ANALYSIS OF

DR. ROBERT KEHOE'S MEDICAL SUMMARY OF

MRS. [redacted] CASE HISTORY

N 5251

PREFACE

In order to assimilate the following rebuttal material to Dr. Kehoe's report, the reader must refer to the Kehoe report paragraph by paragraph, as the analysis of Dr. Kehoe's remarks are so arranged in this discussion.

The reader is further encouraged to refer to the sources noted as the basis for the discussion where technical matters are necessarily dissected and examined.

Some graphic charts are included at the end of this article further to elucidate technical discussion.

Definitions of Terms used in Paragraph I

1. "chronic cholecystolithiasis" - refers to chronic gallbladder inflammation with gallstone formation (treated by gallbladder removal)

2. "endometrial disfunction with an hemorrhagic condition of the endrometrium" - refers to abnormal vaginal bleeding due to hormonal disturbances (quite common in women).

3. "influenza with hysterical manifestions" - refers to an episode of virus flu (what Dr. Kehoe refers to as "hysterical manifestions" is unknown to me)

4. "acute states of anxiety" - refers to episodic stress reaction to real organic disease processes, quite common to any really sick individual.

5. "migraine" - refers to a type of severe headache, the exact cause of which is still quite obscure to medical science.

6. "acute urinary retention" - refers to episodes of difficulty in passing urine, secondary to bladder infections (quite common in women)

7. "anxiety neurosis with conversion" - refers to stress reactions to real organic disease states (again noted to be quite commonly seen in sick individuals)

8. "gastritis and functional pylorospasm" - refers to episodes of inflammatory reaction in the stomach associated with apasm of the muscular outlet valve of the stomach, the pylorus.

9. "probable pyelonephritis" - refers to infection of the kidneys (also common in women)

10. "subdeltoid bursitis" - refers to an inflammatory condition of the bursa (a structure which cushions the action of tendons and muscles across joints) located at the shoulder under the deltoid muscle - a very common condition.

11. "myalgia and arthralgia" - refers to episodes of pain in muscles and joints (a condition common to many usual and unusual illnesses)

12. "cystic ovaries" - a condition of the female ovary in which normal egg follicles fail to ripen, the egg degenerating, and the follicles enlarging, filling with fluid- again, a common female disorder.

13. "multiple pelvic and abdominal adhesions" - refers to scar tissue formation occuring in nearly all persons who have undergone surgery, in the abdominal and pelvic regions underlying the operative sites.

14. "recurrent lumbosacral abnormalities of the spinal column"- refers to well substantiated organic disease of the low back in this case ruptured vertebral disc and its sequelae, requiring surgery.

15. "sciatic neuritis" - refers to an inflammatory condition of the sciatic nerve (located from low back, through buttock, and into into thigh and leg, to foot).

16. "gastric ulcer" - refers to ulceration (via chronic inflammation) of the mucus membrane of the stomach.

In this section, Dr. Kehoe reviews the presenting signs and symptoms of Mrs. [redacted] 1969 October admission to Good Samaritan Hospital, during which the diagnosis of Plumbism (lead poisoning) was made. She did indeed present with evidence of bowel inflammation, and my initial impression was that she may be suffering from diverticulitis (small packets of bowel mucus membrane which herniate through small blood vessel openings into the bowel wall, which may become inflammed-- such as in appendicitis). Inflammation, regardless of its cause, may indeed create fever, as infection caused by bacteria, viruses, fungi, or unicellular animal parasites. Nausea is a common feature of any gut inflammatory process.

X-ray examination of the bowel failed to demonstrate diverticulitis, or other bowel disease responsible for the patient's complaints and findings. Consulation with Dr. Sylvan Weinberg (a reputable internal medicine specialist) was obtained. He also was unable to explain the patient's problem. Therefore, a search for exotic causative agents was made. It is known that poisons may cause such a sympton complex, and tests were therefore made for arsenic, zinc, antimony, and lead; urine being the most available source (hair and nail clippings also were submitted blood being omitted due to its transient carrying capacity for such toxic substances).

