[9] C. Bottura, D. P. Neves, E. Mattar and H. L. de Oliveira, "Ulhoa Cintra A.B.—Hypoglucemia y Coma hipoglucémico consecutivo a intoxicación aguda por alcohol etílico," *Rev. Hosp. Clin. Fac. Med. Univ. Sao Paulo*, 4(3), 733 (1949).

[10] P. B. Neame, and S. M. Joubert, "Post Alcoholic Hypoglucemia and Toxic Hepatitis" *Lancet*, 2, 893 (1961).

[11] J. C. Foches and G. M. Duncan, "The Effect of Alcohol on Liver Lipids and on Line and Heart Glycogen," *Quart. J. Studies Alcohol*, 11, 373 (1950).

[12] N. Freinkel, D. C. Singer, C. D. Silbert, and J. B. Anderson, "Studies on the Pathogenesis and Clinical Features of 'alcoholic hypoglucemia,'" *J. Clin. Invest.* 41, 1359 (1962).

[13] D. M. Tennerat, "Factors Influencing the Effects of Alcohol on Blood Sugar and Liver Glycogen," *Quart. J. Studies Alcohol*, 2, 263 (1941).

[14] C. S. Lieter, C. M. Leevy, S. W. Stein, W. S. George, G. R. Cherrick, W. H. Abelmann, and C. S. Davison, "Effects of Ethanol on Plasma Fall Fatty Acids in Man," *J. Lab. Clin. Med.*, 59 826 (1962).

[15] L. H. Cummins, "Hypoglucemia and Convulsions in Children Following Alcohol Ingestion," *J. Pediat.*, 58, 23 (1961).

[16] E. Giménez, N. Vallejo, J. Colombo, A. De Palma, R. Escobari, C. Jarach, M. Larguía, V. Penchazadeh, and O. Stoliar, "Intoxicación alcohólica percutánea," Sociedad Argentina de Pediatría, Mayo, 1967.

[17] J. P. Von Vartburg, J. L. Bethune, and B. L. Valler, "Human Liver: Alcohol Dehydrogenase: Kinetic and Physicochemical Properties," *Biochemistry*, 3, 1775 (1964).

[18] R. Sandler and N. Freinkel, "Interrelationships between the Formation of Gliceride, Glycerol and Glucose from Alanine by Liver Slices," *Metab. Normal Expil.*, 75, 7020 (1966).

[19] N. A. Freinkel, Cohen, R. A. Arky, and A. E. Foster, "Alcohol Hypoglycemia. II. A Postulated Mechanism of Action Based on Experiments with Rat Liver Slices," *J. Clin. Endocrinol.* 25, 76 (1965).

[20] N. Freinkel, D. L. Singer, R. A. Arky, S. J. Bleicher, J. B. Anderson, and C. K. Silbert, "Alcohol Hypoglycemia. I. Carbohydrate Metabolism of Patients with Clinical Alcohol Hypoglycemia and the Experimental Reproduction of the Syndrome with Pure Ethanol," *J. Clin. Invest.*, 42, 1112 (1963).

CLINICAL TOXICOLOGY, 1(1), pp. 49-56, March, 1968

P9.

The Treatment of Poisoning: A Program for the Medical Curriculum*

Eric G. Comstock, M.D.†
Houston, Texas

The hazard of poisoning is an inescapable by-product of the increasing chemosynthetic accomplishments of modern civilization. In no previous era has there been so conveniently available such a variety of potent poisons for accidental or intentional self-destruction. The magnitude of the problem is indicated by the occurrence of over 1 million cases of poisoning and 8000 deaths each year [1].

