

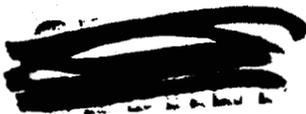
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M. M. Haring  
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HEALTH DIVISION RESEARCH PROGRESS REPORT

J. L. Svirebely  
Health Division Director

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HEALTH DIVISION RESEARCH PERSONNEL

G. Bowen, G. Caplinger, R. Cowden, J. Cron, C. Ens, W. Petty, P. Glass, I. Grafton, B. Guthals, D. Hall, C. Hemler, W. Hood, W. Jolley, J. Lyons, D. McGinnis, J. Mendicino, R. Miller, G. Norris\*, E. Parsons, A. Rogers, T. Schilling, E. Spoerl\*\*, J. Svirbely, L. Talley, P. Trucksis, J. Williamson, and I. Zuroweste

\* Joined Group August 2, 1948

\*\* Joined Group August 18, 1948

ABSTRACT

The LD<sub>50</sub> per os experiment on rats was augmented by further experimentation using six additional dosage levels.

The experiment to determine the LD<sub>50</sub> of postum for mice by per os administration and intravenous injection is being continued.

An experiment was initiated to evaluate procedures used in the preparation of injection and dummy solutions

Data are presented giving assay of activity recovered from tails of intravenously injected rats.

The experiment was completed on percentage recoveries of postum from rats administered postum by caudal vein injections.

Determination of the postum content of the tails of mice used in the LD<sub>50</sub> studies is being continued.

A spectrophotometric curve for the determination of nonprotein nitrogen has been developed.

A study concerning some of the factors which may affect the deposition of postum on copper discs is being conducted.

Due to the illness of the statistician, no work for the Statistical Sub-Group is reported for this period.

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The experiment to determine the amount of postum that is retained by waxed paper cups was continued.

An experiment to determine the practicability of utilizing higher ion-collection potential gradients to shorten the resolving time in the parallel plate alpha chamber is being conducted.

An experiment to determine the relationship between alpha chamber microphonic response and chamber length is being run.

A project whose purpose is the development of an autoscaler for low level alpha counting has been initiated.

An experiment has been initiated to determine whether a stable, logarithmic rate meter can be developed for neutron monitors, utilizing a diode coupled integrating circuit.

Declassification proceedings have been initiated on Operations Manuals (MLM-147 and MLM-148) for parallel plate alpha counting systems which utilize our CZT2 scale of eight scaler or CZT3A scale of sixty-four scaler, together with the CZT1B parallel plate alpha chamber.

#### DETAILED REPORT

##### A. BIOLOGICAL GROUP

1. PATHOLOGY SUB-GROUP - B. Cowden, J. Cron, P. Glass, W. Jolley, J. Lyons, D. McGinnis, J. Mendicino, and L. Talley

(A) The per os experiment with Sprague-Dawley white rats was continued to obtain more complete data for statistical calculations of the LD<sub>50</sub> dose.

The general procedures used were identical with those reported in the Health Research Progress Report, MLM-121, May 1-31, 1948.

The following theoretical dosage levels were administered:

|          |               |   |
|----------|---------------|---|
| Level I  | 9 female rats | 910 microcuries per kg. of body weight  |
| Level II | 9 female rats | 1300 microcuries per kg. of body weight |

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|           |                              |   |   |   |   |   |   |   |   |
|-----------|------------------------------|---|---|---|---|---|---|---|---|
| Level III | 10 male and<br>9 female rats | 1820 microcuries per kg. of body weight |   |   |   |   |   |   |   |
| Level IV  | " " "                        | 2340                                    | " | " | " | " | " | " | " |
| Level V   | 10 male rats                 | 2860                                    | " | " | " | " | " | " | " |
| Level VI  | " " "                        | 3380                                    | " | " | " | " | " | " | " |

Clinical symptoms, gross pathology, and mortality data will be reported later. Assay results of the dummy solutions, as compiled by the Biochemistry Sub-Group are reported in Table I.

(B) The experiment to determine the LD<sub>50</sub> of postum, by per os administration and intravenous injection, for white mice is being continued. The mortality data showed such a wide range of variance that no correlation or analysis of data is possible. Therefore, additional dosage levels will be run.

An experiment to evaluate procedures used in the preparation of injection and dummy solutions is in progress.

(C) It is believed that this experiment will provide data indicating the degree of accuracy which can be expected in the reproducing of activity injection solutions by hypodermic syringe, lambda pipette, and serological pipette and in the assay of radioactive solutions by the glass slide and copper disc methods.

