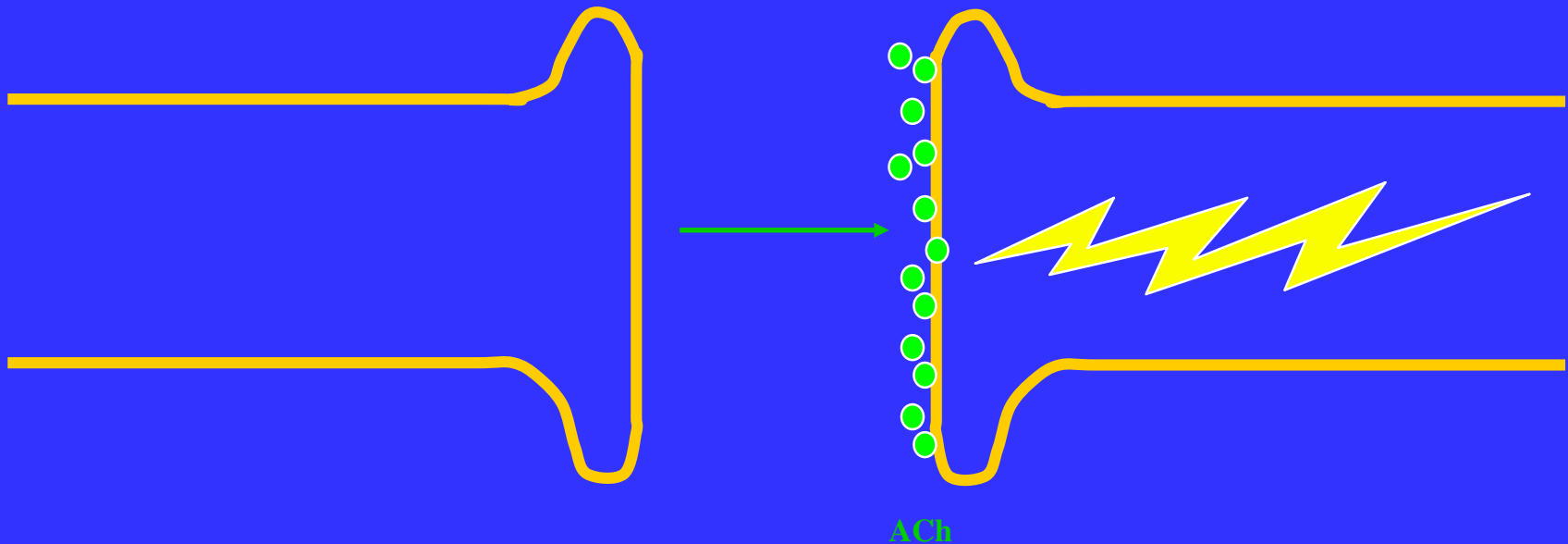


(Slide from US Army Medical Research Institute of Chemical Defense)



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Nerve Transmission: Nerve to Nerve