The problem of poisoning is widely recognized. Congress has authorized the President of the United States to designate the third week of March as National Poison Prevention Week. The hazard of poisoning by the diverse chemicals packaged for use in the home has been further recognized by Congress through the enactment of the Federal Hazardous Substances Labeling Act which provides for cautionary labeling on millions of packages which enter the American home. Very recently, the Food and Drug Administration, impressed with the urgent need for effective induction of vomiting removed the prescription requirement for bottles of 30 ml or less of syrup of ipecac so that it could be available in the home as a first aid measure when its use is advised by a physician. The American Registry of Pathology at the Armed Forces Institute of Pathology maintains the Registry of Tissue Reactions to Drugs which serves to collect and evaluate tissue reactions to drugs. There has been established a nationwide network of poison information centers to serve the physician treating cases of poisoning. The package insert of virtually all pharmaceuticals contains comments on overdose and poisoning. Most pharmaceutical companies and many chemical companies provide for special routing of calls from physicians who need information on the treatment of acute poisoning. The U.S. Department of Health, Education, and Welfare has a pharmacology-toxicology program within the National Institue of General Medical Sciences to encourage fundamental research on problems of toxicology. The U.S. Public Health Service Office of Pesticides supports the Community Studies Section which has been organized for "In-depth clinica and biochemical evaluation of individuals with acute and/or chronic exposure to pesticides."

*Presented at the Tenth Annual Meeting of the American Association of Poison Control Centers, Shoreham Hotel, Washington, D.C., October 23, 1967.

†For correspondence or reprints: P.O. Box 2565

Many professional training programs include an emphasis on poisoning and its treatment. The veterinary schools provide elaborate courses on poisoning as it relates to veterinary practice, and the schools of pharmacy devote some time to the problem of poisoning as it relates to the practice of pharmacy. In 1964 the Poison Control Branch of the Public Health Service's Division of Accident Prevention published "A Guide for Teaching Poison Prevention in Kindergartens" [2]. Since that time several states have had teaching programs on poisoning in their kindergartens.

It is time for the medical schools to acknowledge the problem of poisoning and to provide practical training which will prepare the physician to manage acute poisoning emergencies effectively.

The present status of medical management of acute poisoning is defensible by a variety of pleadings, each one of which sums to inadequacy. In nearly every instance the case of acute poisoning descends upon the physician as a surprise event. Often no training in the management of acute poisoning has been available to him, and any insight he may have has come from clinical reports of one or a few cases of poisoning published by physicians whose training has not prepared them as investigators. Such reports may be poorly documented and the conclusions may be frankly erroneous, but they gain authenticity by virtue of their publication. The case of poisoning is treated as though it were the first and with the fervent hope that it will be the last case which the physician has occasion to see. No useful information is accumulated and nothing is contributed to the state of the art of the treatment of poisoning. When the case is one for which there exists a specific and effective therapeutic approach, the necessary materials frequently are not available. It is more commonly the case that a specific antagonist or course of therapy does not exist and valuable time and occasionally the patient is lost while searching for one. In the emergency situation, approaches to therapy are used which would be avoided by better knowledge of the chemistey or pharmacology of the substance involved. An example is the time lost needlessly by the protracted administration of syrup of ipecac to induce vomiting after ingestion of centrally acting antiemetic phenothiazine derivatives. Quite recently a review was circulated nationally to resident physicians advocating hemodialysis as the approach of choice for severe glutethimide intoxication. However, the amount of glutethimide recovered from the body by aqueous hemodialysis is very small because of the low solubility of glutethimide in water. Where benefit appears to have been derived from aqueous dialysis, it is probable that the improvement reflects normalization of the more readily diffusible constituents of blood. In contrast, the lipid solubility of glutethimide has been utilized advantageously in a technique of lipid dialysis. The equilibration of blood with lipid separated by a membrane has been demonstrated to remove glutethimide from the blood [3]. Another promising approach, which is now experimental, is the passage of blood through a column of charcoal, the gluethimide being retained on the charcoal stationary phase [4].

Because of the unusual pressures and because of the uncertainties which occur in the acute poisoning situation, the physician may be inclined to pursue exotic and unproved techniques of therapy directed toward the poison while overlooking lifesaving procedures directed toward support of the patient. Glutethimide intoxication is an example of a clinical situation where more emphasis on treating the patient and less emphasis on treating the poison would result in the salvage of virtually every case reaching medical attention before anoxic injury has occurred.

