VII. RESEARCH NEEDS

Despite its decreasing usage, relatively large quantities of parathion are currently being manufactured, formulated, mixed, and applied to various crops in the United States. Accordingly, the following research is recommended in order to add to our existing knowledge of parathion:

(1) Animal experiments to determine whether or not permanent effects on the central nervous system occur as the result of chronic low-level exposure. Well-designed and controlled behavioral studies should be undertaken as a major part of the attempt to better define the effects of parathion on the central nervous system.

(2) Animal experiments to determine the mutagenic, teratogenic, and carcinogenic potentials of parathion in realistic doses.

(3) Electromyographic testing of human subjects exposed to parathion to determine particularly whether low concentrations of the insecticide produce adverse effects on the neurologic system.

(4) Studies to determine whether parathion exerts any toxicity by a mechanism, or mechanisms, other than inhibition of tissue ChE.

(5) Additional studies to more clearly define the environmental factors responsible for the demonstrated conversion of parathion deposited on surfaces to other toxic substances.

(6) An epidemiologic study of a worker population exposed to parathion for a long period of time. In the event that an adequate cohort of workers exposed to parathion cannot be identified, a retrospective morbidity and mortality study of a worker population exposed to parathion and other ChE-inhibiting organophosphorus pesticides would be of great use in determining the long-term effects, if any, of these compounds.

(7) A program to develop more effective and satisfactory protective clothing for employees working with parathion as well as other pesticides (eg, cool, lightweight, and impervious to parathion).

(8) Studies to develop an accurate and precise solid sampling system for airborne parathion. In addition, the recommended impinger device should be thoroughly evaluated in order to determine its sampling efficiency and the overall precision of the recommended sampling and analytical method.

(9) A research effort to develop an improved biologic test method to supersede blood ChE determinations.

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APPENDICES

IX. APPENDIX I

SAMPLING AND CALIBRATION PROCEDURES

The sampling method recommended is based on those described by Miles et al,[118] and the *NIOSH Manual of Analytical Methods*.[197] As stated previously in Chapter IV, the sampling efficiency and the overall precision of the recommended sampling and analytical method are unknown. In addition, the Environmental Protection Agency has withdrawn the impinger (with ethylene glycol) sampling method from its pesticide manual. (RH Hill, Jr, written communication, March 1976) However, the recommended method remains the best one presently available for collecting and determining the concentration of parathion in air.

Atmospheric Sampling

When sampling is performed for determination of compliance with the recommended workplace air standard, the sample shall be taken within the breathing zone of the exposed employee to ascertain the employee's actual exposure to airborne parathion. A description of sampling location and conditions, equipment used, time and rate of sampling, and any other pertinent information shall be recorded at the time of the sample collection.

(a) Equipment

The sampling train consists of a midget impinger filled with 15 ml of ethylene glycol, an absorption tube, and an air pump. A prefilter unit consisting of the filter media and cassette filter holder can be used if needed.

(1) Midget impinger: All portions of the impinger which may contact the collection medium or the air stream before collection is effected must be made of glass. The collection medium is ethylene glycol. The ethylene glycol used must be free of substances that will produce interfering peaks upon hexane extraction and subsequent gas liquid chromatographic analysis. Consequently, the only ethylene glycol suitable is that which has been preextracted and found to be free of interfering substances by gas-liquid chromatography using a flame photometric detector.

(2) Absorption tube: An absorption tube loosely packed with a plug of glass wool is inserted between the exit arm of the impinger and the air pump to protect against splash-over or water condensation.

(3) Air pump: Any air mover capable of drawing the desired flowrate through the impinger may be used, so long as the flowrate does not vary more than ±5% during the sampling period. The sampling pump must be capable of operating at a pressure drop of 1 inch of mercury while providing the designated flow rate of 1-2 liters/min. The flowrate of the pump must be calibrated and this calibration checked periodically to ensure that it has not changed.

(4) An integrating volume meter such as a dry-test or wet-test meter.

(5) Thermometer

(6) Manometer

(7) Stopwatch

(8) Filter cassette with glass-fiber filter, 8μ, 37 mm.