All studies were negative except for the finding of a grossly abnormal lead level found in the urine. The diagnosis of lead poisoning was thereby established; the patient's symptoms being due to colic (spasm) in the gastro-intestinal tract secondary to the toxic effects of lead.

Comment

Dr. Kehoe's remarks in the third paragraph seem to imply that the diagnosis was arrived at by "spontaneous generation", as if by "divine revelation", rather than by good investigative, logically deduced, procedure.

A search for red blood cell basophillic stippling was made (a condition of precipitation of Wright's stain blue dye in the red blood cells as seen under the microscope on a slide prepared from peripheral blood). A search for elevated content of urinary porphyrins also was made (a chemical present in urine as a result of abnormal breakdown of the red blood cells and its oxygen bearing molecule, hemoglobin). Both tests were negative. These, when positive, are considered ancillary evidence of the presence of a toxic substance (heavy metal - lead, etc.).

It should be noted that stippling and porphyria are mostly evident in cases of acute lead poisoning (large doses in a short period of time), in small children who are exposed to paint lead sources (crib rails, wall paint, etc.). In children, whose metabolic processes are accelerated (building all tissues rapidly, including bone, bone marrow, and red blood cells) it is consistent that since lead complexes with, and deposits in bone, that the metabolic processes of the red blood cell, a product of the marrow, should therefore become abnormal, and that stippling and porphyria would be present. Children also (because of accelerated bone growth) will show a "lead-line at growth-plate metaphyses of long bones by x-ray, when they become poisoned by lead. A "lead-line" can be seen in their gums; for the same reason, with the growth of their teeth, when poisoned with lead.

However, in an adult, with no growth proceeding, but only repair

and degenerative processes of metabolism, and in a case of chronic exposure to lead (over a long period of time); it would not be unusual to not find basophillic stippling of the red blood cells, nor a lack of increased porphyrins in the urine.

Dr. Kehoe's description of a patient afflicted by lead toxicity (in "uncomplicated plumbism") is vivid and perhaps accurate. Mrs. [redacted] did in deed suffer gastro-intestinal colic as described, on many occasions (resultant in ulcer formation, stress reactions, abnormal gut metabolism, with reactivehypoglycemia, secondary pancreatitis, etc.). She did in deed grimace, and grind her teeth. She held her left side and abdomen many times - perhaps this was an attempt to relieve her distress as Dr. Kehoe describes. And, as Dr. Kehoe has so aptly noted, she did suffer many secondary infections and inflammations, which complicating her lead problem, did in deed cause her fever. Fever was a factor, which rather than casting doubt on the diagnosis, substantiated the existence of inflammatory reaction and complication of her lead problem.

Comment

I therefore reject Dr. Kehoe's conclusion that the absence of stippling, absence of porphyrins, and presence of fever, mitigate finally against the diagnosis of plumbism. I also object to this line

of reasoning and conclusion (for the above stated explanation), made by a physician not engaged in clinical practice, who has never examined by history or physical the actual patient, and who makes such rash statements by virtue of his perusal of records alone. By being this patient's physician, actively engaged in her health problems for the past number of years, I submit I am therefore infinitely more qualified to judge her condition and make the appropriate diagnosis.

Dr. Kehoe decries the use of urine as a source of material for the examination and detection of lead, and obviously prefers blood as a source. This is directly opposed (see Goodman & Gilman, The Pharmacological Basis of Therapeutics, 1956 Edition, Pages 1007-8) in modern investigative theory. In acute lead poisoning, blood in deed would be a readily available source, with its high transient level secondary to an acute ingestion of lead in high concentration. It is known that in subacute, and in chronic exposures to small doses of lead, blood levels are very transient and low in concentration. Upon leaving the blood, lead enters the bone and complexes with its calcium lattice structure, with lead reaching an equitibrium chemical balance at low concentration with blood levels. Lead may then leave the bone under the influence of EDTA lead complexing therapy, into the blood, and can readily be detected in the urine upon kidney filtration of the blood.

Whenever a lead source is discontinued, blood levels of lead drop (as do urine levels). Bone levels rise, and will only decomplex when treatments are instituted. Therefore urine is a better source for lead determination, and is especially so in a case of chronic lead poisoning - as in Mrs. [redacted] case.