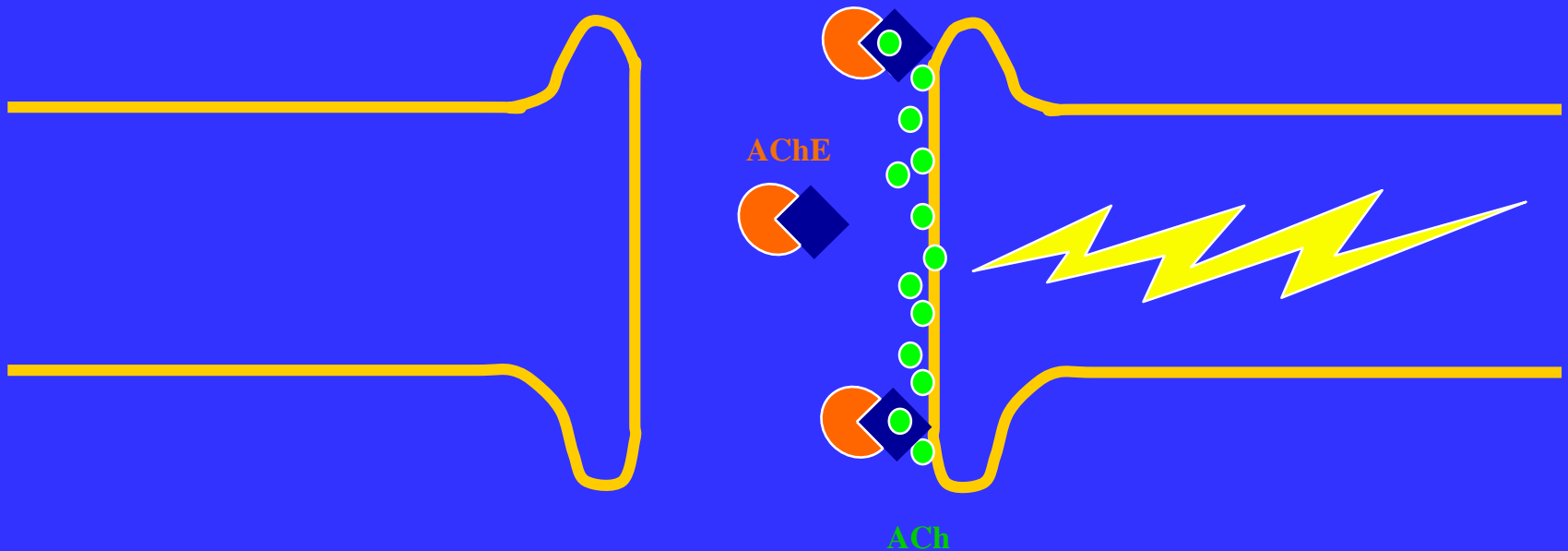


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Impulse Termination: The Role of AChE

