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This document consists of 279 page(s).
Number 1 of 6 copies, Series A

707088

CURRENT STATUS AND CURRENT RESULTS

of the

DIVISION OF PHARMACOLOGY

Compiled April 1946

In order to utilize the results of the work on the toxicology of T performed by the Pharmacology Division of the Rochester Project, summary reports are requested.

One volume of this report is to be a scientific monograph dealing with all work on T toxicity carried out at Rochester. The treatment of subject matter is to be critical, i.e., including only reliable data, selected, organized and meaty. Pertinent data from the literature are to be included in each chapter where appropriate. If desirable, a chapter on human exposures is to be provided by Captains Howland and Goldring, summarizing industrial information.

Microphotographs of typical histological sections, especially of kidney lesions, should be included where necessary for clarity and easy description. Photographs of novel or special apparatus or of other subjects are to be included where these facilitate the presentation of data.

The key persons in charge of various parts of the work are the ones best suited to prepare these summary reports. For these key persons the writing is to be an important part of their work. It is not an extra duty to be accomplished by voluntary over-time labor. These key persons are to adjust their programs to permit time for writing. The adjustment will consist of delegating responsibility where necessary and hiring additional personnel when necessary, the latter subject to the approval of the Project Direator.

The preparation of these summary reports must be carried out under pressure of a deadline. Immediate need for speedy progress is made imperative by the expected termination of the contract and by the de-

parture of key personnel for permanent positions. As a consequence, the persons writing these project reports must give the writing priority over routine obligations.

It is recommended that Dr. Voegtlin assume the responsibility for the preparation of these reports. He has full authority to direct and coordinate the writing. He is to call on the authors of the various chapters to spend any time needed for meetings, discussions and writing.

A second volume would deal in a more detailed fashion with all of the data. This detailed compilation is to be a more comprehensive scientific summary of the experimental data with descriptions and interpretations. This volume is to be midway in treatment of subject matter between the extremely detailed final reports and the condensed monograph.

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PERSONNEL

PERSONNEL

DIVISION OF PHARMACOLOGY

Harold C. Hodge, Chief of Division

15 April 1946

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DIVISION OF PHARMACOLOGY

Chief:	Hodge, Harold C.
Office:	Carman Backus
Library:	Kujawski

5 February 1946

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INHALATION SECTION

Assignment of Personnel
as of March 15, 1946

UNIT	HEAD	ASSISTANTS
11	Dygert	Wichser*, Oberg**, Booth, Vernarelli
2X	Rothstein[1)]	Dittman, Fisher, Berke
3	Roberts[2)]	Bishop, Pettengill, Amdur[3)], Mogridge, Baxter
5	Pozzani	Wilson, Youtzy, Yaeger
7	Spiegl[3)]	Minor, Marx, Doran
12	Rothermel	Finegan, Harrison, Miss Ward
10	Sprague	Poole

1) Dr. Rothstein — in charge of Lung Retention Studies — Assisted by: LaBelle, Todd

2) Dr. Roberts — in charge of Renal Clearance Tests — Assisted by: Baxter, Tornaben

3) Dr. Spiegl — in charge of Emergency Toxicity Tests — Assisted by: Amdur

Dr. Field — in charge of Liver-Function Tests

Laskin — in charge of Dust Particle-Size — Assisted by: Miss Reid, Fiorica, Glover (part-time) Scott (part-time)

Tornaben — in charge of Tissue Sampling, Autopsies — Assisted by: (Bleeding, Assisting at Operations) Miss Hofschneider

Cucci, Miss Walsh — 31 Analyses

Mrs. Dygert, Miss Zorsch, Miss Bascom - Stenographers

* To leave in April
** To leave in March

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ENGINEERING DEPARTMENT PERSONNEL

18 January 1946

Murphy	- *	Section Chief -	Army
Wolf	*	Army	
Maier	*	Army	
Same	- **	Army Engineers -	7700
Baurmash	*	Army	
Wilson	**	Army -	7500

** discharged - rehired by Manhattan Department

* discharged - no longer here 4/15/46

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ENGINEERING DEPARTMENT

Specific Assignments

18 January 1946

Murphy	-	Supervision
Wolf	-	Maintenance
Maier	-	Alpha count studies
Same	-	Air distribution studies
Baurmash	-	Alpha count studies
Wilson	-	Air distribution studies

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ANALYTICAL

Flagg

Ass't. Chiefs - F.A. Smith and Voss

Research:	Flagg
	Tishkoff
C-216:	Voss
	Boggs
	Gardner
Routine:	Smith, Frank
	Crossman
	Sullivan
	Lucas
	Morabito
	Smith, Nancy
	Wright

Dr. Bloor

19 January 1946

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ANALYTICAL SECTION

PERSON-JOB SCHEDULE, AS OF DECEMBER 15, 1945

Chief of Section: Dr. John F. Flagg
Assistant Chiefs: Dr. Frank A Smith and Sgt. Marion Voss

DIVISION I

Routine Analytical Laboratory

Personnel	Duties Performed
Smith, Frank A.	Administration, choice of methods, validity of data, library research, liaison between units and laboratory.
Crossman, Myrtle	Assists in administration, recording of data, performs routine analyses.
Lucas, Doris	Dishwashing.
Morabito, Angelica	Performs routine analyses.
Smith, Nancy	Performs routine analyses.
Sullivan, Virginia	Performs routine analyses.
Wright, Joan	Performs routine analyses (part time).

DIVISION II

Fluoride Analysis Laboratory

Voss, Marion	Supervision of laboratory, calculation of results; performance of analyses; improvement of methods.
Boggs, Sheila	Performance of fluoride analyses.
Gardner, Dwight	Performance of fluoride analyses; assistance in supervision.

DIVISION III

Research

Flagg, John F.	Supervision of laboratory, research and consultation on methods of uranium and fluoride analysis.
Tishkoff, G.H. (two-thirds time)	Research on methods of uranium analysis.

19 January 1946

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PHARMACOLOGY

Haven

Ass't Chiefs:	Maynard Neuman
Ingestion:	Maynard Richardson Downs Meskill Moore McGuire Burmeister Goodwin Hollenbeck ~~Lehman~~ Miller
Skin:	Orcutt
Dental	Dale ~~Orcutt~~ Clark Pagano
Distribution Excretion and Storage:	Neuman Carlson O'Connell Mulryan Potter O'Leary Proctor
Isotope work:	
Heads:	Haven Neuman Crossland Randall Carlson Kaley
Routine Fluorimetric T Analysis	Neuman Orcutt Wenning

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Pharmacology (continued)

Bone:	Neuman, M.
Acute Toxicity:	Miller
Office:	Rissberger Thompson
Animal Care:	Kesel McKenzie
Technician's Helper:	McLaughlin

January 21, 1946

PHARMACOLOGY ~~SECRET~~

Chief	Haven	
Ass't Chiefs	Maynard Neuman	
Ingestion	Maynard	Ingestion toxicity studies with rats on the following compounds: TNO_3, TO_2F_2. Ingestion toxicity studies with dogs on the following compounds: TNO_3, TO_2F_2, and TCl_4. Writing of final reports of preliminary experiments with various T compounds as fed to rats.
	Richardson	General supervisor in charge of caretakers at Bronson Avenue Laboratory.
	Downs	Making radiographs of rats from ingestion experiments. Paired feeding studies.
	Meskill	Assistant Chief Animal Caretaker. In charge of feeding rats on ingestion experiments.
	Moore	Mixing of diets for rat ingestion experiments, assisting hematology technicians with rat blood work at Bronson Avenue Laboratory.
	McGuire Burmeister	Animal Caretakers engaged in care and feeding of the rat breeding colony.
	Goodwin	Animal Caretaker engaged in the care of rats in the Bronson Avenue Experimental Room.
	Hollenbeck	Secretary-stenographer for ingestion unit and for general office work at Bronson Avenue Laboratory.
	Miller	Acute toxicity studies with TNO_3, TO_2F_2 and TCl_4 on rats.
Skin	Orcutt	Detailed study of toxicology of $TO_2(NO_3)_2$ following percutaneous absorption. Completed except for final report. Effects of TCl_5 on the skin and on the eye. Completed except for final report. Effects on the eye and skin of compounds of current toxicology interest. Summary report.