A brief outline of the experiment follows. Eighteen injection solutions were prepared according to standard procedures, nine using a low activity stock postum solution, and nine using a high activity solution. The stock activity solution was measured with a lambda pipette, a 1/4 cc. tuberculin syringe, and a serological pipette. Five dummy solutions were prepared from each injection solution, and two glass slides made from each dummy solution. This experiment will be duplicated by another technician, and the results will be reported later.

(D) Reference is made to the LD<sub>50</sub> intravenous injection experiment on rats, reported in the Health Research Progress Report, MM-140, June 1-30, 1948. More work will be done on this problem before it can be ascertained whether a significant amount of activity is retained in the tail of the rat at the site of injection.

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Table I  
ASSAY OF DUMMY SOLUTIONS

| Dosage Level | Copper Discs Assay                               |   |                      |  | Glass Slides Assay                            |                      |  | Total Time of Administration Minutes |
|--------------|--|---|----------------------|--|---|----------------------|--|--------------------------------------|
|              | Calculated Dose, Microcuries Per kg. Body Weight | Average Dose, Microcuries Per kg. Body Weight | % of Calculated Dose | Range of Dose, Microcuries Per kg. Body Weight | Average Dose, Microcuries Per kg. Body Weight | % of Calculated Dose | Range of Dose, Microcuries Per kg. Body Weight |                                      |
| I            | 910  | 680.7   | 74.8                 | 663.9-712.3                                    | 651.9   | 72                   | 625.1-686.5                                    | 18                                   |
| II           | 1300   | 909.38  | 69.9                 | 847.7-946.7                                    | 865.2   | 67                   | 845.4-877.5                                    | 17                                   |
| III          | 1820   | 1315.7  | 72.2                 | 1276.0-1356.0                                  | 1332.7  | 73                   | 1264.5-1428.6                                  | 42                                   |
| IV           | 2340   | 1668.9  | 71.4                 | 1558.8-1789.5                                  | 1693.5  | 72                   | 1613.0-1794.5                                  | 29                                   |
| V            | 2860   | 2087.2  | 73.0                 | 2002.5-2135.0                                  | 2089.6  | 73                   | 2051.5-2116.0                                  | 23                                   |
| VI           | 3380   | 2396.8  | 70.9                 | 2297.0-2518.0                                  | 2421.8  | 72                   | 2304.5-2575.5                                  | 16                                   |

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### FUTURE PLANS

In addition to the plans outlined in the previous reports, there will be initiated a study of the effects of rutin on the control of ecchymoses in rats exposed to postum. Vitamin P, toluidine blue, and protamin will be investigated to determine their effects on clotting time. Pilot studies of the compatibilities of rutin and protamin will be carried out on rats exposed to postum.

2. BIOCHEMISTRY AND PHYSIOLOGY SUB-GROUP - G. Caplinger, W. Fetty, D. Hall, E. Spoerl, P. Trucksis, and I. Zuroweste

(A) Percentage Recoveries of Postum from Rats Administered Postum by Caudal Vein Injections.

This experiment was started during the month of July, 1948, and the details are given in the Health Research Progress Report, MM-164, July 1-31, 1948. The ten rats which were used in this experiment weighed approximately 100 grams. Of the six rats used as experimental animals, three received an actual administration of 2.3 microcuries of postum, while the other three received 4.3 microcuries of postum. Four rats served as the controls. Two of the controls (I and II) received injections of the phosphate buffer solution, prior to the injections of the experimental animals. The other two controls (IX and X) were treated in like manner after the experimental animals received their administrations of postum. The experimental as well as the control animals were killed with chloroform 15 minutes after their injections. The tail of each rat was severed and digested separately from the remainder of the rat. The postum concentration of suitable aliquots taken from the diluted acid - residues was determined by plating on the copper discs.

The results of this study are given in Table II.

(B) Determination of the Postum Content of the Tails of Mice used in the LD<sub>50</sub> Studies.

The details of the procedure are given in the Health Research Progress Report, MM-164, July 1-31, 1948. After the death of the mice, which were given postum intravenously by way of the caudal vein, the tails were severed. Following the digestion of the tails with a perchloric acid - nitric acid mixture, the postum content of aliquots of the neutralized and