It is also true as Dr. Kehoe points out, that lead is ubiquitous, and that healthy urban dwellers may have lead detected in the urine (most often from inhaling the products of combustion of leaded gasoline in the engines of automobiles - this fact I understand Dr. Kehoe's entire research experience has been dedicated to discredit, as it has been sponsored by the petroleum industries. However, when lead levels reach a certain high point of concentration in the urine, a point which has been established by medical research, it is known to be toxic to the individual tested, and is capable of producing symptoms. Mrs. [redacted] urine lead levels were twice as high as this known toxic level (see attached table of laboratory results).

Dr. Kehoe's example of two men working side by side takes into account only exposure by inhalation (or at least a source common to both, at the same concentration to both), not as in Mrs. [redacted] case by her usual inhalation exposure (as she is a city dweller) plus an ingestion exposure source. She has been, as Dr. Kehoe has pointed out, not a healthy working male,

disease states.

As to the "deplorable" conditions under which Mrs. [redacted] laboratory studies were ordered, collected, and examined, I invite him to inspect Good Samaritan Hospital's Special Chemistry Clinical Laboratory, and discuss any phase in question with the hospital pathalogists responsible for its operation, the PhD, who actually conducts the testing, or the RN's of the Nursing Service who follow my orders and who are responsible for the collection of all specimens. A copy of the exact technic used in the Laboratory with reference material is attached to this report.

Comment

Analysis of Dr. Robert Kehoe's "consideration of the alleged source of lead, allegedly absorbed by the patient, Mrs. [redacted]

Comment

After the diagnosis of lead poisoning was established in Mrs. [redacted] case, a search was instituted for a possible source of lead in her immediate environment. Inasmuch as Mr. Robert [redacted] her husband, was also intimately exposed potentially to the same environment, a twenty-four hour urine was collected on him and examined for lead. No toxic lead level was detected,

effectively ruled out.

It is known that certain ceramic kitchenware may contain a glaze which may incorporate lead. The [redacted] possessed such a possible source, a teapot, purchased at McCrory's Store, which was imported from Japan, its site of manufacture being obscure.

Mrs. [redacted] alone brewed and drank tea from this ceramic pot. The pot was analyzed, and did in deed contain high quantities of lead. Moreover, it was ascertained, that between hospitalizations (during which she was treated, unexposed to more lead, and subsequently improved), it was her habit to consume tea, which is commonly given to recuperating patients especially with gastrointestinal disorders, from this pot. In short order, she would again experience episodes of severe gastrointestinal colic and require re-hospitalization (for "pylorspasm, ulcer, diverticulitis, and the "like", without benefit of knowledge of the truth of the source of her complaints). It is all too clear, at this point that lead was in deed the culprit, and that the innocent teapot, the veritable source.

Dr. Kehoe quite obviously questions the results of the testing of the ceramic pot in question, I leave the disputation of the analytical results and methods of testing to the experts. As far as I am concerned, tannic acid (tea solution) is of sufficient potency (especially if brewed strongly) to create a weak solution of lead (extracted from the lead-based ceramic glaze), which when ingested regularly, over a period of time, is quite adequately the source of toxic

poisoning in the case of Mrs. [redacted] I can appreciate the inadequate result obtained by the reknowned Kettering Laboratory, of actual lead extraction from the teapot in question, when one realizes that the same teapot had been subjected to strong acidification (not a weak solution of tea-tannic acid) by two previous laboratory examinations (WPAFB & Bowser-Morner).

Respectfully submitted,

G.H. Dennis, II, M.D.