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Dental	Dale Clark Pagano	Decalcifying teeth, embedding, cutting colloidin, staining sections and separating tissues from heads.
Distribution, Excretion and Storage	Neuman	Head
	Carlson	Electrolytic separation of interfering substances.
	O'Connell	Aliquoting, evaporating, fusing and analyzing samples.
	Mulryan	Assisting in running analyses by fluorimetric method.
	Potter	Analyzing industrial urine samples by fluorimetric method.
	O'Leary	In charge of isolation of T from biological samples. Ashing of biological samples and isolation and measurement of T therefrom. In charge of recording of data.
	Proctor	Fluorimetric analyses of tissue samples for pharmacology section.
Isotope work	Haven Neuman	Heads
	Crossland	Writing final report on the degree of unsaturation (iodine numbers) of fatty acids of liver and kidney of T poisoned rats. The degree of unsaturation of fatty acids of blood of T poisoned rats.
	Randall	Citric acid excretion in T poisoning.
	Kaley	Alpha counts.
Routine Fluorimetric T Analysis		
	Neuman	Head
	Orcutt Wenning	Routine tissue analyses from Stokinger's studies.

January 21, 1946

Bone	Neuman, M.	Mechanism of T deposition in bone.
Acute Toxicity	Miller	Acute toxicity of various T compounds
Office	Rissberger	Secretary
	Thompson	Charts
Technician's Assistant	McLaughlin	Washing glassware and cages
Animal Care	Kesel	Chief
	McKenzie	

19 January 1946

[redacted]

MECHANISM

Dounce, Head

Wills, Assistant Chief
Lan, Assistant Chief

Main
Fanta
Tishkoff
Kaley
Rothermel, D.

[redacted]

[redacted]

MECHANISM

Chief - Dounce

Assistant Chiefs - Wills
Lan

Lan	Effect of heavy doses of T on rabbits. Writing reports. Effects of heavy metals on catalase excretion.
Wills	Kidney function studies.
Main	Assists in technical phases of kidney function studies.
Fanta	Titration of proteins in the presence of T compounds.
Tishkoff	Platinum electrode studies. Writing reports.
Kaley	Catalase determinations.
Rothermel	Catalase determinations on urines of rabbits, cats, dogs given repeated doses of T.

21 January 1946

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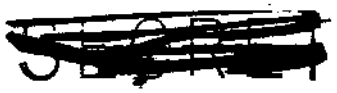

PHARMACOLOGY DIVISION

Hodge	Chief	
Carman	Office	1530 (39.6 hrs.)
Backus	Office	.61å/hr.
Kujawski	Library	2500

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TOXICOLOGY

Amdur	Army	Heininger	2080
Bascom	1900	Hofschneider	1500
Baere	2080	Hollerin	2080
Baxter	2800	Hoyt	2080
Berke	3600	Kesel, R.	2900
Bishop	2800	Kesel, J.	2080
Booth	2200	Laskin	Army
Bunn	2080	LaBelle	3000
Burmeister	2080	Leach	[illegible]
Cucci	2400	Mason	2080
Darrah	2080	Marx	2400
Dittman	Army	Mennerlyn	1820
Doran	2200	Minor	2500
Dygert, H.	1900	Mogridge	2000
Dygert, P.	1.31/hr.	Myrick	2080
Enos	2200	North	2000
Field	3000	Papke	2340
Fiorica	1800	Pettingill	2200
Fisher	2000	Poole	2200
Glover	1.18/hr.	Pozzani	3000
General	2080	Prescott	2000
Harrison	2400	Price	2080

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Roberts	4000
Rothstein	4000
Rothermel	3400
Reid	1800
Rewald	2080
Scott	1.09/hr.
Semmel	2080
Sprague, E.	1695
Sprague, G.	3200
Spiegl, C.	4000
Stokinger	6000
Todd	2400
Tornaben	2600
VanScoyk	2080
Vernarelli	2000
Walsh	1500
Ward	2000
Wilson	2600
Yaeger	2200
Youtzy	2000
ZanButo	2000
Zorsch	1600

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ANALYTICAL

Bloor	1000
Crossman	2200
Flagg	2500 (half time)
Lucas	1300
Smith, N.	1700
Smith, F.	3600
Sullivan	2000

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PHARMACOLOGY

Carlson	2300
Clark	1500
Crossland	1.529/hr.
Cummins	2080
Dale	Army
Downs	2400
Dzuiba	~~Army~~
Goodwin	1820
Haven	4500
Hartman	2080
Haig	.568/hr.
Hollenbeck	1600
MacKenzie	2340
Maynard	4800
McLaughlin	.655/hr.
McGuire	2080
Meskill	2340
Moore, G.	2080
Mulryan 4	1600
Neuman, M.	1.31/hr.
Neuman, W.	4000
O'Connell	Army
O'Leary	3000
O'Malley	3000
Orcutt	3500
Pagano	1300
Plain	2080
Proctor	.786/hr.
Randall	.786/hr.
Richardson	2340
Rissberger	1183 (30.8 hrs.)
Sullivan	2080
Thompson	.655/hr.
Valentine	Army
Wenning	1800
Wheele	1800
Lull	.795/hr.

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MECHANISM

Dounce	4000
Fanta	2400
Kaley	3300
Lan	3700
Main	3300
Rothermel, D.	2[redacted]00
Tishkoff	Army
Wills	4000

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CURRENT STATUS

CURRENT STATUS TOXI

TOXICOLOGY SECTION

Herbert E. Stokinger, Chief of Section

15 April 1946

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INHALATION SECTION

Current Status Index

[redacted]

Project No. 110	Changes in Blood Potassium and CO_2 in Acute T Poisoning.
Project No. 111	The Retention and Absorption by Alveolar Transport of Inhaled T Dust.
Project No. 120	Inhalation Toxicity Studies of Tribnol, Chlorthane, 890, 891.
Project No. 137	The Use of Blood Clotting Time as an Early Index of Toxicity Resulting from T and C-216 Compounds.
Project No. 138	Toxicity of $Na_2T_2O_7 \cdot 4H_2O$ Dust by Inhalation.
Project No. 139	Toxicity of 'HI-Grade' Ore by Inhalation.
Project No. 140	Toxicity of $TO_4 \cdot 3H_2O$ Dust by Inhalation
Project No. 141	Toxicity of $(NH_4)_2T_2O_7$ Dust by Inhalation
Project No. 155	The Study of Particle Size, Particle Count and Concentration of T Dusts in Industrial Areas and in Laboratory Studies.

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDIES
Revised January 1946

	UNIT 10 Control	UNIT 11 TO_2		UNIT 2X TF_4		UNIT 3 T-Nitrate		UNIT 5 T-Nitrate		UNIT 7 TF_6		UNIT 12 TCl_4	
Level Mg T/m^3	0 0	High 10	Low 1	High 3	Low 0.5	High 1.0	Low 0.15	High 0.45	Low 0.05	High 0.2	Low 0.05	High 0.2	Low 0.05
Species													
Dog	12	20	20	18	18	22	22	19	19	17	17	21	21
Rat	175	150	150	150	150	225	175	150	150	175	150	150	150
Rabbit	15 H.E.*, 15	18	-	31	-	20	20	-	-	12	-	20	-
Guinea Pig	15 H.E.*, 15	30	-	21	-	30	30	-	-	-	30	30	-
MORTALITY AND SACRIFICE RECORD													
WEIGHT RECORD	Dogs and Rats: Weekly, month 1-3; semimonthly, months 4-13; Rabbits and Guinea Pigs: Weekly, months 1 and 2; biweekly, months 3-10.												
HEMATOLOGY	10 dogs, 15 rats each level, semimonthly.												
PATHOLOGY	Plan No. 1 (altered)	No.2	No.2	No.2	No.2	No.1 (with specialties)	No.1	No.2	No.2	No.1	No.1	No.2	No.2
RENAL BIOPSY AND MICROSCOPIC URINE EXAMINATIONS		also hepatic		2 dogs each level, initial, 10 day, 4 and 3 months.									
BIOCHEMISTRY	Plan No. 1 AAN/Creatinine	No.2 Rabbits: Urea	No.2 No Catalase	No.1	No.1	No.2 Rabbits Catalase	No.1 No AAN Creatinine	No.2	No.1	No.1 No Catalase	No.1	No.1 No AAN or Catalase, Rabbits	No.2
LIVER FUNCTION TESTS	5 dogs 10 rats 5 rabbits						5 Dogs 10 Rats 5 Rabbits		5 Dogs 10 Rats		5 Dogs 10 Rats 5 Rabbits	5 Dogs 10 Rats	
RENAL CLEARANCES						3 Dogs	3 Dogs						
TISSUE ANALYSES	No.2 (modified)	No.1	No.2	No.1	No.2	No.1	No.2	No.2	No.2	No.2	No.2	No.2	No.2

*Head Exposure

1019160

22 January 1946

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDY - continued

Renal Clearance (Dr. Roberts)

Baxter

Ashenberg

Tornaben

6 days - 3 on 0.15 and 3 on 1.35 mg. T/m^3 as TNO_3.