An emergency room program for the treatment of poisoning which consists of a book on toxicology and the telephone number of the poison information center simply is no longer adequate. An emergency room program must provide for an inventory of drugs and equipment necessary for the treatment of poisoning and for a means of keeping these inventories up to date. Methods for first aid for poisoning must be posted and the paramedical personnel who are likely to encounter the patient first must be provided training in the use of first aid for poisoning. A schedule for the orientation of the house staff must be established and supervised by an attending physician, with special interest in the clinical management of poisoning. Protocol for the collection of suitable specimens for the diagnosis of poisoning should be posted and provisions made to prevent the discarding of valuable materials such as lavage fluid. Laboratory personnel must be made aware of the rapid procedures for the determination of toxic substances in biological specimens and they must be trained in the use of these procedures so that they are available to the physician on an emergency basis.

Only the physician can establish an emergency room program and only an interested and knowledgeable physician can see that it is carried out effectively. The training required to improve the emergency treatment of poisoning can be provided in the medical school and it can be provided for the practcing physician as a 1-day intensive training program. An important goal of such a course is the reorientation of medical thought from the concept that poisoning is a detached and catastrophic event to the concept that poisoning is a regularly occurring clinical entity which yields to the application of the same principles of sound medical practice as are applied daily in other circumstances. The management of the poisoned patient differs from that of any other acutely stressed patient by only a handful of special drugs and a few fundamental concepts which would be presented during the course. Table 1 presents an outline of the content of such a course.

Practical experience with the management of poisoning can be achieved only in the emergency room and during the subsequent hours of continuous attendance in the intensive care unit. The basic organization to provide practical experience in the treatment of poisoning is the poison team to which members of the house staff are assigned. The chief should be an individual on 24-hr call. During this assignment the physician will become intimately familiar with any special supplies or equipment used in the treatment of poisoning. He will be responsible for the continuous state of readiness of the poison room. The poison team should include an assistant from the intern staff; on-call residents in surgery, pediatrics, anesthesiology, and neurology; and follow-up members from physical medicine and psychiatry. Medical students assigned to this team can provide a great deal of practical assistance in clinical management. Assignment of responsibility for care of the varied needs of the acutely poisoned patient among the team members should provide for maximally effective use of resources both for treatment and for training. The poison team must be supported by the consulting staff, whom they may call upon as special problems arise.

Table 1
Outline of a Course in Clinical Toxicology

I. Introduction
- A. Definition: the scope of clinical toxicology
- B. Prevention of poisoning
  1. Private, community, and governmental resources
  2. The role of the physician
  3. Teaching poison prevention in the public schools
- C. Resources available to the physician
  1. Cautionary labeling
  2. Local and regional poison information centers
  3. Chemical and Drug manufacturers
  4. Private and governmental service organization
  5. Other professional specialties
     a. Medical: pathologists, clinical chemists, clinical pharmacologists, industrial physicians, pharamacists, clinical toxicologists
     b. Industrial: industrial hygienists, industrial hygiene chemists, organic chemists, analytical chemists, botanists
  6. Bibliography of recent texts and papers of a review type

II. First Aid for Poisoning
- A. First aid for poisoning in the home
- B. Training of paramedical personnel
- C. An outline of methods for first use for poisoning (printed manual to be distributed)
- D. Organization of the community hospital for first aid and initial treatment of poisoning

III. Diagnosis of Poisoning
- A. Diagnostic criteria and their relative reliability
- B. Clinical diagnosis
  1. History
     a. Past history and preexisting illness
     b. Current drug therapy and drug-use history (emphasis on need for maintenance therapy or possible withdrawal reactions)
     c. Physicians seen and prescriptions received over past year, particularly where injury may have been intential
     d. Employment history, especially recent job changes
     e. Avocations and unusual activities
     f. Changes in attitudes or personal habits
  2. Present illness
     a. Time last known to be well
     b. Time of onset and nature of first symptoms
     c. Activities immediately prior to onset
     d. Environmental survey for possible containers of toxic substances and clues to route of contamination, for example, toxic or asphyxiant gases
  3. Physical examination: points of special emphasis (note time)
     a. Voluntary or involuntary activity
     b. State of consciousness
     c. Skin: stains, burns, contaminating oils, trauma, puncture wounds, capillary beds, sweating