(b) Calibration

Since the accuracy of an analysis can be no greater than the accuracy of the air volume measurement, the accurate calibration of a sampling pump is essential. How often the calibration must be performed is dependent on the use, care, and handling of the pump. Pumps should also be recalibrated if they have been misused or if they have just been repaired or received from a manufacturer. If the pump receives hard usage, more frequent calibration may be necessary. Regardless of use, maintenance and calibration should be performed on a regular schedule and records of these kept.

Ordinarily, pumps should be calibrated in the laboratory both before they are used in the field and after they have been used to collect a large number of field samples. The accuracy of calibration is dependent upon the type of instrument used as a reference. The choice of calibration instrument will depend largely upon where the calibration is to be performed. For laboratory testing, primary standards such as a spirometer or soapbubble meter are recommended, although other standard calibration instruments (such as a wet-test meter or dry-gas meter) can be used. The actual setups will be similar for all instruments.

Instructions for calibration with the soapbubble meter appear below. If another calibration device is selected, equivalent procedures should be used.

Since the flowrate given by a pump is dependent on the pressure drop of the sampling device, in this case a midget impinger, the pump must be calibrated while operating with a representative midget impinger in line. The calibration train thus consists of a soapbubble meter, a midget impinger, an absorption tube, a pressure gauge capable of measuring 20 inches of water, and an air pump.

(1) The voltage of the pump battery is checked with a voltmeter to ensure adequate voltage for calibration. The battery is charged if necessary.

(2) The pump is turned on. The inside of the soapbubble meter is then moistened by immersing the buret into the soap solution and drawing bubbles up the inside until they are able to travel the entire buret length without bursting.

(3) The pump rotameter is adjusted to provide the desired flowrate.

(4) A water manometer is checked to ensure that the pressure drop across the sampling train is maintained at approximately 12 inches of water at 2 liters/min.

(5) A soapbubble is started up the buret, and the time required for the bubble to move from one calibration mark to another is measured with a stopwatch.

(6) The procedure in (5) is repeated at least twice, the results averaged, and the flowrate calculated by dividing the volume between the preselected marks by the time required for the soapbubble to traverse the distance.

(7) Calibration data which are to be recorded include the volume measured, elapsed time or number of strokes, pressure drop, air temperature, atmospheric pressure, serial number of the pump, date, and name of the person performing the calibration.

(c) Sampling Procedure

Breathing zone samples representative of the individual employee's respiratory exposure are collected with the midget impinger by fastening the impinger to a coat lapel or shirt collar, or by holding the impinger near the face of the employee during the sampling period. The duration of sampling shall be such that a concentration of 10% of the recommended environmental standard, as specified in Chapter I, Section 1(a), may be detected accurately by the recommended analytical method. An air sample of 25-50 liters should be collected. The temperature and pressure of the atmosphere being sampled are measured and recorded.

After a sample is taken, the impinger stem is removed and washed with 2-5 ml of ethylene glycol. This wash solution is included in the impinger, and the amount of washing solution recorded. The top of the impinger is sealed tightly with a hard, nonreactive stopper (preferably Teflon). Do not seal with rubber. The impinger is placed upright in a carrying case, with care taken to prevent losses due to spillage or evaporation. The trapped parathion is extracted into hexane and analyzed as described in Appendix II. Other collection methods shown to be equivalent or superior may be used. If shipment of the impingers with the stems is preferred, the outlets of the stems should be sealed with paraffin sheet or other nonrubber covers, and the ground glass joints should be sealed (ie, taped) to secure the tops tightly. A "blank" impinger should be handled as the other samples (fill, seal, and transport) except that no air is sampled through this impinger. Where a prefilter has been used, the filter cassettes are capped and placed in an appropriate cassette shipping container. One filter disc should be handled like the other samples (seal and transport) except that no air is drawn through it. This is labeled as a blank.

X. APPENDIX II

ANALYTICAL METHOD FOR PARATHION

The gas-liquid chromatographic method presented in the *NIOSH Manual of Analytical Methods*[197] is recommended for analysis of parathion in air. NIOSH classifies the method as Class C (tentative), which is described as a method in wide use and which has been adopted as a standard method or recommended by another government agency or one of several professional agencies.

Principle of Method

Parathion in workplace air is trapped in ethylene glycol contained in a midget impinger. The ethylene glycol solution is diluted with water and extracted with hexane. The resulting solution of parathion in hexane is concentrated and subjected to gas-liquid chromatographic analysis using a phosphorus-specific flame photometric detector.