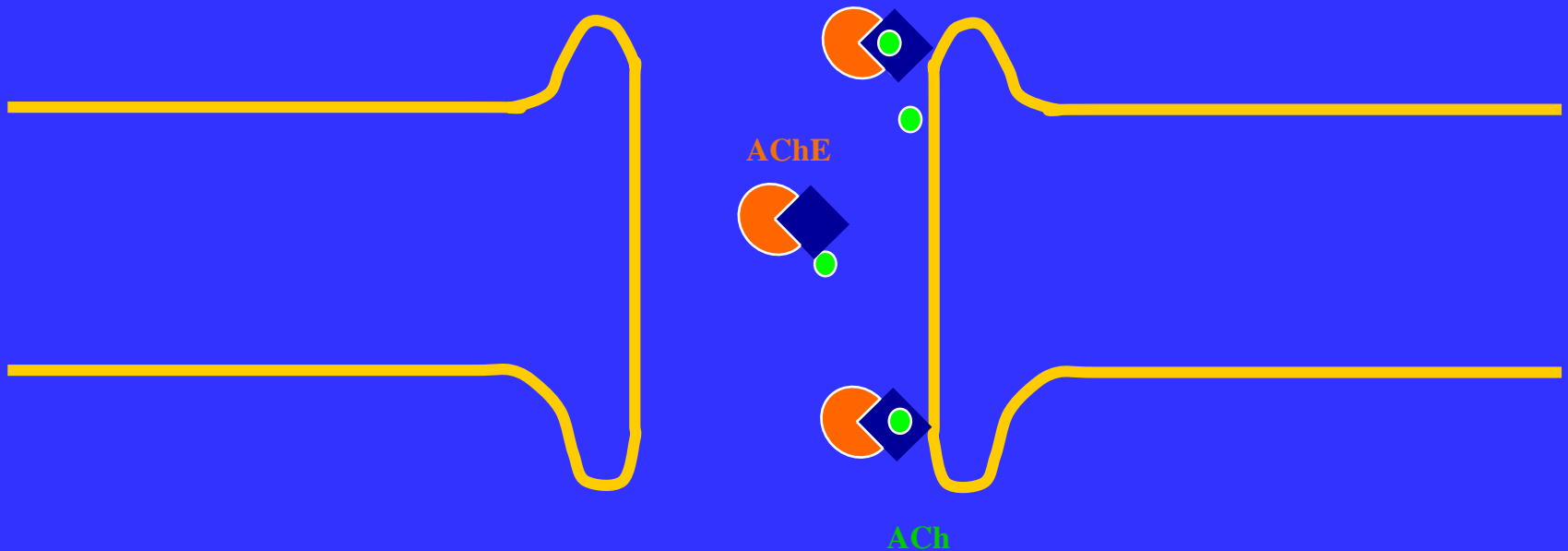


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Impulse Termination: The Role of AChE