3 each week.
Exposure to begin January 28 on low level, February 4 on high level.

Diodrast)
Inulin) clearances
Chloride)

Microscopic exam of urines

Catalase

Protein

Amino Acids

Hematology

Blood N.P.N.

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDIES (continued)

Renal Clearance (Dr. Roberts)

Baxter
Ashenberg
Tornaben

6 days - 3 on 0.15 and 3 on 1.35 mg. T/m^3 as TNO_3

3 each week
Exposure to begin January 28 on low level, February 4 on high level

Diodrast)
Inulin) clearances
Chloride)

Microscopic exam of urines
Catalase
Protein
Amino Acids
Hematology
Blood NPN

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDIES (continued)

LIVER-FUNCTION TESTS - Dr. Field

Material	Unit	Level	Test	Interval
		5 dogs - not hematology animals 10 rats - separate groups from all others		
Control	10	-	P,F,B	Before; week 1, 4 and monthly.
01	3	High	P,F,B	Before; 1, mo. 1; week 1,2,4 mo. 2; monthly
01	5	Low	P,F,B	Before; 1, mo. 1; week 1,2,4 mo. 2; monthly
07	12	High	P,F,B	Before; 1, mo. 1; week 1,2,4 mo. 2; monthly
12	7	Low	P,F,B	Before; 1 mo. 1; week 1,2,4 mo. 2; monthly
		5 rabbits		
Control	10	-	P,F	Before; Calendar-day 4, 10, 21, 36
01	3	Low	P,F	and every 4 weeks
12	7	Low	P,F	thereafter

P = Prothrombin; F = Fibrinogen; B = Bromsulfalein

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDIES (continued)

Project No. 108 — Renal Function Tests
Renal Clearance Studies on Dogs

Current Status — Clearance studies of inulin, chloride and diodrast have been made for a preliminary period preparatory to similar studies on the animals following exposure to two different levels of T nitrate dust; 0.15 and 1.0 mg. of T per cubic meter.

Personnel — Dr. Eugene Roberts, Head
Messrs. Baxter, Ashenburg, Tornaben

Tests Completed — 3-month control studies.

Tests Projected — Clearance of inulin, chloride and diodrase will be made 10 days after the start of exposure to be followed by determinations at two week intervals for the following six weeks, month intervals thereafter.

Concurrently determinations of blooc NPN, cellular constituents of the blood and urinary catalase, protein, and amino acid nitrogen as well as microscopic examination of the urine are to be made; also creatinine.

GENERAL PROCEDURES OF ONE YEAR INHALATION STUDIES (continued)

CHEMISTRY PLAN NO. 1

BLOOD

NPN - 10 dogs - Hematology Group - Semimonthly, month 1; weekly, month 2; monthly, month 3-13

10-12 rabbits - Semimonthly, month 1; weekly, month 2; monthly, month 3 to end.

URINE

Protein - 10 dogs - Hematology Group - Semiweekly, month 1; thrice weekly, month 2; 5 days per month, month 3-13.
10-12 rabbits - Twice weekly, month 1; thrice weekly, month 2; 5 times monthly to end.

Catalase - 2-4 dogs - Renal Clearance Group - (Specially prepared by exteriorized bladder or vaginal operation), Semi-weekly, month 1, 2; 5 days per month, month 3-13.
10-12 rabbits - Daily months 1-2; 5 consecutive days per month, months 3 to end.

Amino Acid Nitrogen-Creatinine Ratio - Dogs same schedule as for protein.
10-12 rabbits twice weekly, month 1; 3 times weekly, month 2; 5 times monthly, month 3 to end.

Sugar - qualitative as requested.

CHEMISTRY PLAN NO. 2

BLOOD

NPN - 10 dogs - (Heamtology Group, if done) - Semimonthly, month 1, weekly, month 2; monthly, month 3-13.
10-12 rabbits - Semimonthly, month 1; weekly, month 2; monthly, month 3 to end.

URINE

Protein - 10 dogs - Semiweekly, month 1, thrice weekly month 2; 5 days per month 3-13.
10-12 rabbits - Twice weekly, month 1; thrice weekly, month 2; 5 times monthly, month 3 to end.

Sugar - qualitative as requested.

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CAPACITY AND PROCEDURES OF THE SERVICE DEPARTMENTS FOR THE INHALATION SECTION FOR THE PERIOD JUNE 1, 1945 TO JULY 1, 1946

CAPACITY OF HEAMTOLOGY SECTION

Capacity of 25 counts to be taken semi-monthly on 10 levels for 13 months. In addition to this we can arrange for one acute run at a time, blood counts for which can be taken at weekly intervals. The counts on all runs are to be done on 10 dogs and 15 rats. It is also understood that should any bleeding for other purpose be done on either dogs or rats, that the amount of blood drawn and the frequency of this bleeding shall be the same for all chronic runs. These runs are to start on consecutive week-days Monday thru Friday as: 1st Monday; second Tuesday; third, Wednesday; fourth, Thursday; fifth, Friday. The next Monday, sixth run; Tuesday, seventh run; Wednesday, eight run; Thursday, ninth run; Friday, tenth run.

Signed George M. Suter

CAPACITY OF ROUTINE CHEMICAL ANALYSIS LABORATORY

The maximal daily capacity of this laboratory, for short periods of time, is indicated in Table I.

TABLE I

Maximal Daily Capacity of Routine Chemical Analysis Laboratory

Alternative Daily Schedules
(either schedule 1 or 2, etc., but not 1 and 2, etc.)

	URINE					BLOOD	
	Amino Acid						
Schedule	Rabbit	Human	Protein	Sugar	Chloride	NPN	Urea
1	20	20	200	0	0	60	0
						or	
2	30	10	150	50	0	40	30
3	40	0	100	100	0	as above	
4	10	10	100	100	30		
5	15	5	100	100	30		

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This capacity could only be maintained for periods of ten days to two weeks, with intervals in between for recuperation.

Totals of 30 ureas, 200 proteins, 60 NPNs, and 40 urinary amino nitrogen determinations are the absolute maximum. Alternative schedules other than those listed may be possible, as long as the above maximums are not exceeded.

The average monthly capacity of the laboratory is listed in Table II.

TABLE II

Optimal Monthly Capacity of Routine Chemical Analysis Laboratory

Determination	Number
Urinary Amino Nitrogen	200
Urinary Protein	2000
Urinary Sugar	2000
Urinary Chlorides	600
Blood NPN	1200
or	
NPN	800
Urea N	600

Signed Frank A. Smith

[redacted]

PROCEDURE OF TISSUE ANALYSES BY MR. ORCUTT'S GROUP
under direction of Dr. W. Neuman

PLAN #1

1 dog sacrificed at 10 day and 4, 6, 8 and 12 months of exposure.

2 rats each sacrificed after 6, 12, 18, 24, 30, 36, 42, 48, 54, 60, 120, 140, 180, 250 and 300 hours of exposure and every 4 weeks thereafter to the termination of the exposure.

At each sacrifice, the lung, liver, kidney, and femur will be analysed for T by the photofluorometric method. In addition to these tissues the following tissues will be taken on each sacrificed dog and on 2 rats each at the 6 and 12 month periods.