Range and Sensitivity

The linear range of the flame photometric detector is 0.5-25 ng for parathion. For a 50-liter air sample carried through the following procedure to solution in 1 ml of hexane, 2 μl of which is injected into the gas chromatograph, the range of workplace air concentrations over which analysis is linear is 5-250 $\mu g/m^3$. These limits can be lowered or raised by changing (1) the volume of air sampled, (2) the volume of the final hexane solution, or (3) the size of the aliquot injected into the gas chromatograph.

Interferences

Phosphorus compounds having retention times close to that of parathion will interfere with the analysis. The equipment used must be scrupulously cleaned to remove any traces of phosphate detergents. Glassware should, in addition, be rinsed with hexane immediately prior to use.

Advantages and Disadvantages

(a) The method is very sensitive and the detector exhibits high specificity for phosphorus compounds. The analysis is performed directly on the compound of interest. Separation and quantification are accomplished in a reasonable amount of time.

(b) The cost of the equipment and supplies may be somewhat expensive for some laboratories. The sensitivity of the equipment depends on careful adjustment of the operating parameters. Contamination can occur easily through equipment and reagents. If interfering compounds are anticipated, a lengthy cleanup procedure is required.

Apparatus

(a) Forceps.
(b) Glass stirring rods.
(c) Separatory funnels, 60-ml and 125-ml with Teflon stopcock.
(d) Beakers, 100-ml.
(e) Funnels, 65- or 75-mm (diameter at top).
(f) Glass wool (preextracted with hexane).
(g) Hot water bath.
(h) Kuderna-Danish evaporator-concentrator, consisting of a 125-ml Erlenmeyer-type flask, 3-ball Snyder column, and 10-ml receiver graduated in milliliters.
(i) Glass beads, 3-mm.
(j) Volumetric flasks for standards.
(k) Graduated cylinders, 25- or 50-ml.
(l) Syringes, 5- or 10-μl and 100-μl.
(m) Transfer pipets, volumetric.
(n) Gas chromatograph, with attendant equipment, including a phosphorus flame photometric detector. The following modification is suggested for operation of the GC with flame photometric detection and is generally applicable to any GC. A switching valve should be interfaced between the gas chromatographic column and the detector. The valve, which is heated with a 432-watt 2 ½" x 24" insulated heating tape, permits interchange of column effluent and nitrogen purge. The nitrogen purge flow rate is adjusted to equal the flow from the gas chromatographic column so that when an interchange of flows is made for the purpose of venting solvent, no change is observed in the recorder baseline. This arrangement avoids extinguishing the flame when sample injections are made.
(o) Gas chromatography column constructed from 6 ft x 4 mm inside diameter borosilicate glass (silanized) packed with one of the following:
(1) 10% DC-200 (12,500 cst) on 80-100 mesh Gas Chrom Q.

(2) 15% QF-1 (10,000 cst)/ 10% DC-200 (12,500 cst) on 80-100 mesh Gas Chrom Q.

(3) 2% diethylene glycol succinate (DEGS) (C6 stabilized) on 80-100 mesh Gas Chrom Q.

(4) 4% SE-30/6% OV-210 on 80-100 mesh Chromosorb W, HP.

Columns 1 and 2 are conditioned by heating 2-4 days at 240-250°C under nitrogen flowing at 60 ml/min, then primed by repeated injections of standard parathion solution under the conditions of analysis given below. Column 3 is conditioned by heating 12 hours at 225-230°C under nitrogen flowing at 60 ml/min. Column 4 is conditioned for at least 3 days at 245°C under nitrogen flowing at 60 ml/min. A column of 10% Carbowax 20M on 80-100 mesh silanized support (2 in x 4 mm inside diameter glass tubing) is then attached before column 4 and the assembly is heated at 230-235°C for 17 hours under nitrogen flowing at 20 ml/min. The 10% Carbowax 20M column is subsequently removed.

Reagents

(a) Ethylene glycol, interference-free (pesticide quality).

(b) Hexane, interference-free (pesticide quality).

(c) Distilled water, interference-free.

(d) Saturated aqueous sodium chloride, interference-free.