See Attached Tables

APPENDIX

1. Dr. Kehoe's Report

2. Table of Urinary Lead Determinations

3. Lead - In Blood or Urine

4. Table of Porphyrin Metabolism as relates to Lead

5. Table of Abnormally Produced Red Blood Cell Metabolism

TABLE OF URINARY LEAD DETERMINATIONS

performed by

The Special Chemistry Laboratory
(headed by Dr. Haddox -
a Ph.D. in Biological Chemistry)
of Good Samaritan Hospital

[redacted]

Date Test Ordered (24 hr. urine collection)	Date Done	Result mgm/l	Control mgm/l
10/24/69	10/29/69	0.170	0.015
10/31/69	11/ 3/69	1.130	0.020
11/ 6/69	11/10/69	0.044	0.018
as OP	12/ 5/69	0.021	0.020
" "	1/20/70	0.068	0.030
" "	2/ 5/70	0.120	0.020
" "	5/ 6/70	0.042	0.022
" "	5/21/70	0.040	0.015
" "	8/25/70	0.002	0.018
	[redacted] (husband)		
as OP	10/30/69	0.001	0.015

Normal lead level (urine)	0.01 to 0.030
Toxic level (according to Kehoe & Associates in 1947)	greater than 0.070 mgm/l

(2)

LEAD - In Blood or Urine

I. DIGESTION

1. A 100 ml. aliqnot of 24 hr. urine specimen or 10 ml. of blood placed in round bottom flask with several glass beads.

2. Add 150 ml. HNO_3 + 6 ml. H_2SO_4. Heat until volume is approximately 50 ml. (Boil gently at first to avoid foaming over).

3. Remove flame and add 50 ml. more of HNO_3 and (carefully and slowly) add 5.0 ml. of conc. perchloric acid. (72%)

4. Heat again until solution clears and white SO_3 fumes are copiously evolving. Usually occurs when volume is down below 4.0 ml. Remove heat. (If not a clear colorless syrupy liquid, add a few more ml. of HNO_3 and heat again until SO_3 fumes copious. Should be repeated until get the clear liquid).

II. COPPER and IRON REMOVAL

5. Add 15 ml. of AMMONIUM CITRATE and 1.0 ml. of HYDROXYLAMINE HCl. Cool and add NH_4OH until just alkaline to phenol red. Then add 5.0 ml. of KCN solution. (If precipitation occurs, add just enough citrate solution to dissolve it).

III. DITHIZONE EXTRACTION

6. Transfer to separatory funnel (50 to 125 ml).

7. Add 5 ml. of dithizone extraction solution. Shake and drain off into another separatory funnel (125 to 250 ml). (The dithizone will turn red if Pb. present).

8. Continue adding 5 ml. portions of the dithizone extraction solution until all the lead is removed and the solution remains green. Each portion is in turn combined with the previous portion.

9. Add 50 ml. of the Buffer solution (pH 3.4) to get the lead in the aqueous phase. Shake thoroughly. After settling, discard the chloroform phase(which should be a light green).

IV. COLORIMETRIC DETERMINATION

10. Add 10 ml. pure chloroform to separatory funnel to remove any residual dithizone. Discard this chloroform wash.

11. To the buffer solution in the separatory funnel, add 10.0 ml. of the proper Dithizone standard solution (estimated from steps 7 & 8 above) and 10 ml. of ammonia-cyanide solution;add the solution well shaken.

12. After separation of layers, flush the funnel stem with the first few drops. The remainder is run directly into the colorimeter tube for reading at 510 mm. (Read against reagent blank (see #13) if available on a pure lead free Dithizone solution.

LEAD - In Blood or Urine (continued)

13. The results are compared with the standard curve to obtain the amount of lead in the sample taken. (Appropriate calculation follow to adjust to blood % on urine/ 24 hr.)

14. A reagent blank should be run at same time, beginning with step #1 using 100 or 10 ml. of HOH in place of urine or blood resp.

REAGENTS:

(1). AMMONIUM CITRATE solution - 400 gm. citric acid dissolved in HOH. Sufficient NH_4OH added to make the solution alkaline to phenol red. Dilute to(1)liter with HOH.

(2). HYDROXYLAMINE HYDROCHLORIDE - 20.0 gm. + HOH to 100 ml.

(3). POTASSIUM CYANIDE (KCN) - 10.0 gm. + HOH to 100 ml.

(4). DITHIZONE EXTRACTION solution - 10 mg. DIPHENYL THIOCARBAZONE + 400 ml. CHLOROFORM. (Not important as to exact weight or volume). (Solution should be aged several days before use)

(5). DITHIZONE STANDARD solution - Solutions kept in dark bottles out of light in refrigerator. Main standard - 20 mg. dithizone + chloroform to 1,000 ml.