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Table II

PERCENTAGE RECOVERIES OF POSTUM FROM RATS ADMINISTERED POSTUM BY CAUDAL VEIN INJECTION

| Rat No. | Level of Postum Microcuries per kg. Body Weight | Amount of Postum Administered Expressed in Microcuries |        | Recovery of Postum (Microcuries) |                   | Percentage Recovery of Postum |
|---------|---|--|--------|----------------------------------|-------------------|-------------------------------|
|         |   | Theoretical  | Actual | Tails                            | Rest of Rat Total |                               |
| I       | Control   | -  | -      | 0.03                             | 0.08              | 0.11<br>Dummy Injection       |
| II      | Control   | -  | -      | 0.05                             | 0.05              | 0.10<br>"                     |
| IX      | Control   | -  | -      | 0.00                             | 0.08              | 0.08<br>"                     |
| X       | Control   | -  | -      | 0.01                             | 0.07              | 0.08<br>"                     |
| III     | 25  | 2.5  | 2.3    | 2.49                             | 0.14              | 2.63<br>114.3                 |
| IV      | 25  | 2.5  | 2.3    | 1.80                             | 0.68              | 2.48<br>107.8                 |
| V       | 25  | 2.5  | 2.3    | 0.34                             | 2.17              | 2.51<br>109.1                 |
| VI      | 50  | 5.0  | 4.3    | 0.30                             | 3.65              | 3.95<br>91.9                  |
| VII     | 50  | 5.0  | 4.3    | 0.04                             | 5.06              | 5.10<br>118.6                 |
| VIII    | 50  | 5.0  | 4.3    | 0.07                             | 4.31              | 4.38<br>101.9                 |

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diluted acid residues were determined. The results of this work will be reported by the Pathology Sub-Group.

(C) Development of a Spectrophotometric Curve for the Determination of Nonprotein Nitrogen.

Since an increase in nonprotein nitrogen has been shown to result following administration of uranium salts to animals (See classified Report CH-3710) it is possible that this increase may also accompany administrations of postum. A spectrophotometric curve was developed for the determination of nonprotein nitrogen content of blood using concentrations of ammonium sulfate corresponding to 25, 50, and 100 milligrams of N.P.N. per 100 ml. of blood. One ml. of each standard solution was treated with 1 ml. of 18 N sulfuric acid and 15 ml. of Nessler's solution. After dilution with water to 35 ml. and mixing the optical densities of the resulting colored solutions were read in the spectrophotometer at a wave length of 5440 mu. The instrument was set to zero density with a blank consisting of 1 ml. of sulfuric acid and 15 ml. of Nessler's solution diluted with water to 35 ml. By plotting concentrations of N.P.N. against their density readings a straight line curve was formed. The percentage recoveries of nitrogen added to blood were next determined. A sample of blood whose N.P.N. had been determined was used as the stock sample. Weighed quantities of ammonium sulfate were added to measured volumes of this blood and the nonprotein nitrogen contents of these prepared blood samples were determined. The procedure involved precipitation of the blood proteins with trichloroacetic acid, digestion of an aliquot of the protein free filtrate with 18 N sulfuric acid and subsequent oxidation with 30 per cent hydrogen peroxide. The acid residues were nesslerized and diluted to 35 ml. with distilled water. After mixing, their densities were determined in a spectrophotometer. By interpolation from the curve previously prepared the nonprotein nitrogen values were read.

The results of this work are given in Table III. Recoveries ranged from 97.6 to 101.2 per cent.

Table III

| <u>N.P.N. Originally Present, mg. per 100 ml. Blood</u> | <u>Amount added, mg./100 ml. Blood</u> | <u>Amount Recovered, mg. per 100 ml. Blood</u> | <u>Per Cent Recovered</u> |
|---|--|--|---------------------------|
| 35.6  | 5.0                                    | 41.1   | 101.2                     |
| 35.6  | 30.0                                   | 64.1   | 177.2                     |
| 35.6  | 35.0                                   | 69.8   | 95.2                      |

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(D) A Study Concerning Some of the Factors Which May Affect the Deposition of Postum on Copper Discs.

An examination of the data accumulated during the past few months shows a marked variation in the percentage of postum deposited on copper discs during successive two hour periods of plating. These plating solutions containing postum are aliquots of the neutralized and diluted perchloric acid - nitric acid residues of animal tissues.

Variations in the ionic concentrations of the acids and their salts present in the plating solutions probably have an effect on the deposition of postum on the copper discs. During successive two hour plating periods, copper is dissolved from the discs due to the action of the acids present in the plating solutions. The presence of these copper ions may also have a bearing on the plating of postum on the copper discs.