Lung (with pulmonary nodes)	Washed Intestine and Contents
Kidney	A. Rat - entire
Liver	B. Dog - from bowel ca 3", terminal ileum
Elbow	
Tooth	Gastrocnemius
Brain	Spleen
Eye Balls	Pancreas
Thyroid (dog only)	Gall Bladder (with contents)
Heart	Adrenal (dog only)
Aorta and Contiguous Vessels	Testis
Pulmonary Lymph Nodes (dog only)	Bladder Urine

PLAN #2

This plan resembles Plan #1 except that fewer sacrifices of rats will be made in the initial stages of exposure. Two rats each will be sacrificed after 6, 12, 18, 24, 30, 54, 66, 120, 140, 180, 250 and 300 hours of exposure and every 4-weeks thereafter to the termination of exposure.

(kwz) February 5, 1946

[redacted]

[redacted]

PATHOLOGY PLAN I

Dog: Serial: 10 days; 4, 6, and 8 months.

Final: 15 dogs.

Biopsy: 2 dogs initial; 10 days, 4 and 8 months.

Procedures: 1. Complete tissues on all dogs without brain.
2. Bone marrow smears on terminal dogs.

Rat: Serial: 1, 2, 3, 5, 7, 14, 21, and 30 days, and every 2 weeks from there on. (*Extra 3 animals for these times.)

Final: 50 rats. 25 with complete tissues.
25 with kidney only.

Procedures: 1. 3 rats at each designated time interval.
2. Lung, liver, and kidney on all rats. Complete tissues are saved.
3. Complete tissues on 25 animals at the end.
4. Bone marrow smears on terminal 50, if indicated by hematology.

Rabbit: Kidney only.

PATHOLOGY PLAN II

Dog: Serial: 10 days; 4, 6, and 8 months.

Final: 15 dogs.

Biopsy: 2 dogs Initial 10 days, 4 and 8 months.

Procedures: 1. Complete tissues all dogs, without brain.

Rat: Serial: 3, 5, 7, 14, 21, 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, and 330 days. (*3 additional animals at these points.)

Final: 50 rats.

Procedures: 1. 3 rats at each designated time interval.
2. Lung, liver, and kidney on all rats. Complete tissues are saved.
3. Complete tissues on 25 animals at end. 25 with kidney only.

Rabbit: Kidney, lung on insoluble dusts only.

[redacted]

Lung, liver, and kidney will be done on any and all dying animals for each

[redacted]

chronic run. In case of a severe epidemic with many deaths, this could not be done.

It is suggested that, if there are animals not scheduled for pathology upon which the experimenter would particularly like to have all of the tissues, he could do his own autopsy and save the tissue in 10% formalin. The reading of such tissues might be done if time ever developed.

SPECIAL PATHOLOGY PROCEDURES

A. Eugene Roberts — Plan 1 (Nitrate)

1. Additional Animals.

   a. Rabbits: Kidney of selected rabbits. (Also Spiegl and Rothstein)
   b. Adult rats: Serial sacrifice for 6 months to have lung, liver and kidney. Three rats at each sacrifice schedule (weekly for one month and semi-monthly thereafter.)

2. Bone Marrow Smears:

   a. To be done on all terminal rats and dogs, if there is dramatic change in hematology.

B. Paul Dygert: — Follow Plan 2 for both runs (TO_2).

C. U. C. Pozzani: — Plan 2 (Nitrate)

D. Charles J. Spiegl — Plan 1 (TF_6)

E. J. J. Rothermel — Plan 2 (TCl_4)

F. A. Rothstein — Plan 2 (TO_2)

G. George Sprague — Plan 1 (altered) (control)

Dogs - terminal (all tissues of dogs).
Dogs - 2 biopsy dogs, initial 10 days, 4 and 8 months.
Rats - 3 animals per week for one month; semi-monthly thereafter.
50 terminal rats, 25 with kidney only.

Tissues: lung, liver, and kidney
No Bone marrow smears on terminal animals, unless done on experimental animals

R. G. Metcalf, Capt. M.C.
Pathology Division

(kwz) 1019170 February 5, 1946

[redacted]

SCHEDULE OF EXPOSURE OF ANIMALS OF INHALATION SECTION

1945 - 1946

UNIT	MATERIAL	START OF 28-DAY PRE-EXPOSURE CONDITIONING PERIOD			START OF 1-YEAR EXPOSURE PERIOD		
		Dog	Rat	Remarks Rabbits and Guinea Pigs	Dog	Rat	Remarks Rabbits and Guinea Pigs*
2X	TF_4	July 23	July 23	Nov. 5†	Aug. 20	Aug. 20	Dec. 11
3	T-nitrate	June 6	June 6	Nov. 5	July 2	July 2	Dec. 11
5	T-nitrate	July 11	July 11	-	Aug. 8	Aug. 8	-
7	TF_6	Aug. 1	Aug. 1	Nov. 5**	Aug. 29	Aug. 29	Dec. 11
10	Control	June 15	June 15	Nov. 5	July 13	July 13	Dec. 11
11	TO_2	June 8	June 8	Nov. 5† Rats on both levels killed June 30 because of enteric bacterial infection. Replaced with rats from S.M.H.	July 6	-	Dec. 11
			July 20			Aug. 17	
12	TCl_4	June 20	June 20	Nove. 5† Rats on both levels killed July 1-5 because of enteric bacterial infection. Replaced with rats from S.M.H.	July 18	-	Dec. 11
			July 18			Aug. 16	

18 January 1946

* 6 months only.

** Rabbits on high level, guinea pigs on low level.

† High level only.

1019171

INHALATION SECTION
LIST OF FINAL REPORTS OF ACUTE RUNS COMPLETED AND OUTSTANDING

COMPOUND	LEVEL	AUTHOR	STATUS
T nitrate	20.0	Roberts	In progress
	20.0	Dygert	
	4.5	Roberts	Completed
	2.0*	Roberts	
	0.9*	Pozzani	
	0.5	Roberts	In progress
	0.3*	Roberts	
	0.1*	Pozzani	
TO_2	22.0	Dygert	Completed
	10.0	Rothstein	
	10.0*	Dygert	
	2.0	Rothstein	
	1.0*	Dygert	
T_3O_8	17.0	Stokinger	Completed
TF_4	22.0	Dygert	Completed
	5.0	Dygert	
	3.0*	Rothstein	
	0.5	Dygert	In progress
	0.5*	Rothstein	
TO_4	20.0	Dygert	In progress
TO_3	19.0	Rothstein	Completed
TCl_4	18.0	Cobler	Completed
	3.3	Cobler	In progress
	1.0	Rothermel	
	0.26	Rothermel	In progress
	0.20*	Rothermel	
	0.10	Rothermel	
	0.05*	Rothermel	
TO_2F_2	12.0	Stokinger	Completed
	2.5	Rothstein	
	0.65	Rothstein	
	0.2	Rothstein	In Progress
TF_6	13.5	Spiegl	Completed
	2.03	Spiegl	In progress
	0.20	Spiegl	In progress
	0.20*	Spiegl	
	0.05*	Spiegl	

* First 30 days of chronic study.

[redacted]

COMPOUND	LEVEL	AUTHOR	STATUS
C-212	0.1	LaBelle	In progress
890	50 ppm.	Weil	Completed
	20 ppm.	Weil	In progress
Tribnol	100 ppm	Weil	Completed
	100 ppm	Weil	Completed
	15 ppm	Weil	Completed
'Hi-Grade'Ore	20.0	Dygert	In progress
	5.0	Pozzani	In progress
	1.4	Weil	Completed
$Na_2T_2O_7$	20.0	Rothstein	In progress
$(NH_4)_2T_2O_7$	20.0	Dygert	
C-216	100 to 10,000 ppm.	Eriksen	In progress
	25.0	Eriksen	Completed
	8.0	Eriksen	Completed
	0.8	Eriksen	In progress
	3.0	Eriksen	In progress
HF	25.0	Eriksen	In Progress
	7.0	Eriksen	In progress
891	73.0	Weil	Completed
Control	091K (90 day)	Sprague	In Progress
	092K (90 day)	Sprague	In Progress
	21AC (30 day)	Sprague	In Progress
	21BC (36 day)	Sprague	In Progress

Total number of final reports - 60
Number of reports completed - 16
Number of reports in progress - 23
No. of reports to be written - 21

Signed H. E. Stokinger

13 December 1945

[redacted]

[redacted]

PROJECT NO. 16 INHALATION TOXICITY STUDIES OF TF_6 AND PRODUCTS

Current Status

Two 1-year exposure studies of dogs, rats, guinea pigs and rabbits to 0.05 mg. T and 0.2 mg. of T as TF_6 per cubic meter.