The Main Standard Used With 0 - 100 µg Range

Dilute ½ for 0-50 µg range (i.e. to 10 mg./L)
Dilute ¼ for 0-10 µg range (i.e. to 5 mg./L)
(Age before use for several days)

(6). AMMONIA-CYANIDE solution - Dissolve 20 gm. of KCN in HOH. Add 150 ml. NH_4OH. Dilute to(1) liter with HOH.

(7). BUFFER SOLUTION (pH 3.4) - To 500 ml. of double distilled water add 9.1 ml. of nitric acid and a few drops of bromo-phenol blue (or appropriate indicator); bring the pH to 3.4 with NH_4OH. Add 50 ml. of Clark-Lubs buffer double strength, then dilute the solution to 1.0 liter.

(Clark-Lubs buffer double strength: 50 ml. of 0.2 M potassium acid phthalate and 9.95 ml. of 0.2M HCl + HOH to 100 ml.)

(8). STANDARD LEAD NITRATE solution: 0.160 gms. dried lead nitrate diluted to 100 ml. with 1% HNO_3 (equivalent to 1 ml. of lead). For use dilute in 1% HNO_3 to give 1 µg and 10 µg per ml.

LEAD - In Blood or Urine (continued)

(9). STANDARD CALIBRATION CURVE: To a measured quantity of lead nitrate solution add 50 ml. of pH 3.4 buffer solution and follow procedure as outlined in procedure steps #10 thru. #13.
(Suggest values of 10, 2, 5, 10, 20, 100 µg Pb.)

NORMAL = < 0.080 mg/Liter Urine

BORDERLINE = 0.081 mg/Liter Urine to ca. 0.25 mg/L urine. (Borderline ca 0.12 mg/l) depending on [illegible]

DEFINITE = > 0.25 mg/Liter Urine

See: "Clin. Toxicology" Thienes 4th Ed. } discussion
pp 58?-582
pp 136-

"Colorimetric Analysis of Trace Elements" Kolthoff & Sandell } method
(1964) pp 287-315

TABLE OF PORPHYRIN METABOLISM
as relates to Lead (Heavy Metal Intoxication)

Porphyrin Tetrapyrrole Ring

+

Fe

↓

Heme Molecule

+

Protein

↓

Hemoglobin Molecule
(incorporated into Red Blood Cell in
Bone Marrow)

↓ 120 day life cycle

Splenic Degradation

↓

Disrupted Tetrapyrrole Ring

↓

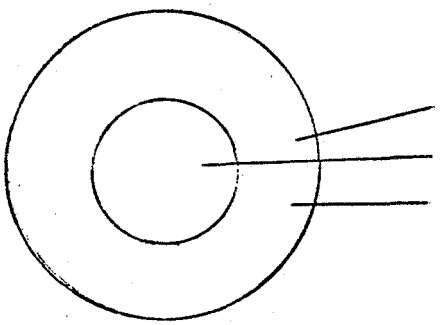
Renal (Kidney) Excretion
of porphyrin material

(May appear in urine of child or individual acutely poisoned with lead or other heavy metal)

<u>Not necessarily</u> seen in urine of
chronically poisoned patient

TABLE OF ABNORMALLY PRODUCED
RED BLOOD CELL METABOLISM

Immature Red Cell:

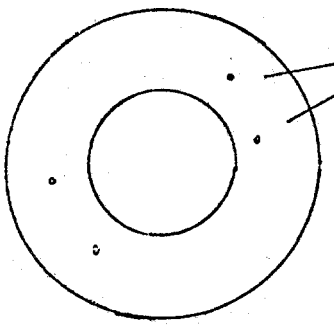


Cell protoplasm
Nucleus with RNA
Mitochondria with RNA-DNA complex

+

Lead

↓



Basophillic stippling noted as a result of lead precipitation of mitochondria - seen in peripheral blood 50 cells/100,000 examined of child or individual acutely poisoned by lead or other heavy metal

↓

Breakdown as noted on Table of Porphyrin Metabolism as relates to Lead

Porphyrins in urine

<u>Not necessarily</u> seen in blood of chronically poisoned patient.