(e) Anhydrous sodium sulfate.

(f) Parathion of known purity.

Procedure

(a) The sample in 17-20 ml of ethylene glycol is transferred to a 125-ml separatory funnel. (The reagent quantities and glassware sizes specified below apply to a sample in 20 ml of ethylene glycol and must be scaled proportionately for different volumes.) Wash the sample container with a measured amount of water and add the washings to the separatory funnel. Dilute the ethylene glycol with a total of 70 ml of water.

(b) Extract the aqueous solution 3 times with 12-ml portions of hexane (total of 36 ml).

(c) Extract the combined hexane extracts 2 times with 10-ml portions of distilled water.

(d) Dry the hexane solution by passing it through 2.6 g of anhydrous sodium sulfate contained in a funnel with a glass wool retaining plug at the top of the stem. Collect the eluate in a 125-ml Kuderna-Danish flask which has been fitted with a 10-ml receiving tube containing one 3-mm glass bead. When the extract has eluted, rinse the separatory funnel with 3 consecutive 2-ml portions of hexane, washing down the walls of the funnel. Allow each rinse to elute before adding the next. Finally, rinse the funnel and the sodium sulfate with 2 more 2-ml portions of hexane.

(e) Set the Kuderna-Danish assembly in a boiling water bath and concentrate the extract to about 5 ml. Remove the assembly from the bath and, after it is cool, disconnect the receiving tube from the flask, rinsing the joint with a little hexane. Place the tube under a nitrogen stream at room temperature and further concentrate the extract to about 0.5 ml. Rinse down the wall of the tube with hexane, delivered from a 100-μl syringe, diluting the extract to exactly 1.0 ml, and stir.

(f) Inject a 2-μl aliquot of the hexane solution into the gas chromatograph and obtain a chromatogram. The chromatographic conditions are:

Column temperature	220 C for columns 1 and 2 210 C for column 3 200 C for column 4
Injection port temperature	225 C
Detector temperature	200 C
Transfer line temperature	235 C
Switching valve temperature	235 C
Carrier gas (nitrogen) flow	120 ml/min for columns 1 and 2; 60 ml/min for column 3; and 75 ml/min for column 4.

The retention times (relative to parathion) at these conditions for parathion, related analytes, and some interfering organophosphorus pesticides are tabulated Table X-1.

The solvent-flush sample injection technique is recommended. Duplicate injections should be made. The hexane, which precedes the parathion should be vented according to (n) under Apparatus so that the detector flame is not extinguished. The conditions of the run should be such that no parathion is lost during the venting process.

(g) By comparison to standard curves for parathion, average of the area under the parathion peak is converted to the amount in ng of parathion seen by the detector. Paraoxon, if present in the sample, can be quantitated by comparison of its peak area with a standard curve for paraoxon.

TABLE X-1
RETENTION TIMES — PARATHION AND OTHER COMPOUNDS OF INTEREST

OP Compound	Column 1	Column 2	Column 3	Column 4
Parathion	1.00 (4.4 min)	1.00 (8 min)	1.00 (3.4 min)	1.00
Paraoxon	0.77	1.13	1.23	1.17
Methyl parathion	0.73	0.78	1.18	0.76
Methyl paraoxon	0.56	0.88	1.41	0.90
Amino parathion	1.04	0.78		
Dursban	1.00			
Fenthion	0.97			
Ruelene		1.01		
Phosphamidon				1.12

Adapted from *NIOSH Manual of Analytical Methods* [197].

Calibration and Standards

(a) Prepare at least 3 standard solutions in the concentration range 100-10,000 ng/ml from a stock solution of parathion in hexane.

(b) Make duplicate injections of aliquots of each parathion standard solution onto the chromatographic column and determine the peak areas.

(c) Plot the amount in ng of parathion seen by the detector vs the peak area. A straight line passing through the origin should result. If these conditions are not observed, either the linear range of the detector has been exceeded or a system malfunction has occurred.

(d) Injections of standards should be interspersed among sample injections in order to monitor detector sensitivity.