Personnel

Dr. Charles Spiegl - Unit Head
Messrs. Schepartz, Minor and Marx - Assistants

Tests Completed

Three 30-day studies

13.5 mg of T/m^3
2.0 mg of T/m^3
0.2 mg of T/m^3

Tests Projected

None

23 January 1946

1019174

[redacted]

[redacted]

PROJECT NO. 17 TOXICITY OF UO_2F_2 DUST BY INHALATION

CURRENT STATUS: No current work.

TESTS COMPLETED: Exposure for 30 days to

a) 12 mg/m³ UO_2F_2
b) 2.5 mg/m³ of air
c) 0.65 mg/m³
d) 0.2 mg/m³

TESTS PROJECTED: None

18 January 1946

1019175

[redacted]

[redacted]

PROJECT NO. 18 — INHALATION TOXICITY STUDIES OF T NITRATE DUST

Current Status — Four 1-year exposure studies of dogs, rats, guinea pigs and rabbits to 0.05, 0.15, 0.45, and 1.5 mg T/m^3 as T nitrate.

Personnel — Dr. Eugene Roberts - Unit Head (0.15 and 1.0 mg T)
Messrs. Bishop, Pettengill, Laush, Amdur

Mr. U. C. Pozzani - Unit Head (0.05 and 0.45 mg T)
Messrs. Ashenburg, Wilson, Sanford

Tests Completed — Four 30-day studies

Two at 20 mg T nitrate/m^3
One at 4.5 mg T nitrate/m^3
One at 0.5 mg T nitrate/m^3

Tests Projected — None

23 January 1946

1019176

[redacted]

[redacted]

PROJECT NO. 19 — INHALATION TOXICITY STUDIES OF TF_4 DUST

Current Status — Two 1 year exposure studies of dogs, rats, guinea pigs and rabbits to 0.5 and 3.0 mg T as $TF_4/m3$.

Personnel — Dr. Aser Rothstein - Unit Head
Messrs. Dittman, Berke, Fisher

Tests Completed — Three 30-day studies

22.0 mg TF_4/m^3
5.0 mg TF_4/m^3
0.5 mg TF_4/m^3

Tests Projected — None

21 January 1946

1019177

[redacted]

PROJECT NO. 21 — INHALATION TOXICITY STUDIES OF TO_2 DUST

Current Status — Two 1 year exposure studies of dogs, rats, guinea pigs and rabbits to 1.0 and 10.0 mg T as TO_2 per cubic meter.

Personnel — Mr. Paul Dygert - Unit Head
Messrs. Oberg, Wichser, Boothe, Baxter

Tests Completed — Three 30-day studies

22.0 mg TO_2/m^3
10.0 mg TO_2/m^3
2.0 mg TO_2/m^3

Tests Projected — None

21 January 1946

~~SECRET~~

PROJECT NO. 22 INHALATION TOXICITY STUDIES OF C-212

CURRENT STATUS: None

TESTS COMPLETED:
a) Acute pilot exposure to 10, 5, 1, 0.5, 0.1 ppm. All animals (10 mice, 10 rats, 8 rabbits, and 20 guinea pigs) died within 3 hours and 26 minutes.
b) 30 day exposure to 0.1 ppm. Dogs, rabbits, guinea pigs, rats, mice.

TESTS PROJECTED: None

18 January 1946

1019179

~~SECRET~~

[redacted]

PROJECT NO. 23 TOXICITY OF T_3O_8 DUST BY INHALATION

CURRENT STATUS: No current work.

Personnel

None

TESTS COMPLETED: Exposure for 30 days to 17 milligrams per cubic meter of T_3O_8.

TESTS PROJECTED: None

18 January 1946

1019180

[redacted]

[redacted]

PROJECT NO. 24 TOXICITY OF TO_3 DUST BY INHALATION

CURRENT STATUS: No current work.

TESTS COMPLETED: Thirty-day exposure to 19 mg./m^3.

TESTS PROJECTED: None

18 January 1946

[redacted]

[redacted]

PROJECT NO. 8R V513 INHALATION TOXICITY STUDIES OF TCl_4 DUST

Current Status	Two 1 year exposure studies of dogx, rats, guinea pigs and rabbits to 0.05 and 0.2 mg T as TCl_4/m^3.
Personnel	Mr. J. J. Rothermel - Unit Head Messrs. Harrison, Finegan and Miss Ward
Tests Completed	Five 30-day studies 18.0 mg of TCl_4/m^3 3.3 mg of TCl_4/m^3 1.0 mg of TCl_4/m^3 0.3 mg of TCl_4/m^3 0.1 mg of TCl_4/m^3
Tests Projected	None

21 January 1946

1019182

[redacted]

~~SECRET~~

PROJECT NO. 28 INHALATION TOXICITY STUDIES OF C-216

CURRENT STATUS: No current work.

TESTS COMPLETED:
a) Pilot tests at high concentrations for very short periods, 10,000 to 100 ppm.
b) Exposure for 30 days to 25 milligrams of C-216 per cubic meter; for 30 days to 8 milligrams per cubic meter and for 30 days to 3 milligrams (and to 0.8 mg.) of C-216 per cubic meter.

TESTS PROJECTED: None

18 January 1946

~~SECRET~~

[redacted]

PROJECT NO. 29 INHALATION TOXICITY STUDIES OF HF

CURRENT STATUS: No current work.

TESTS COMPLETED: a) 30 day exposure to 25 milligrams of HF per cubic meter, and 30 day exposure to 7 milligrams of HF per cubic meter.

TESTS PROJECTED: None

18 January 1946

1019184 [redacted]

~~SECRET~~

PROJECT NO. 30

TESTS OF EFFICIENCY OF RESPIRATORY PROTECTIVE DEVICES IN ATMOSPHERES OF T COMPOUNDS CONTAINING C-216.

Current Status: No current work.

Experiments Planned: None

Tests Completed: Respiratory protective devices have been tested against dust of TO_2, TO_4; $3H_2O$, T_3O_8, TF_6, TF_4, $TO_2(NO_3)_2 \cdot 4H_2O$, $(NH_4)_2T_2)_7 \cdot 4H_2O$, 'Hi-Grade' Ore, and C-716 and fractions.

Personnel: None

18 January 1946

~~SECRET~~

SECRET

PROJECT NO. 92 C-216 ANALYSIS

Mr. Schlamowitz has demonstrated the inhibition of liver esterase activity by C-216. This effect was applied to the quantitative determination of C-216 in aqueous solution. Comparison with the chemical method has been quite satisfactory. Application of the enzymatic method of C-216 analysis to sampling of chamber air containing C-216 has been made successfully.

18 January 1946

SECRET

PROJECT NO. 93 STAINING OF PHOSPHATASE AND RENAL TISSUE OF T POISONED ANIMALS

CURRENT STATUS: Results difficult to interpret. No further work current.

15 January 1946

[redacted]

PROJECT NO. 109 — CARBOHYDRATE METABOLISM IN T AND F POISONED ANIMALS.

Current Status — Report being written as a thesis by Charles Bishop.

Personnel — Roberts, Bishop

Tests Projected — None

[redacted]

[redacted]

PROJECT NO. 110

CHANGES IN BLOOD POTASSIUM AND CO_2 IN ACUTE T POISONING

Current Status

To date, severe U poisoning either by pulmonary or parental routes has been found to cause reduction in total blood CO_2 but little or no change in the level of blood potassium.

Personnel

Roberts

[redacted]

SECRET

PROJECT NO. 111	THE RETENTION AND ABSORPTION BY ALVEOLAR TRANSPORT OF INHALED T DUST
Current Status	Preliminary testing of equipment with animals is in progress.
Personnel	Messrs. LaBelle and Todd, Dr. Rothstein
Tests Completed	Equipment of unique design has been constructed. This includes a small exposure chamber, a new type of dust feed which maintains a very constant dust concentration, a system for obtaining all exhaled air of an animal without interfering with breathing, two sets of apparatus to obtain dust of a given size-range and an apparatus for making rapid determinations of particle size on bulk dust.
Tests Projected	Measurements of lung retention as outlined in the project statement.