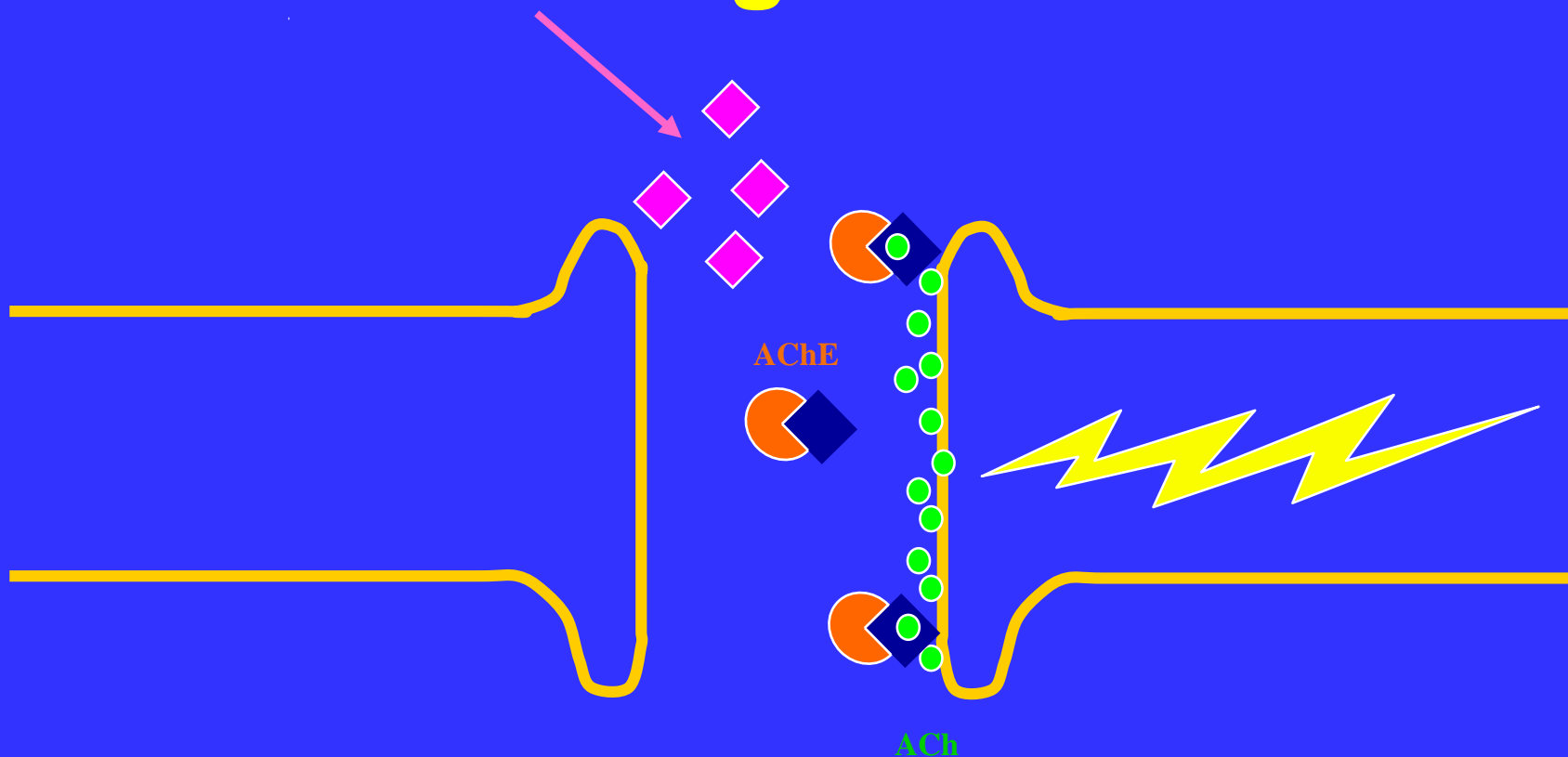


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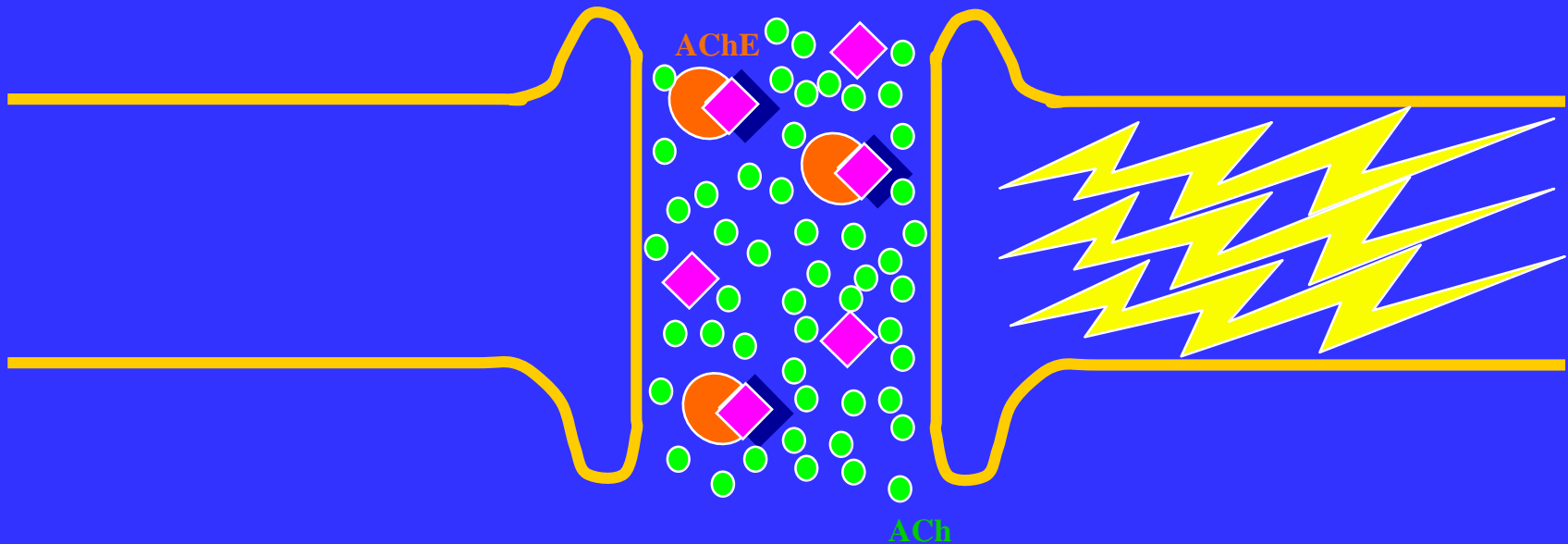
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Exposure to a Cholinesterase Inhibiting Pesticide



(Slide from US Army Medical Research Institute of Chemical Defense)

Exposure to a Cholinesterase Inhibiting Pesticide



(Slide from US Army Medical Research Institute of Chemical Defense)