     d. Head: hair distribution, scalp lesions, trauma
     e. Eyes: movement, pupil size and reactions, reflexes fundi, chemical damage to mucous membranes or cornea
     f. Mouth: stains, burns, irritation, coagulation necrosis, foreign bodies, trauma to mucous membranes
     g. Chest: respiratory rate, pattern, excursion, auscultatory findings
     h. Heart: rate, rhythm, valve sounds, murmurs
     i. Abdomen: distention, bowel sounds, tenderness, palpable organs
     j. Gentialia and rectum: excoriation, irritation, foreign bodies
     k. Muscles: tone, tics, fasciculation, paresis, paralysis, muscle mass loss
     l. Neurological: orientation, hallucinations, sensory perception, motor disturbances, tremors, convulsive activity, normal and pathological reflexes, depth of coma
- C. Routine (conventional) laboratory examination: pointing out procedures with toxicologic implications
  1. Lumbar puncture: pressure, gross appearance, cell count, chemistries
  2. X-ray
     a. Chest: initial and after 24 hr
     b. Abdomen: radio-opaque particles: mercury, lead, dirt, etc.
  3. Electrocardiagram
  4. Electroencephalogram
  5. Blood chemistries: electrolytes, enzymes on admission and after 24 hr
  6. Urine: gross appearance, microscopic morphology, chemical examination
- D. Analytical toxicology: chemical identification of the toxic substance or its metabolites (manual to be distributed lists approximately 500 toxic substances with information on specimens to be collected and notes on interpretation)
  1. The original material
  2. Emesis or lavage fluid
  3. Blood specimens
  4. Urine specimens
  5. Stool specimens
  6. Skin washings
  7. Fat biopsy
  8. Expired air
  9. Other specimens
- E. Rapid methods for chemical diagnosis of poisoning in the emergency room; numerous relatively simple laboratory methods have been developed for detection of toxic substances in body fluids within minutes to 1 hr (manual of rapid procedures will be provided)
- F. Pitfalls in the diagnosis of poisoning as illustrated by case presentation
- G. Multiple etiology: discussion of hazards involved when thorough laboratory studies are not performed, with case presentation illustrating misinterpretations which result

IV. Principles of the Treatment of Poisoning
- A. Decontamination
  1. Clothing
  2. Hair, skin, finger nails, eyes, mouth

3. Gastrointestinal tract
   a. Induction of vomiting: how, when, for what
   b. Gastric lavage: how, after how long, for what
   c. Purgation: with what, for what, when

B. Prevention of absorption
   1. Immiscible phase
   2. Adsorbants: activated charcoal, etc.
   3. Formation of insoluble derivatives
   4. Reaction with a fixed ion, ion-exchange resins

C. Neutralization
   1. Acids
   2. Bases

D. Increase in rate of excretion
   1. Diuresis: chemical, osmotic, pH control
   2. Enteroenteric, enterohepatic circulation, interruption by binding material in the gut
   3. Dialysis
      a. Peritoneal
      b. Extracorporeal
         (1) Aqueous
         (2) Lipid
         (3) Other: charcoal column
   4. Ionic trapping
   5. Conversion to a more readily excreted form

E. Prevention of the formation of a more toxic derivative, i.e., methanol treated with ethanol

F. Removal of dependence on a sensitive system, i.e., hyperbaric therapy for methemoglobinemia

G. Blocking the sensitivity of an end organ: i.e., atropine block of hypercholinergic crisis by stabilizing the polarized cell membrane

H. Reversal of enzyme inhibition, i.e., proto-PAM

I. Conversion to less toxic form

J. Nonspecific
   1. Supporting vital function
   2. Awareness of delayed effects: how long should a patient be observed when he is asymptomatic

K. Formulary of drugs useful in the treatment of poisoning

L. Contraindications: what are they and how should they be interpreted

M. An emergency room program for the treatment of poisoning (booklet to be distributed which outlines an emergency room program with inventory of drugs and equipment, first aid program, and numerous practical aids for the physician who wishes to establish a program in the community hospital)