23 January 1946

SECRET

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PROJECT NO. 120 INHALATION TOXICITY STUDIES OF TRIBNOL, CHLORTHANE, 890, 891

CURRENT STATUS: No current work.

TESTS COMPLETED: A. Acute CT-Studies, completed

1. Tribnol - Pilot toxicity exposures to 20, 36, 150, 370 and 700 ppm.
2. Chlorthane - Pilot toxicity exposures to 20, 50, 85 and 100 ppm.
3. 890 - Pilot toxicity exposures to 20, 40, 100, 200, 350, 400, 500, 600, 700, 850, 900, 1000, 1500, 2000, 3000, 3500 and 4500 ppm.

B. Thirty day studies completed or in progress.

1. Tribnol - 30 day exposure to 100 ppm.
1a. Repeat 30-day exposure to 100 ppm. (Tribnol)
2. 890 - 30-day exposure to 50 ppm.
3. 890 - 30-day exposure to 20 ppm.
4. 891 - 30-day exposure to 70 mg/m^3.
5. Tribnol - 9-day exposure to 20 ppm.
6. Tribnol - 30-day exposure to 15 ppm.

TESTS PROJECTED: None

18 January 1946

1019191

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[redacted]

PROJECT NO. 137

THE USE OF BLOOD CLOTTING TIME AS AN EARLY INDEX OF TOXICITY RESULTING FROM T AND c-216 COMPOUNDS

Current Status

Light borderline hepatic damage was observed in animals exposed to the low levels of T nitrate, TF_6 and TCl_4 in the present one-year series of exposures. Dysfunction was detectable after the first two to four weeks of exposure. After a prolonged period of normalcy signs of dysfunction reappeared. Six months later they are still frequently observed.

Tests Projected

Continuation of one year exposures.

Tests Completed

See Current Results.

Personnel

John Field

10 April 1946

[redacted]

1019192

~~SECRET~~

PROJECT NO. 138 TOXICITY OF $Na_2T_2O_7 \cdot 4H_2O$ DUST BY INHALATION

CURRENT STATUS: No work current

Personnel:

None

TESTS COMPLETED: 30-day exposure to 20 mg/m^3

TESTS PROJECTED: None

18 January 1946

1019193

~~SECRET~~

[redacted]

PROJECT NO. 139 TOXICITY OF 'HI-GRADE' T ORE BY INHALATION

CURRENT STATUS: No work current.

Personnel:

None

TESTS COMPLETED: 30-day exposure to 20 mg/m³ of Hi-Grade T Ore.
30-day exposures to 5 mg. and to 1 mg./m³.

TESTS PROJECTED: None

18 January 1946

[redacted]

[redacted]

PROJECT NO. 140 TOXICITY OF $TO_4 \cdot 3H_2O$ DUST BY INHALATION

CURRENT STATUS: No work current.

Personnel:

None

TESTS COMPLETED: 30-day exposure to 20 mg./m^3 of TO_4.

TESTS PROJECTED: None

18 January 1946

1019195

[redacted]

SECRET

PROJECT NO. 141 TOXICITY OF $(NH_4)_2T_2O_7$ DUST BY INHALATION

CURRENT STATUS: None

Personnel:

None

TESTS COMPLETED: 30-day exposure to 20 mg/m³.

TESTS PROJECTED: None

18 January 1946

SECRET

[redacted]

PROJECT NO. 155

THE STUDY OF PARTICLE SIZE, PARTICLE COUNT AND CONCENTRATION OF T DUSTS IN INDUSTRIAL AREAS AND IN LABORATORY STUDIES

Current Status

Determination of mean particle weight size of the 5 T dusts used in the chronic inhalation studies.

Personnel

Mr. Laskin and Dr. Rothstein - head
Messrs. Fiorica, Glover and Miss Reid

Tests Completed

Routine weekly samples of each of 10 exposure levels of 4 T dusts taken by means of the Cascade Impactor, TCl_4, T nitrate, TF_4 and TO_2. The products of TF_6 are being studied by electron-microscope technique.

Projected Tests

None.

23 January 1946

1019197

[redacted]

[redacted]

[redacted]

CURRENT STATUS

ENGINEERING SECTION

Neil Murphy, Chief of Section

ENGR

January 1946

1019198

[redacted]

[redacted]

ENGINEERING SECTION

Current Status

Present assignments include normal chamber maintenance, studies on air velocity distribution in chambers, and determination of the effect of variables upon estimated dust concentrations predicted from alpha emission rats of filter paper samples.

22 January 1946

[redacted]

1019199

[redacted]

ANALYTICAL SECTION

Current Status Index

Project No. 97	Analytical Methods for Mx, My and Mz.
Project No. 164	Solubility of T Compounds. Approximate Measurement Rate in Solution of T Compounds in Serum and in Water.

[redacted]

[redacted]

PROJECT NO. 97 ANALYTICAL METHODS FOR MX, MY, and MZ

Current Status

Consultation
- a. Polarographic Studies (Dounce)
- b. Analysis of Soil Samples (Tybout)

1. The use of organic reagents to recover traces of T from a highly contaminated effluent solution
   Testing the reactions of known and available organic reagents.
   The purpose of these investigations is to disclose a reagent that will either
   - a. precipitate T directly from the solution, without contamination of the precipitate by iron, copper, nickel or chromium, or
   - b. remove these latter elements, leaving the T in solution.
2. My measurements are anticipated occasionally.
3. Glass electrode to measure T in solution.
4. Solubility of T compounds in plasma.
5. Polarographic analyzer.
6. Writing reports.

Personnel

John Flagg, Head
Tishkoff

30 January 1946

1019201

[redacted]

[redacted]

PROJECT NO. 164

SOLUBILITY OF T COMPOUNDS
Approximate Measurement Rate in Solution of T Compounds in Serum and in Water.

Current Status

Rate of solubility of 11 T materials in serum and in water at 37° C.

Personnel

Mr. Tishkoff under the direction of Drs. Flagg

[redacted]

CURRENT STATUS

PHARMACOLOGY SECTION

Frances L. Haven, Chief of Section

PHARM

15 April 1946

[redacted]

[redacted]

PHARMACOLOGY SECTION

Current Status Index

Status of Final Reports on Ingestion

Ingestion Toxicity Calendar

Project No. 1	Chronic Toxicity of T Nitrate for Rats
Project No. 2	Chronic Toxicity of TF_4 for Rats
Project No. 3	Chronic Toxicity of TO_3 for Rats
Project No. 4	Chronic Toxicity of TO_2 for Rats
Project No. 5	Chronic Toxicity of T_3O_8 for Rats
Project No. 6	Chronic Toxicity of CoF_3 for Rats
Project No. 7	Chronic Toxicity of TO_4 for Rats
Project No. 8	Chronic Toxicity of TCl_4 for Rats
Project No. 9	Chronic Toxicity of TO_2F_2 for Rats
Project No. 10	Chronic Toxicity of TO_2Ac_2 for Rats
Project No. 11	Chronic Toxicity of TO_2 for Dogs
Project No. 12	Chronic Toxicity of TNO_3 for Dogs
Project No. 13	Chronic Toxicity of TCl_4 for Dogs
Project No. 14	Chronic Toxicity of TO_2F_2 for Dogs
Project No. 15	Chronic Toxicity of TF_4 for Dogs
Project No. 118	Chronic Toxicity of High Grade T Ore for Dogs
Project No. 129	The Tolerance to an Acute Dose of T Induced by Repeated Administration of Small Doses of T.
Project No. 132	Distribution, Storage and Excretion of T Administered by Various Routes, Chronic and Acute

[redacted]

[redacted]

Project No. 148	Lipids in T Poisoning
Project No. 149	The Use of the Radioactive Isotope in the Study of Distribution, Storage and Excretion of T in the Animal Body.
Project No. 150	The Effect of Various Agents on T Nitrate and TO_2F_2 Toxicity.