Calculations

(a) Determine the total amount in ng of parathion present in the sample:

$$\text{Sample weight of parathion (ng)} = \text{ng(0)} \times \frac{\text{Solution volume}}{\text{Injection volume}}$$

where:

ng(0) = nanograms of parathion determined from calibration curve based on peak area responses

Solution = volume in μl of the final hexane volume solution (usually 1 ml)

Injection = volume in μl of the aliquot of the volume final hexane solution injected into the gas chromatograph

(b) Convert the volume of air sampled to standard conditions (25°C, 760 mmHg):

$$V(s) = V \times \frac{P}{760} \times \frac{298}{(T + 273)}$$

where:

V(s) = volume of air in liters at 25°C and 760 mmHg

V = volume of air in liters as measured

P = barometric pressure in mmHg

T = temperature of air in degrees Celsius

(c) The concentration of parathion can be expressed in ng/liter or $\mu g/m^3$:

$$\text{(u) g/cu m} = \text{ng/liter}$$

or

$$\text{(u) g/cu m} = \frac{\text{total ng}}{V(s)}$$

XI. APPENDIX III

METHOD FOR BIOCHEMICAL DETERMINATION OF BLOOD CHOLINESTERASES

The method of Wolfsie and Winter,[147] a micromodification of the Michel method,[133] is recommended for the measurement of cholinesterase activity.

Reagents

All reagents should be at least ACS reagent grade.

(a) Buffer Solution I (for erythrocytes)

For 1 liter of buffer, dissolve 4.1236 g sodium barbital (0.02 M), 0.5446 g potassium orthophosphate, di-H (0.004 M), and 44.730 g potassium chloride (0.60 M) in 900 ml of distilled water; 28.0 ml of 0.1 N hydrochloric acid is added while shaking the solution, and the flask is brought to volume with distilled water. The pH of Buffer I should be 8.10 at 25°C.

(b) Buffer Solution II (for plasma)

For 1 liter of buffer, dissolve 1.2371 g sodium barbital (0.006 M), 0.1361 g potassium orthophosphate, di-H (0.001 M), and 17.535 g sodium chloride (0.30 M) in 900 ml of distilled water and add 11.6 ml of 0.1 N hydrochloric acid before bringing to volume. The pH of Buffer II should be 8.00 at 25°C.

The pH of the buffer solutions will decrease over a period of several weeks. The pH should be checked before using and, if it has dropped more than 0.03 pH units, it should be discarded and a fresh solution made.

(c) Acetylcholine Substrate (for erythrocytes)

This is 0.11 M acetycholine chloride (2.000 g in 100 ml of distilled water).

(d) Acetylcholine Substrate (for plasma)

This is 0.165 M acetycholine chloride (3.000 g in 100 ml of distilled water).

A few drops of toluene are added to each acetylcholine substrate solution as a preservative, and the solutions are refrigerated when not in use. The acetylcholine solutions should not be retained for more than 1 week.

(e) Saponin Solution

This is 0.010% saponin (100 mg in 1,000 ml of distilled water). This solution should be made fresh as needed.

Apparatus

(a) Centrifuge capable of 3,500 rpm and holding capillary sample tubes.

(b) A pH meter, calibrated to 0.01 pH units.

(c) 0.02 ml Sahli-type hemoglobin pipet.

(d) Constant-temperature bath, 25°C.

(e) 100- and 1,000-ml volumetric flasks.

(f) Heparinized capillary tubes.

(g) A Bunsen burner.

Sampling, Handling, and Preparation

Blood is collected from a clean, dry fingertip in a heparinized glass capillary tube. The blood is allowed to flow into the capillary tube until the tube is approximately ¾ full, leaving one end free by 1-1.25 inches, to permit flame-sealing of the tip of the tube without overheating the blood sample.

The finger should be pricked deeply and care should be taken to collect only free-flowing drops of blood in order to guard against the initiation of the clotting process before the blood contacts the heparin lining in the wall of the capillary.

One end of the capillary is plugged with solid (room temperature) paraffin and the other (free) end is sealed in the flame of a Bunsen burner. The capillary may now be labeled with an adhesive tape tag bearing a serial number or name and date. The sample should then be centrifuged at 3,000-3,500 rpm for 50-60 minutes. When the sample has been so treated, it may be shipped to a laboratory, if necessary, or stored for several days (preferably in a refrigerator) without appreciable change.