Organophosphates

- Binding with acetylcholinesterase is a two step process
 - Initial binding is reversible
 - After “aging”, bond becomes irreversible. Time to “aging” varies with the OP but usually begins after 6 hours
- Some organophosphates: Chlorpyrifos (Dursban, Lorsban), malathion, parathion, diazinon



N-methyl Carbamates

- Binding with acetylcholinesterase is reversible
 - Do not undergo “aging”
- Do not cross as well into the central nervous system
- Some carbamates: Aldicarb (Temik), carbaryl (Sevin), carbofuran, methomyl



Cholinergic Syndrome

- **Muscarinic Receptors**

- Diaphoresis
- Eyes - miosis, lacrimation, blurred vision, discomfort
- Resp - Wheezing, cough, SOB, bronchorrhea
- Cardiac - Bradycardia, hypotension
- GI - Salivation, nausea, vomiting, defecation, incontinence, diarrhea, abdominal pain
- GU - Urinary incontinence, frequency



Cholinergic Syndrome

- **Nicotinic Receptors**
 - Cardiovascular – Tachycardia, hypertension
 - Musculoskeletal – Fasciculations, muscle weakness, paralysis, cramps, weakness of muscles of respiration
- **CNS Receptors**
 - Headache, anxiety, confusion, psychosis, ataxia, dysarthria, tremor, seizures, stupor, coma, respiratory depression, Cheynes-Stokes respiration



Which Signs and Symptoms Can Help Make the Diagnosis

- Signs and symptoms are variable. Many are non-specific. Certain combinations, esp. if the MD has a high of index of suspicion, can lead to the diagnosis
- Some signs are reasonably specific and are good clues
 - Excessive salivation
 - Lacrimation
 - Muscle fasciculations and weakness
 - Pupil constriction
 - Urinary incontinence
 - Fecal incontinence
 - Smell of hydrocarbon constituents

(Bardin et al. 1994)

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Mnemonics

- SLUD or SLUDGE

Salivation

Lacrimation

Urination

Defecation

Gastrointestinal
cramping

Emesis

- DUMBBELS

Diarrhea

Urination

Miosis

Broncospasm

Bronchorrhea

Emesis

Lacrimation

Salivation

- MUDDLES

Miosis

Urination

Diarrhea

Defecation

Diaphoresis

Lacrimation

Emesis

Salivation



**Which is the “critical”
organ system in an
organophosphate or
carbamate poisoning?**

(All organ systems are important!)



Respiratory System

- Primary cause of death is respiratory failure
 - Tsao et al. 43 of 107 with OP or carbamate poisoning developed respiratory failure.
 - Of these forty-three, 51.2% died.
 - 100% of pts. without respiratory failure survived.
- Bronchospasm and bronchorhea in combination with weakness of the muscles of respiration and depression of medullary respiratory centers can cause respiratory arrest (can be sudden)
- Pneumonia can develop



Routes of Absorption

- **Inhalation**
 - Fastest
- **Ingestion**
 - Used in suicides
 - Children
- **Dermal absorption**
 - Slower
 - Symptoms may not appear for 6-12 hours after exposure
 - Most occupational exposures
- **Need to observe patient with significant exposures**



Lab Tests

- **Plasma Cholinesterase Activity**

- (aka pseudo, serum, or butyryl cholinesterase)
- More labile
- More actively inactivated
- More rapidly regenerated
- Preferentially lowered by some pesticides
(eg. chlorpyrifos, mevinphos)

- **RBC Cholinesterase Activity**

- (aka true or acetyl cholinesterase)
- Same as enzyme in nervous system
- Depressed slower
- Thought to reflect inactivation at neuroeffector site more accurately
- Regenerates slower
- Preferentially lowered by some pesticides (eg. phosmet, dimethoate)



