Research Plan

Childhood Lead Poisoning: Comparative Studies in the Baboon

Objectives and Background

Lead poisoning in children resulting from the ingestion of peeling or chipped paint, is a well known problem of most major cities in this country. The objectives of the following proposed study are to clarify many of the metabolic aspects of lead toxicity and at the same time to provide information useful for selection of the most effective therapy for children exposed to excessive amounts of lead. For the coming year it is expected that more than 1,000 children will develop lead poisoning in New York City. At the present time the only screening test in use for lead exposure is the blood lead determination. In addition to being highly dependent upon the time at which exposure to lead occurred, the blood lead concentration has been cited as a poor indicator of body burden and the probability of developing symptoms of lead toxicity (Kehoe, 1964-1966). It is conceivable that treatment should occur at early stages of exposure to prevent clinical effects and sequelae in children.

To date there exists in the scientific literature many reports on the ability of several biochemical tests to give early indication of lead exposure before symptoms

develop. The greatest value of these tests, used singularly or in combination is not entirely understood for the evaluation of lead exposure in children. A review of the topic of lead intoxication has recently been published which considers these and other questions which are currently unanswered (Hammond, P. B. 1969).

Specific Aims

The proposed study will be designed to consider the following questions:

1. What are the interrelationships between exposure, time and the symptomatology of toxicity?
2. What clinical test or combination of tests best define(s) the history of exposure and the propensity for developing lead poisoning?
3. Based on the metabolic data obtained in answering the first two questions and data on body burden distributions from concurrent projects, this will provide information which should allow logical understanding of existing studies on therapy for abnormal lead body burdens.

Rationale and Significance

The rationale for this approach is that only by considering the interrelations between the various metabolic parameters of lead ingestion will some of the inconsistencies in the literature be resolved. It is essential in this

respect to first achieve an understanding of the most probable exposure history. This study has been designed to provide a basis for classification as to dose and time relationships. Fundamental data such as clearance times from various body organs (blood, liver, etc.) and transfer times between such organs are being obtained in ongoing work sponsored by the U. S. Atomic Energy Commission and National Institutes of Health. These constants can be used to convert the most probable exposure history to an estimated body burden and organ distribution pattern.

This should provide a basis for the answers to many questions. For example, what is the reason for the so called "re-poisoning" that has been noted even after removal from the source of lead (Guinee, V. P. 1970). Is the blood lead level in itself the best indicator of lead body burden and/or the probability of developing symptoms of toxicity? Are the various tests for heme precursors and enzymes as useful for diagnoses with children as for adults and what combination of biochemical and clinical examinations are required to give the best indication of exposure?

Proposed Plan of Investigation

To answer these questions the following research plan has been developed.

Approximately eight young (15mo. old) baboons will be

exposed to selected amounts of lead by both the injection and ingestion routes. For the injection cases tracer quantities of ^{210}Pb will be included in the injection material.

I) Determination of acute and chronic toxicity levels by intravenous injection.

A) Inject four young baboons with selected amounts of lead containing tracer quantities of ^{210}Pb; Study animals for clinical, chemical and hematological effects associated with lead poisoning; Control animals will be injected with tracer ^{210}Pb only.

1. Dr. Goldstein will be responsible for the definitive clinical examinations and will periodically examine all animals under study. On a daily basis the medical and veterinary personnel of the Laboratory for Experimental Medicine and Surgery in Primates will conduct these examination. The routine examinations will be made for manifestation of typical symptoms including tiredness, lassitude, constipation, abdominal discomfort or pain, weight loss, anorexia, altered sleep, irritability, anemia, pallor, diarrhea, nausea, blue line in gums (Burton's line), reduction of muscle power-(Wrist drop); muscle tenderness, sensory changes; symptoms or signs of neuropathy or encephalopathy.

2. Routine chemistries and hematology will

be performed for urinary ∂-aminolevulinic acid (ALA), coproporphyrin (CP), erythroctic protoporphyrin (PPE), hemoglobin, differential blood analysis, hyprochromic and stippling erythrocyte counts, urobilinogen, urobilin and amino acid assay.

3. Blood feces, and urine lead levels will be determined and "whole body" counts taken to determine ^{210}Pb concentrations in blood and total body at onset of clinical symptoms and degree of absorption at different stable lead levels.

II) Determination of absorption across intestinal wall by chronic feeding of lead and time related toxic symptoms with paint pigments.

A) Establish "normal" lead levels in all young animals - i.e., by atomic absorption spectroscopy (at importation, and after 45 days quarantine period).

B) Feed "food" pellets with known lead content to four young animals.

1. Surveillance as in Part IA, 1 to 3 Clinical, chemical and hematological on test and control animals.

Summary

The program is designed to define the parameters which determine blood lead concentrations due to ingestion of paint by children and the relation of symptoms and

clinical tests to these concentrations.

A comparative study will be performed using the baboon as a test animal. These animals serve as excellent human models based on known physiological data and ongoing lead distribution work.

Sufficient comparative data will be obtained on extremely young baboons to provide for comparison with the known parameters of lead intoxication in adult humans. Concurrent studies funded by other sources will provide knowledge of body burden distributions by tissue and/or organ.

Location of Facilities

The Anthony J. Lanza Laboratory of the Institute of Environmental Medicine, New York University Medical Center and the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP) are located in Sterling Forest, Tuxedo, New York. The animal housing, treatment and observation will be handled at the latter facility.

Chemical, radiological and clinical testing will be performed in the appropriate laboratories of both facilities. Special examinations such as X-ray radiography will be performed when appropriate by transporting the animals to the medical center in New York City.

References

1. Guinee, Vincent F. - Personal Communication.

2. Hammond, P. B., Lead Poisoning. An Old Problem with a New Dimension, Essays in Toxicology, ed. Blood, F. R., Academic Press (1969) 115-155.

3. Kehoe, R. A., Normal Metabolism of Lead, Arch. Environ. Health 8, 232-243 (1964).

Proposed Budget

Salaries and Wages	Annual Rate	Budget
Dr. David H. Goldstein* 15% Dr. Theodore J. Kneip* 20% Dr. Norman Cohen* 33 1/3% Dr. Elizabeth Muchmore* 25% Dr. Wendell Niemann* 10%	$ 12,000.00	$ 4,000.00
Technicians (1.5) 100%	8,000.00	12,000.00
Clerk (1) 25%	6,800.00	1,700.00
Salaries Total		$ 17,700.00
Fringe (10% of Salaries)		1,770.00
		$ 19,470.00
Other		
Animal Costs 6 animals at $95.00 each		570.00
Animal Care (Medication, Handling) (Technician charges) (Transportation, Sampling)		2,500.00
Animal days - (Space charges) Estimated 1810 days 2-365 days each 2-270 days each 2-180 days each 2- 90 days each		2,800.00
Supplies		2,500.00
Travel		500.00
Miscellaneous		1,000.00
		$ 9,870.00
Total Direct		$ 29,340.00
Indirect (31% of Salaries)		5,487.00
Total		$ 34,827.00

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