Analysis

For analysis, the capillary is cut cleanly with a sharp ampul file. From the packed-cells section of the capillary, draw 0.02 ml directly into a Sahli-type hemoglobin pipet. The ends of the capillary must be cut evenly to provide satisfactory juxtaposition with the tip of the pipet. Discharge the contents of the pipet directly into 1.0 ml of 0.01% saponin solution in a microbeaker, and rinse the pipet well (3 times) into the solution. Glass vials, 1 inch (2.5 cm) deep by ¾ inch (19 mm) in diameter, are convenient for electrometric testing. They

will fit in the carrier of a standard pH meter, and, when used with a clean rubber stopper, will eliminate transfer of the sample from a test tube for each pH measurement. Plasma is taken from the appropriate section of the capillary in the same manner as the packed erythrocytes and discharged into 1.0 ml of distilled water, the Sahli pipet being rinsed into the solution (3 times) as with the erythrocytes.

Erythrocyte Cholinesterase Assay

(a) One milliliter of hemolyzed erythrocyte solution is added to 1 ml of buffer solution I and placed in a 25°C water bath.

(b) After a 10-minute equilibrium period, the initial pH_i is determined to the nearest 0.01 pH unit with the pH meter.

(c) Two-tenths milliliter of 0.11 M acetylcholine chloride solution is added with rapid mixing and the time is recorded.

(d) The reaction proceeds for 1-1.5 hours before the final pH_f is noted.

The beaker containing the solution should be shaken when the glass electrode is introduced to speed the establishment of equilibrium.

Note: The buffer solution I is designed to yield a pH of 8.00 after the addition of hemolyzed human erythrocytes.

Plasma Cholinesterase Assay

(a) One milliliter of diluted plasma is mixed with 1 milliliter of buffer solution II.

(b) The solution is allowed to equilibrate in a 25°C water bath for 10 minutes.

(c) At the end of 10 minutes, the initial pH_i is noted to the nearest 0.01 pH unit.

(d) Two-tenths milliliter of 0.165 M acetylcholine chloride solution is added with rapid mixing.

(e) The reaction mixture is incubated for 1-1.5 hours before the final pH_f is noted.

Calculations

The final units derived from this assay are ΔpH/hour:

$$\text{Delta pH/hour} = \frac{\text{pH (i)} - \text{pH (f)} - \text{bc}}{\text{t (f)} - \text{t (i)}}$$

where:

pH (i) = initial pH

pH (f) = final pH

t (f) − t (i) = time elapsed in hours between reading pH (i) and reading pH (f)

b = nonenzymatic hydrolysis corresponding to pH (f)

c = correction for variations in delta pH/hour with pH, corresponding to pH (f)

The b and c correction factors are given in Table XI-1.[133] Average baseline values of erythrocyte and plasma cholinesterase activity determined by this method for healthy nonexposed men and women are given in Table XI-2.[145,147] The value for average RBC ChE activity for men is drawn from Wolfsie and Winter.[147] The value for women is obtained by multiplying the average RBC ChE activity figure for men[147] by the ratio of mean ΔpH/hr for women to mean ΔpH/hr for men derived from the data of Rider et al.[145] The use of the data of Wolfsie and Winter[147] allows for the increased packing and possible contamination of RBC's by plasma ChE. Plasma ChE values were selected from Rider et al,[145] since their larger data base probably provides a closer approximation of the true population mean of normal values for plasma ChE activity. For the same reason, their data provide the most reliable women/men ratio for RBC ChE activities.

TABLE XI-1
CORRECTION FACTORS FOR USE IN EQUATION FOR ΔpH/HR

	Erythrocyte/ Cholinesterase Corrections		Plasma/ Cholinesterase Corrections	
pH (f)	b	c	b	c
7.9	0.03	0.94	0.09	0.98
7.8	0.02	0.95	0.07	1.00
7.7	0.01	0.96	0.06	1.01
7.6	0.00	0.97	0.05	1.02
7.5	0.00	0.98	0.04	1.02
7.4	0.00	0.99	0.03	1.01
7.3	0.00	1.00	0.02	1.01
7.2	0.00	1.00	0.02	1.00
7.1	0.00	1.00	0.02	1.00
7.0	0.00	1.00	0.01	1.00
6.8	0.00	0.99	0.01	1.00
6.6	0.00	0.97	0.01	1.01
6.4	0.00	0.97	0.01	1.02
6.2	0.00	0.97	0.01	1.04
6.0	0.00	0.99	0.01	1.09

Adapted from Michel [133].