V. The Management of Coma

A. Determining and monitoring the depth of comma

B. Respiratory support
   1. Airway
      a. Oropharyngeal
      b. Intratracheal intubation
      c. Tracheotomy
   2. Intermittant positive pressure respiration
      a. Mouth to mouth
      b. Face mask and bag

      c. Anesthesia machine
      d. Atuomatic positive pressure respirator
   3. Inhalation therapy
      a. Choice of gases
      b. Aerosol and mist therapy
   4. Routine maintenance of the respiratory tract during prolonged coma

C. Support of blood pressure
   1. Intravenous access
   2. Blood volume
   3. Choice of IV fluids
   4. Use of vasopressors
   5. Use of CNS stimulants

D. Fluid and electrolyte balance in prolonged coma

E. Renal function and maintenance of urinary output

F. Nursing care during prolonged coma

VI. Clinical Management of Poisoning due to Specific Substances (this section to be adjusted to accommodate the time available)

A. Sedative drugs
   1. Polar
   2. Nonpolar

B. Insecticides

C. Carbon monoxide

D. Toxic metals

E. Etc.

Beyond the benefits to be derived from the personal experience in the sound management of poisoning, additional benefits are to be gained from a training program in clinical toxicology. These include the following:

1. A treatment center to serve the immediate vicinity by providing sound emergency care for acute poisoning by a resident staff who is expecting poisoning to occur and where special needs for treatment have been anticipated and immediately are available

2. Specialized laboratory needs for establishing etiology chemically and for monitoring the efficacy of therapy are avilable using techniques which provide necessary data within clinically useful time limits.

3. Appreciation of the unique research opportunity in clinical pharmacology which each poisoned patient presents will provide for suitable clinical and biochemical documentation of each case. This will make available the needed data on route of excretion, chemical nature of metabolites, and the correlation of clinical and chemical findings required to develop and evaluate courses of therapy.

4. As functioning units, such treatment centers will serve as prototypes and they will establish a minimum level of competence for any emergency facility for the treatment of poisoning.

5. Reports from such a training program will emerge in the medical literature and will constitute the sound clinical and chemical basis which is required for progress in clinical toxicology.

Now is the time for medical schools to incorporate an urgently needed program in clinical toxicology into their training curriculum.

References

[1] J. McBay, "Law-Medicine Notes: Poison Control," *New Engl. J. Med.*, 277, 534 (1967).

[2] United States Department of Health, Education, and Welfare Public Health Service, Division of Accident Prevention, "A Guide for Teaching Poison Prevention in Kindergartens and Primary Grades," Publ. 1381, Sept. 1965.

[3] J. H. Shinaberger, L. Shear, L. E. Clayton, K. G. Barry, M. Knowlton, and L. R. Goldbaum, *Trans. Am. Soc. Artificial Internal Organs*, 11, 173 (1965).

[4] M. H. De Myttenaere, J. F. Maher, and G. E. Schreiner, Hemoperfusion through a Charcoal Column for Glutethimide "Poisoning," *Trans. Am. Soc. Artificial Internal Organs*, 13, 190 (1967).

CLINICAL TOXICOLOGY, 1(1), pp. 57-61, March, 1968

p,p'-DDE and p,p'-DDT Residues in Human Placentas, Cords, and Adipose Tissue*

Richard T. Rappolt, Sr., M.D.
Department of Public Health
Emergency Hospital Service
San Francisco, California

and

Wayne E. Hale, B.S.
Berkeley, California

INTRODUCTION

The finding of certain deposited chlorinated hydrocarbon residues in various human tissues [1-4] has led to speculation as to which tissue and which residue might best be used in routine analysis to determine whether such deposits are increasing, decreasing, or holding their own in the human body. The possible use of obstetrical material was investigated because studies encompassing occupational or household usage patterns would be more meaningful with living subjects to describe exposures. Also, subsequent placentas and umbilical cords would indicate qualitative and quantitative trends in residue deposits in the population.

Any implication as to mortality and morbidity concerning DDT and its metabolites in the human population is not within the scope of this article.

*Presented at the Tenth Annual Meeting of the American Association of Poison Control Centers, Shoreham Hotel, Washington, D.C., October 23, 1967. This research was supported by the Pesticides Program; Department of Health, Education, and Welfare; Public Health Service; National Communicable Disease Center; Atlanta, Georgia; under Contract Number PH 86-65-87.