Factors Affecting Cholinesterase Activity Levels

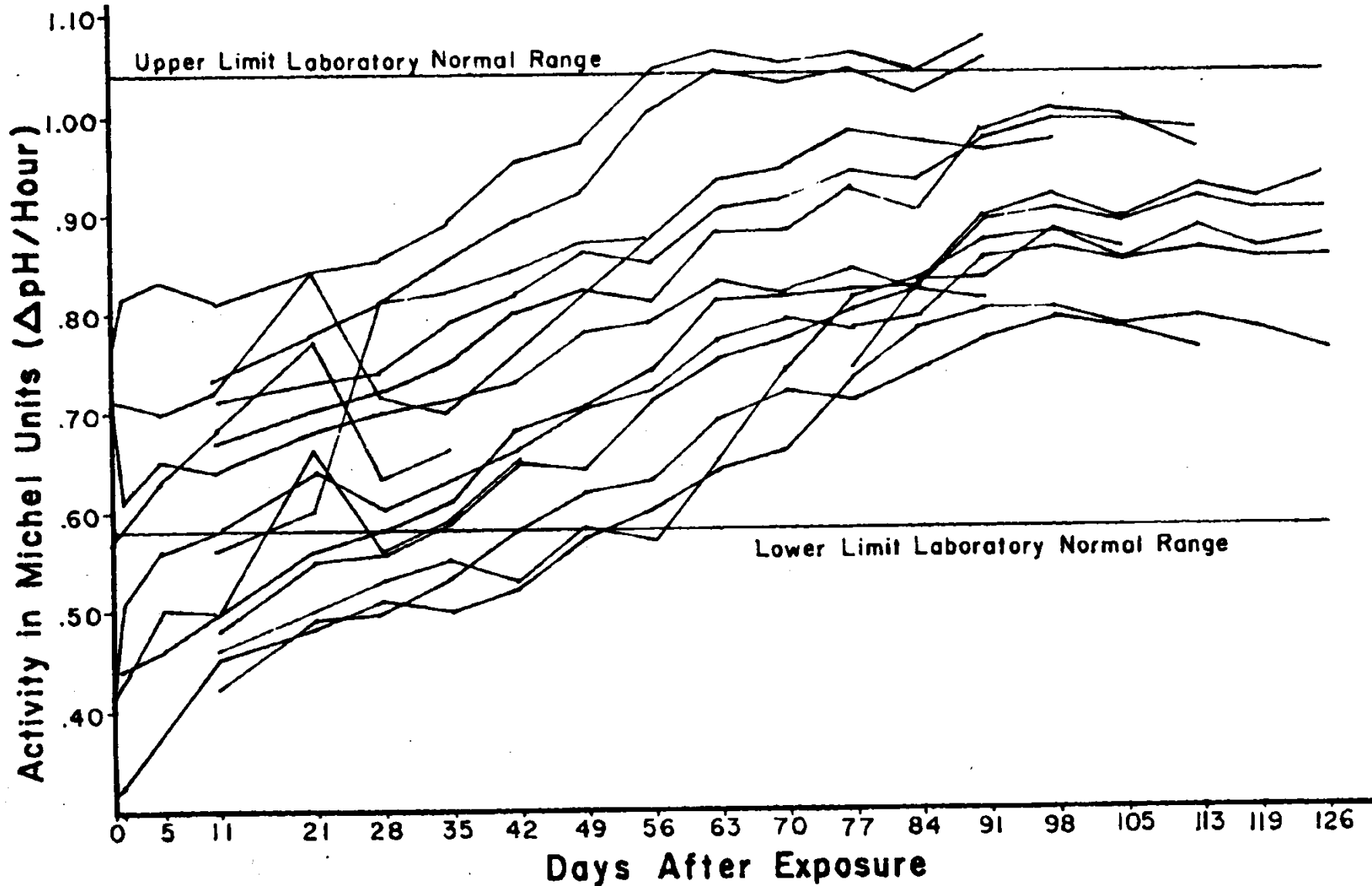
- **Plasma cholinesterase activity level**
 - 3% have genetically determined lower level and are susceptible to a muscle paralyzer, succinylcholine, but not to organophosphates. They have normal RBC ChE.
 - Can be lowered by liver disease, malnutrition, alcoholism, nephrotic syndrome, early pregnancy, cocaine, carbon disulfide, organic mercury, birth control pills, and metoclopramide.
- **RBC cholinesterase activity level**
 - can be affected by hemolytic anemia, pernicious anemia, recovery from hemorrhage, and conditions associated with reticulocytosis.