[redacted]

[redacted]

FINAL REPORTS

on Ingestion

I. 30 DAY RATS

1. U Nitrate - complete
2. UO_2 - complete
3. U_3O_8 - complete
4. UF_4 - complete
5. UO_3 - complete
6. UCl_4 - complete
7. U Acetate - complete
8. CoF_3 - complete
9. UO_4 - complete
10. UO_2F_2 - In progress
11. UF_4(bluish) - complete
12. U Nitrate - complete (6 mo. old rats)

II. 30 DAY HAMSTERS

1. U Nitrate

III. 30 DAY RABBITS

1. U Nitrate - In progress

IV. 30 DAY DOGS

1. U Nitrate
2. UO_2F_2
3. UO_2
4. UF_4
5. U_3O_8
6. UO_3
7. UO_4
8. UCl_4
9. $Na_2T_2O_7$
10. $(NH_4)_2T_2O_7$
11. U Ore

V. ONE YEAR RATS

1. U Nitrate

VI. ONE YEAR DOGS

1. UO_2F_2
2. U Nitrate
3. UCl_4
4. UO_2
5. UF_4

VII. TWO YEAR RATS

1. U Nitrate - In progress
2. UO_2
3. UF_4
4. UO_2F_2

VIII. BREEDING EXPERIMENT

1. U Nitrate - In progress

IX. PAIRED FEEDING EXPERIMENT

1. U Nitrate - In progress

[redacted]

[redacted]

INGESTION TOXICITY CALENDAR

1946

February - Paired feeding test - T nitrate to rats.

March - 1 year test - T nitrate to rats (VII)

April - 2 year test - TO_2F_2 to rats (V)

May - 1 year test - TO_2F_2 to a dog

August - 2 year test - T nitrate to rats (IIIB)

October - 2 year test - TO_2F_2 to rats (VI)

1947

February - 1 year test - TF_4 to dogs

1 year test - TO_2 to dogs

22 January 1946

1019207

[redacted]

[redacted]

PROJECT NO. 1 CHRONIC TOXICITY OF T NITRATE FOR RATS

Current Status

Two year test: groups of female rats are fed 2, 1, .5, 1. T nitrate in their diets. The feeding has been in progress for nearly 18 months for the oldest group and is to continued until August 1946.

One year feeding experiment. Groups of rats are being fed various levels of T nitrate in the diets for periods of 3, 6, 9 and 12 months. The first group was started on the diets on 20 February 1945.

Paired feeding tests of young and old groups.

Tests Completed

Thirty day tests feeding male and female weanling rats 20, 10, 5, 3, 2, 1 and .5% of T nitrate.

Thirty day tests feeding male and female adult rats 2, .5, and .1% of T nitrate.

Some of the 2 year studies.

Tests Projected

None

Personnel

Mr. Maynard and group.

22 January 1946

[redacted]

1019208

[redacted]

PROJECT NO. 2 CHRONIC TOXICITY OF TF_4 FOR RATS

Current Status — No work current.

Tests Completed

a) Thirty-day feeding test. Groups of male and female rats were fed .5, 2 and 20% TF_4. Final report has been submitted.

b) A supplementary 30-day feeding test was run in August 1944 to test the 'blue-green' salt currently manufactured.

c) 2-year study in which groups of male and female animals are fed diets containing .5, 2 and 20% TF_4, respectively in their diets.

Tests Projected — None

Personnel — None

[redacted]

[redacted]

PROJECT NO. 3 CHRONIC TOXICITY OF TO_3 FOR RATS

Current Status — No work current

Tests Completed — 30-day feeding test in which groups of male and female rats were fed .5, 2, and 20% TO_3 in their diets. This test was fun in September 1943. Final report has been submitted.

Tests Projected — None

Personnel — None

22 January 1946

[redacted]

[redacted]

PROJECT NO. 4 CHRONIC TOXICITY OF TO_2 FOR RATS

Current Status — no work current.

Tests Completed — 30 day feeding tests. Groups of male and female rats were fed 0.5, 2 and 20% of TO_2, respectively in their diets for 30 days in July 1943. Final report has been submitted.

Two year feeding test. Groups of male and female rats were fed 0.5, 2 and 20% of TO_2, respectively, in their diets.

Tests Projected — None

Personnel — None

22 January 1946

[redacted]

1019211

[redacted]

PROJECT NO. 5 CHRONIC TOXICITY OF T_3O_8

Current Status — No work current.

Tests Completed — 30-day feeding test in which groups of male and female rats were fed 0.5, 2 and 20% of T_3O_8, respectively in the diets for 30 days. This test was begun in September 1943. Final report has been submitted.

Tests Projected — None

Personnel — None

22 January 1946

[redacted]

1019212

[redacted]

PROJECT NO. 6 CHRONIC TOXICITY OF CoF_3 FOR RATS

Current Status: No work current

Tests Completed: 30-day feeding tests. Groups of male and female rats were fed 0.5, 2 and 20 per cent of CoF_3 in their diets for 30 days. This test was begun in September 1943.

In January 1944 a supplementary one-month study was carried out using male rats fed 0.01, 0.05, and 0.1 per cent CoF_3, respectively, in the diets.

Tests Projected: None

Personnel: None

22 January 1946

[redacted]

1019213

SECRET

PROJECT NO. 7 CHRONIC TOXICITY OF TO_4 FOR RATS

Current Status — No work current.

Tests Completed

a) 30-day feeding tests in which groups of female rats were fed 0.5, 2.0 and 20 per cent TO_4 in their diets. This test was run in August 1943.

b) 30-day feeding test in which groups of male and female rats were fed 0.25 and 1.0 per cent TO_4 in their diets. This test was run in September 1943.

c) 30-day feeding test in which groups of male rats were fed 0.1, 0.5, and 1.0 per cent TO_4 in their diets. This test was run in November 1943.

d) 30-day feeding test in which an additional group of male rats was fed 2.0 per cent TO_4 in their diets. This test was run in November 1943.

Tests Projected — None

Personnel — None

22 January 1946

SECRET

[redacted]

PROJECT NO. 8 CHRONIC TOXICITY OF TCl_4 FOR RATS

Current Status — No work current

Tests Completed

a) 30-day feeding tests in which groups of female rats were fed 0.5, 2.0 and 20 per cent TCL_4 in their diets. This test was run in September '43.

b) 30-day feeding test in which groups of male and female rats were fed 1.0, 1.5 and 3.0 per cent TCl_4 in their diets. This test was run in November 1943.

c) 30-day feeding tests in which groups of male and female rats were fed 0.2, 0.5, and 1.0 per cent TCl_4 in their diets. This test was started January 1944.

Tests Projected — None

Personnel — None

22 January 1946

[redacted]

1019215

[redacted]

PROJECT NO. 9 CHRONIC TOXICITY OF TO_2F_2 FOR RATS

Current Status

a) 2-year feeding test in which groups of male female rats were placed on a diet of 0.01, 0.05, and 0.25 per cent TO_2F_2. This was started April 1944 to run for 2 years.

b) 2-year feeding test in which groups of male rats were placed on a diet of 0.05, 0.10, and 0.15 per cent TO_2F_2. This was started in October 1944 to run for 2 years.

Tests Completed

a) 30-day feeding tests in which groups of male and female rats were fed 0.5, 2.0 and 20 per cent TO_2F_2. This test was run in December 1943.

b) 30-day feeding tests in which groups of male and female rats were fed 0.25, 1.0 and 5.0 per cent TO_2F_2 in their diets. This test was run in December 1943.

c) 30-day feeding test in which groups of male and female rats were fed 0.05, 0.1, and 0.25 per cent TO_2F_2 in their diets. This test was run in December 1943.

d) 2-year feeding test in which groups of male and female rats were fed 0.25 and .50 per cent TO_2F_2 in their diets.

Tests Projected None

Personnel Mr. Maynard

22 January 1946

[redacted]

1019216

[redacted]

PROJECT NO. 10 CHRONIC TOXICITY OF TO_2Ac_2 FOR RATS

Current Status No work current

Tests Completed 30-day feeding test. Groups of male rats were fed 0.5, 2 and 20% of TO_2Ac_2 in their diets. This test was begun December 28, 1943. Final report has been submitted.

Tests Projected None

Personnel None

22 January 1946

[redacted]

[redacted]

PROJECT NO. 11 CHRONIC TOXICITY OF TO_2 FOR DOGS

Current Status	No work current.
Tests Completed	Thirty-day feeding experiment. One dog was fed 20 g/kg/day and survived thirty days. One dog was fed 5 g/kg/day and survived thirty days.
Tests Projected	One year feeding tests in which two dogs are fed at each of three levels.
Personnel	None

22 January 1946

[redacted]

~~SECRET~~

PROJECT NO. 12 CHRONIC TOXICITY OF TNO_3 FOR DOGS

Current Status — No current work.