TABLE XI-2

MEAN BASELINE VALUES OF ERYTHROCYTE AND PLASMA CHOLINESTERASE IN MEN AND WOMEN [Δ pH/HR]

	Men	Women
Erythrocyte Cholinesterase		
Mean	0.861	0.843
Plasma Cholinesterase		
Mean	0.953	0.817

Adapted from Rider et al [145] and Wolfsie and Winter [147].

TABLE XI-3

NORMAL VALUES FOR CIRCULATING CHOLINESTERASES IN HEALTHY NONEXPOSED PERSONS*

Subjects	Erythrocyte Cholinesterase Activity (Δ pH/hr)			Plasma Cholinesterase Activity (Δ pH/hr)			Reference
	Range	Mean	SD	Range	Mean	SD	
400 men	0.58-0.95	0.766	0.081	0.52-1.39	0.953	0.187	Rider et al** [145]
400 women	0.56-0.94	0.750	0.082	0.38-1.25	0.817	0.187	
255 men	0.554-1.252	0.861	0.091	0.408-1.652	0.912	0.112	Wolfsie & Winter*** [147]
120 men & women	—	—	—	0.58-1.37	0.94	0.16	Vorhaus and Kark [146]
20 men	—	—	—	—	0.95	0.24	Fremont-Smith et al [200]
20 women	—	—	—	—	0.78	0.12	

* All analyses performed by method of Michel. [133]

** Ranges, means, and standard deviations in this study are estimates based on data extrapolated to age 40; ranges reflect elimination of highest 1% and lowest 1% of values.

*** Analytic method modified for smaller blood sample.

XII. APPENDIX IV

DIAGNOSIS AND MEDICAL MANAGEMENT OF PARATHION POISONING

The text appearing immediately below is adapted in large part from a publication entitled *Prevention and Management of Organophosphate Poisoning*. This material, approved in 1970 by the AMA Committee on Occupational Toxicology of the Council on Occupational Health, originally appeared in the Journal of the American Medical Association in 1971.[201]

(a) Diagnosis

A diagnosis of parathion intoxication is based primarily on a definite history of exposure to the material usually 6 hours or less before onset of illness plus clinical evidence of diffuse parasympathetic stimulation. Laboratory verification is based on depression of plasma and RBC ChE to a level substantially (50% or more) below preexposure values determined according to the recommended standard. Monitoring of RBC ChE activity levels, as specified in the recommended standard, is intended to prevent the development of poisoning by removing the exposed worker from the toxic environment at a point prior to the development of signs and symptoms. In actual practice, the ChE test is often of value as a confirmatory, rather than a diagnostic, procedure. In treating patients with moderate to severe parathion poisoning, the clinician should act on his clinical impression and on the history of exposure rather than wait for laboratory confirmation of ChE activity depression.

Initial signs and symptoms of parathion intoxication are usually giddiness, sometimes accompanied by headache, constriction of the pupils (miosis), and tightness in the chest. Nausea, vomiting, sweating, blurred vision, weakness, diarrhea, abdominal cramps, and pallor may follow. In moderate to severe cases of intoxication, signs and symptoms may also include dyspnea, salivation, lacrimation, muscular twitchings, convulsions, cyanosis, shock and cardiac arrhythmias, coma, and possibly death. Greatly increased salivary and bronchial secretions are common. In the case of mild poisoning, where the differential diagnosis may be puzzling, the results of the cholinesterase test may be necessary to establish a definite diagnosis.

(b) Treatment

Treatment of parathion poisoning ranges from simple removal from exposure in very mild cases to the provision of very rigorous supportive and antidotal measures in severe cases. In the moderate to severe cases, weakness of the muscles of respiration may necessitate the use of positive pressure artificial respiration. Careful attention must be paid to removal of secretions and to maintenance of a patent airway. Anticonvulsants, such as trimethadione and sodium thiopental, may be necessary. The critical point is that respiration must be maintained since death usually results from respiratory failure (usually accompanied by a secondary cardiovascular component) due to weakness of the muscles of respiration and to accumulation of excessive secretions in the upper respiratory tract. If therapy is to be effective, it must be instituted with the least possible delay. To relieve the symptoms of excess parasympathetic stimulation, large (heroic) doses of atropine are usually required.