Lab Tests

- **Cholinesterase activity level (for OPP)**
 - Association of symptoms and levels is variable
 - Rapidity of decrease of levels is important
 - Can help make diagnosis if very low
 - Be careful how to interpret if levels normal
 - Can confirm diagnosis retrospectively by obtaining levels acutely and repeating over next few weeks and months





(Midtling et al.)



Tests

- Cholinesterase activity level
 - Not usually useful for carbamate poisoning
 - Binding with cholinesterase does not “age”
- Metabolites. May not be readily available.
- Chest x-ray, EKG and cardiac monitoring if indicated
- “Test dose” of atropine, 0.5–1.0 mg. IV
 - If OPP, then no response
 - If not OPP, then should get atropinization with dry mouth, mydriasis, increased heart rate, flushing



Differential Diagnosis

- Mild cases

- Acute viral syndromes (flu-like illness)
- Gastroenteritis
- Respiratory infections
- Asthma
- Psychological dysfunction
- Allergic dermatitis

- Severe cases

- Acute cerebrovascular accident
- Heat stroke
- Heat exhaustion
- Epilepsy
- Infections
 - Meningitis
 - Encephalitis
 - Pneumonia
- Psychosis



Children

- Study done at Children's Medical Center in Dallas
- 20 patients were transferred from other ER's
 - 16 of these 20 had incorrect diagnoses
 - Difficulties in diagnosis
 - 75% were < 3 years old
 - Developmentally incontinent
 - Lacrimation secondary to anxiety and pain
 - » SLUD difficult to use
- Almost 25% had tonic-clonic seizures

(Zweiner et al)

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6-25-18 Folsom

Office of Environmental Health Hazard Assessment



Children

- 37 patients, 1 month to 11 years old (median age 22 months)
 - 36 (97%) occurred in the home
 - 28 (76%) oral ingestion
 - 25 (70%) drank liquid improperly stored organophosphate
 - 6 (16%) dermal absorption
 - 3 (8%) unknown

(Zweiner et al.)



Diagnosis

- History
- Physical findings
- Cholinesterase activity levels
 - Acutely
 - Retrospectively
- Response to therapy



Management

- Supportive care
 - Endotracheal intubation and mechanical ventilation for oxygenation and to prevent aspiration
- Decontamination
- Anticholinergic med is mainstay of treatment
 - Atropine
- Cholinesterase reactivator
 - Pralidoxime (2-PAM, Protopam)
- Other measures



Atropine

- Atropine competitively blocks the action of acetylcholine at the muscarinic receptor sites
- Correct hypoxia before administering to avoid arrhythmias
- First dose is “test dose”
- Standard dose is 2.0-4.0 mg. IV Q 15 minutes
 - End points
 - Lung rales clear
 - “Dry out” lungs to prevent pneumonia and respiratory failure
 - Reversal of muscarinic signs and symptoms
 - Full atropinization (flushing, dry mouth, mydriasis, tachycardia)



Atropine

- Pediatric dose (<12 y.o.) is 0.05-0.1 mg/kg body weight
- Atropine toxicity can cause fever, muscle fibrillation, delirium
- May need large quantity for treatment (up to 50 mg. in 24 hrs.)
- IV continuous infusion 30 mg. in 200 ml. of saline and titrate against symptoms
- No effect on nicotinic receptor sites (including muscles of respiration)



Case Example

68 y.o. male, hx. of depression, attempted suicide. Drank 3 oz. of concentrated solution of dimethoate. Initially responded to treatment with ipecac, charcoal, atropine, and pralidoxime. Relapsed and treated for the next 5 weeks with supportive care and large quantities of atropine. Some days required over 3000 mg. of atropine to control the hypersecretions. **The total amount of atropine used for this patient was over 30,000 mg.** Discharged with a slight hearing loss and a nonspecific personality change.