A study was begun in which an attempt will be made to evaluate the possible effect of such factors as hydrogen, nitrate, chloride and copper ion concentrations on the plating of postum on copper discs. In the first experiment, twelve 300 ml. Kjeldahl digestion flasks, containing 10 ml. of perchloric acid and 20 ml. of nitric acid measured accurately with burettes were heated until the appearance of the dense white perchloric acid fumes. The acid residues were then transferred to glass stoppered 300 ml. Erlenmeyer flasks calibrated at 250 ml. The solutions were neutralized with a concentrated sodium hydroxide solution using a methyl red - methylene blue solution as the indicator, 10.5 ml. of concentrated hydrochloric acid was added to each solution and upon diluting to the 250 ml. mark the solutions were approximately 0.5 N in respect to hydrochloric acid.

A procedure for determining the nitrate concentration of each of the above solutions was set up using pyrogallol sulfonic acid. In the presence of this reagent and concentrated sulfuric acid a pink solution is formed with nitrates which has a maximum absorption at 485 mu. Aliquots ranging from 0.05 to 1 ml., depending on the nitrate concentration, were used in determining the nitrate content and a solution of potassium nitrate containing 0.44 grams of nitrate per liter was used as the standard. The densities of the standard and of the aliquots were determined and the nitrate concentrations of the twelve acid residues were determined.

The acid concentrations of the solutions determined after dilution to 250 ml. ranged from 0.4764 to 0.5100 normal.

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Three 25 ml. aliquots of each solution were measured with a burette and to each aliquot 25 ml. of 0.5019 N hydrochloric acid was added with a burette. One aliquot from each of the twelve solutions was stirred for two hours using copper discs in the same manner as is used for the plating of postum. Another series was stirred for two two-hour periods using a different copper disc for each period, while the third series was stirred for three two-hour periods using different discs for each period. The copper discs were weighed before and after immersion in the acid solutions and loss determined.

After further work on this pilot study has been done, known amounts of postum will be added to digestion flasks and the experimental procedure will be repeated. An attempt will be made to correlate the concentrations of the various ions present in the plating solutions with the percentages of postum deposited on the copper discs during the three different plating periods.

#### FUTURE PLANS

The digestion of mice tails for the LD<sub>50</sub> study will be continued.

A procedure for hemoglobin determination using an oxyhemoglobin instead of an alkaline hematin method will be set up.

Experimental work concerned with the effect of various factors on the plating of postum on copper discs will be continued.

#### 3. STATISTICAL ANALYSIS SUB-GROUP - C. Ens

The work of this group is not reported for this period due to the illness of the statistician.

#### B. SPECIAL PROBLEMS GROUP

##### 1. ANALYTICAL SUB-GROUP - G. Bowen and E. Parsons

Work was continued on the waxed paper cup experiment as detailed in Health Research Progress Report, MM-93, April 1-30, 1948.

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FUTURE PLANS

To continue work on the determination of the amount of activity retained by waxed paper cups.

C. INSTRUMENT GROUP - I. Grafton, B. Cuthals, C. Hemler, W. Hood, R. Miller, A. Rogers, and J. Williamson

The major efforts of the Research and Development Groups are being directed toward improving the performance of parallel plate alpha counting systems. Current experiments propose to reduce the resolving time and the microphonic response of the parallel plate alpha chamber.

It has been found that the resolving time of the alpha chamber can be reduced approximately 70 per cent to 150 microseconds if the ion - collection, potential gradient is increased approximately 150 per cent to 3000 volts per centimeter. Additional experimentation is needed to determine whether the alpha chamber will have stable counting characteristics under these conditions.

It has been observed that the microphonic response of the alpha chamber can be substantially decreased by shortening the chamber length approximately 40 per cent. The resonance frequency of the chamber is thereby raised above the frequency range of the most prevalent room noises. An alpha chamber has been designed on the basis of this observation and additional experimentation will be carried out as soon as six alpha chambers, now being constructed by the machine shop, are completed.

An experiment has been initiated to determine whether a stable pulse rate meter having a logarithmic response can be developed utilizing a diode coupled integrating circuit. If successful, this circuit will be incorporated into the neutron monitors used in "Y" operations. Results to date have been inconclusive.

A project has been initiated for the purpose of developing an autoscaler for low level alpha counting. Tentative specifications call for a scale of eight scaler, with automatic reset timing. A radio frequency high voltage power supply, a panel mounted electromagnet register and provision for interconnecting an external recorder and timer.

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FUTURE PLANS

To continue the experiment aimed at reducing the microphonic response of the parallel plate alpha chamber.

To determine the factors governing the resolving time in a parallel plate alpha counter and from these data to develop, if possible, a high rate parallel plate alpha counter.

To continue with the experimentation on a logarithmic rate meter circuit for neutron monitors.

To design a portable air sampler.

To continue with the attempt to develop an autoscaler for low level alpha counting.

To determine the practicability of using radio frequency high voltage power suppliers in radiation detection equipment.

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