For adults, as much as 2-4 mg (1/30 g to 1/15 g) should be administered by intravenous or intramuscular injection every 5-10 minutes until signs of atropinization appear: dry, flushed skin; tachycardia as high as 140 beats/minute; dilation of the pupils. Obviously, caution must be exercised in administering these amounts of atropine. No generalization of the amount necessary is possible; the dose is administered according to the patient's condition. As much as 50 mg may be required the first day. A mild degree of atropinization should be maintained as long as symptoms are in evidence.

Although atropine remains the drug of choice, particularly if the treatment must be continued for more than a day or two, pralidoxime (Protopam; 2-PAM) chloride is a commercially available antidote which complements atropine and hastens the reactivation of parathion-inhibited ChE's. For adults moderately to severely poisoned by parathion, pralidoxime chloride should be used along with atropine, injected intravenously as an initial dose of 1 g at a rate not in excess of 500 mg/minute. If weakness is not relieved or if it recurs after 20 minutes, the dose may be repeated. After an overwhelming inhalation, skin exposure, or ingestion of parathion, the doses may be doubled. For children, the usual dose is 25-50 mg/kg of body weight. Treatment with pralidoxime chloride will be most effective if given within 24

hours after poisoning. (Its usefulness after 36-48 hours is questionable.) Together, the 2 antidotes, atropine and pralidoxime chloride, are more effective in treating parathion poisoning than is either one alone. Morphine and other respiratory depressant drugs, theophylline and aminophylline, are specifically contraindicated because they accentuate symptoms.

It is of great importance to decontaminate the patient. The stomach should be lavaged and a saline cathartic administered if parathion has been ingested. However, nothing should ever be given by mouth to an unconscious person. Contaminated clothing should be removed at once and the skin and hair should be washed with generous amounts of water (and preferably soap) or other suitable decontaminating solution. Cleansing may be best accomplished under a shower or by submersion in a pond or other body of water if the exposure occurred in the field. Careful attention should be paid to cleansing of the hair. The patient should be attended and monitored continuously for a minimum of 24 hours, since serious and sometimes fatal relapses have occurred because of continuing absorption of the insecticide or dissipation of the effects of the antidote.

(c) First-Aid Measures

Industrial handbooks discussing the use of various OP compounds typically include a section on first aid.

General signs and symptoms of parathion poisoning are headache, blurred vision, weakness, nausea and vomiting, cramps, looseness of the bowels, and pain or tightness in the chest. Signs and symptoms may also include sweating, pinpoint pupils (even when in the shade), drooling, watering eyes, difficulty in breathing, and convulsions.

If the above warning signs and symptoms are definitely observed and parathion poisoning is suspected, the following measures should be put into effect immediately:

(1) If the patient is not breathing, start artificial respiration.

(2) In all cases of suspected parathion poisoning, call a physician at once.

(3) If parathion has been swallowed, induce vomiting by sticking a finger into the throat, by giving warm salt water (one tablespoonful of salt to a glass of water), or by giving soapy water. Repeat until vomit fluid is clear. Make the victim drink plenty of water or milk, if available; however, NEVER GIVE ANYTHING BY MOUTH TO AN UNCONSCIOUS PERSON.

(4) If the patient has been poisoned by contact with the insecticide, move him away from the possibility of any further exposure. If parathion has been spilled or splashed onto the clothes or skin, remove clothing immediately and wash the skin thoroughly with water (and preferably soap) or other suitable decontaminating solution; use copious amounts of water/decontaminating solution in rinsing. If splashed into the eyes, wash continuously with copious amounts of water for at least 15 minutes. Care should be taken to prevent contamination of the skin and clothing of those providing first aid.

(5) Keep the patient lying down, quiet, and warm. Take him to the nearest source of medical care if not available at the scene of poisoning.

(6) Try to find out the names of all pesticides (including the names of their active ingredients) with which the patient has been working or with which he has been contaminated and tell the physician. Take a label from the container (or a clean, labeled container) to the physician along with any other available literature describing the products involved.