(LeBlanc et al.)

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Pralidoxime

(2-PAM, Protopam)

- Reactivates acetylcholinesterase by removal of the phosphate group bound to the esteratic site
- **Draw blood sample for cholinesterase testing before administering pralidoxime**
- **Most effective before “aging” occurs.** Within the first 6 hours after exposure to OP but reported efficacious up to 24-48 hrs. later. Some initiate with muscle fasciculations
- Dose is 1g IV over 45-60 minutes (give slowly)
 - Can repeat after 2 hours and then Q 12h PRN
 - IV continuous infusion 250-500 mg./h. Titrate to sx's
- Pediatric dose (< 12 y.o.) is 20-50mg/kg of body weight



Decontamination

- Clothes removed and bagged
 - Dispose of shoes
- Patient must be completely washed including skin, skin folds, scalp, and under the fingernails with water and soap or an alkaline detergent
- Flush eyes if indicated
- Protect personnel involved in treatment of the patient



Other Measures

- GI measures
 - Activated charcoal
 - For the unconscious, intubate the airway for protection. Then gastric lavage with a large bore tube followed by use of charcoal
- Furosemide for persistent pulmonary edema after full atropinization
- Hydrocarbon aspiration. Treat as case of acute respiratory distress syndrome
- Monitor cardiac and pulmonary status
- Diazepam or lorazepam for seizure control



Case Example

Three workers in a pesticide formulating plant.

Worker 1. 25 y.o. formulator spilled a 76% solution of parathion on his inguinal and scrotal areas and legs. He removed clothes, showered, changed overalls and boots. 2 days later, developed nausea and diarrhea. Went to ED and was treated with Compazine and sent home.

Did not tell the physician of his exposure.

2 days later, returned to ED with weakness, nausea, and sweating. PE-appeared ill, pupils constricted, nystagmus.

History of parathion exposure was given on this visit. Admitted and treated with atropine and pralidoxime. Did well and discharged the next day.



Worker 2. 23 y.o. formulator developed N & V 12 days after Worker 1's exposure. Worker 2 was sent to ED since his screening cholinesterase was suggestive of OPP, even though he had not worked with any OP's. In ED, had N, V, LOC, apnea, seizures, and fecal and urinary incontinence. Admitted, intubated, mechanically ventilated, treated with diazepam, phenobarb, atropine, and pralidoxime. He regained consciousness and improved rapidly and was discharged the next day.

Worker 3. 18 y.o. formulator developed nausea and vomiting 15 days after Worker 1's exposure. Worker 3 was sent to the ED where he was diaphoretic and had pinpoint pupils. Treated with pralidoxime 1 g. and did well and was discharged.



The plant safety officer was very concerned since there were no poisonings over the previous few years and now there were 3 in a 2-week period. Safety measures were strictly enforced. Coveralls used and respirators and gloves were used when indicated. Clothing contaminated with spilled pesticide was bagged and burned.

What happened?



What Happened?

- Worker 1 immediately changed out of his coveralls and bagged them to be burned
 - **Coveralls were laundered instead of burned**
- Worker 1 wore them subsequently
- After another washing, were worn by Worker 2
- After another washing, were worn by Worker 3
- Analysis of the coveralls showed a very high concentration of parathion. The wash water and other coveralls were found to be contaminated. All coveralls were then destroyed and replaced



Important Points of Case

- Exposure history is most important for the diagnosis
- Pesticide illnesses can resemble other common illnesses
- Physical exam findings can be helpful
- Supportive therapy, especially of the respiratory system, is very important
- Dermal absorption is the most common route of occupational poisoning