Completed Tests

a) Four dogs were fed 10 g/kg/day, 2 g/kg/day, 0.5 g/kg/day and 0.1 g/kg./day, respectively.

b) Two dogs were fed 0.02, .1 and .2 g/kg/day of T Nitrate respectively.

Projected Tests — None

Personnel — None

22 January 1946

~~SECRET~~

1019219

[redacted]

PROJECT NO. 13 CHRONIC TOXICITY OF TCl_4 FOR DOGS

Current Status — Nonurrent work.

Tests Completed

a) Two dogs were fed 5 g/kg/day and 0.5 g/kg/day, respectively. Two dogs were fed 0.1 g/kg/day and 0.02 g/kg/day, respectively.

b) Two dogs were fed 0.05, .01 and .002 g/kg/day of TCl_4, respectively.

Tests Projected — None

Personnel — None

22 January 1946

[redacted]

1019220

[redacted]

PROJECT NO. 124 C-216 ANALYSIS

Current Results

1. A rapid method for the direct titration of C-216-ion in relatively pure aqueous solutions has been developed. The procedure specifies titration with thorium nitrate using Chrome Azurol S, S conc, Geigy, as an indicator. The accuracy of the method, the interference of other ions, and the application to the determination of C-216-ion in HC-216)-air mixtures are discussed.

2. The method used in this laboratory in routine fluoride analysis of a variety of samples specifies isolation of the fluoride from the prepared specimen by a single steam distillation from perchloric acid and back titration of the resulting fluoride compound with thorium nitrate and sodium alizarin sulfonate as indicator. Where preliminary evaporation and ashing of the sample are required lime is used as a fixative. In its present form the analysis, although not rapid, is routine in nature provided that certain precautions are constantly observed. It is estimated that two workers with adequate facilities (12 stills) can do 70 to 90 analyses a week. The procedure is scaled to cover a range of from 10 to 500 ug. With urine analyses recoveries of fluoride are 90 to 95%, with more pure solutions 95 to 100%.

   Since microgram quantities of fluorine are being determined the analysis should not be carried out in a laboratory where other work on fluorine containing compounds might cause traces to be present in the atmosphere. Contamination of the sample by minute amounts of fluoride can easily occur, especially during the alkaline evaporation. For the same reason reagents and apparatus should be carefully selected and guarded, and equipment such as fume hoods, evaporators, and muffle furnaces should not be used for other work involving fluorine compounds. For a comprehensive discussion of the methods and precautions see the report by P. A. Clifford[1].

1. Clifford, P. A., Journal of the Association of Official Agricultural Chemists, 27, 90, 246 (1944).

Personnel: A. Tarbell, M. J. Voss, J. Adolph

District File: M-1694, M-1581

Pharmacology Report Nos.: 334, 22.

1019221

[redacted]

[redacted]

MECHANISM SECTION

Current Results Index

Project 42	Kidney
Project 42	Addendum
Project 101	Proposed Further Experiments on Phosphatase
Project 130	Physical Chemistry of Uranium Compounds in Solution
Projects 31, 42, 75, 130 and 130.	General Current Results
Project 156	Excretion, Transportation and Retention Studies After Administration of T_6 and T_4.

14 April 1946

[redacted]

1019222

MECH

[redacted]

PROJECT NO. 42 KIDNEY

Current Results

The work of the Physiology Department can be classified under the following headings:

1. The Excretion of Uranium by the Kidney. In the rabbit the renal clearance and retention of uranyl uranium vary with the acid-base balance of the animal, as shown in the following compilation:

Treatment	Plasma CO_2 Content	Urine pH	U Clearance % Inulin	Kidney U (ug per gm.)
Oat fed	63	6.26	31.8	65
Normal	71	7.82	74.0	25
$NaHCO_3$	76	8.13	95.4	4

The sum of uranium excretion and retention by the kidney averaged 100.4% of glomerular filtration (calculated from inulin clearance, plasma level of uranium and the filterability of uranium at the existing plasma CO_2 capacity). Infusions of citrates and lactate increased slightly the excretion of uranyl uranium, but there is little doubt that bicarbonate is the most important carrier of uranyl uranium in the kidney. Infusions of Na citrate and $NaHCO_3$ may have increased slightly the urinary excretion of tetravalent uranium, and may have decreased the renal retention of tetravalent uranium to only about 6% of the figure with saline infusion. If the latter finding is correct, tetravalent uranium must be deposited on some endothelial structure of the kidney while hexavalent uranium is fixed entirely on epithelium. An experiment to test the first hypothesis is planned.

2. The Effect of Uranium on Renal Function. In the rabbit small doses of uranyl uranium have no effect on the clearances of substances which enter the urine entirely by glomerular filtration (creatinine, xylose, inulin), increase the clearances of substances reabsorbed in large part in the distal half of the proximal convoluted tubule (chloride and amino acid N), may increase the clearances of substances partially reabsorbed in the proximal convoluted segment (glucose and urea) and decrease the clearances of secreted substances (phenol red, diodrast, hippuran). Large doses of uranyl salts reduce the apparent filtration in the glomerulus by caused blockade of the tubule with epithelial debris and back diffusion of all water-soluble materials across the denuded tubule wall. Under such conditions all clearances are reduced.

[redacted]

[redacted]

PROJECT NO. 42 (continued)

3. The Physiology of Early Catalase Excretion. In the rabbit catalase was found not to be filtered or secreted by the kidney. The amount of catalase appearing in the urine at 1.5 to 2 hours after injection of uranyl uranium was found to be a linear function of the amount of metal given. Hexavalent uranium was about 4 times as effective in causing the early appearance of catalase in the urine as tetravalent uranium.

Reports: The work under heading 3 above has been written up and is to be included in the final report of Project No. 75. Final reports on the other headings are being prepared.

Personnel: E. R. Main
J. H. Wills

26 February 1946

1019224

[redacted]

[redacted]

PROJECT NO. 42 KIDNEY

Addendum to Current Results

The retention of tetravalent uranium by the kidney has been reinvestigated, and it has been found that the original analytical figures for the uranium content of the normal rabbit kidney after injection of U_4 must have been in error. When the recently-obtained values are used, it is seen that infusions of $NaHCO_3$ and Na citrate may have lowered slightly the retention of tetravalent uranium by the kidney at the same time at which they increased slightly the urinary excretion. When these findings are taken into account, it becomes apparent that tetravalent, like uranyl, uranium is fixed probably to epithelial structures of the kidney after glomerular filtration.

12 April 1946

[redacted]

[redacted]

PROJECT NO. 101 PROPOSED FURTHER EXPERIMENTS ON PHOSPHATASE

Current Results — Phosphatase method perfected and used for tissue and urine samples.

Personnel — O'Connell
Dounce
Rothermel

No final report

Monthly Report of Improved Method, February 1945, District File No. M-1644

Pharmacology Report No. 322

25 Februgry 1946

1019226

[redacted]

[redacted]

PROJECT NO. 130 PHYSICAL CHEMISTRY OF URANIUM COMPOUNDS IN SOLUTION

Current Results

A. Uranium Complex Formation. Ultrafiltration experiments, described in detail in the May 1945 Progress Report, show that the filterability of U_6 in the presence of a variety of plasma and serum is a rapidly increasing function of the carbon dioxide content of the medium. The results may be explained on the basis of an equilibrium between uranyl-bicarbonate complex and uranyl-protein complex. The results lead to some predictions regarding the effect of acidosis on the permeability of the glomerulus to U_6 in the plasma. Polarographic investigations on the uranyl-bicarbonate and carbonate complexes have shown that these two complexes are identical.

B. Oxidation-Reduction Studies Including Polarography. The dropping mercury and bright platinum electrodes have been used successfully to evaluate the oxidation-reduction potentials, and the kinetics involved have been elucidated. E_o for the $U_6 - U_4$ system was found to be +0.361 volts vs. N.H.E. for an acetate medium in which hexavalent uranium exists as $UO_2(Ac)_3^-$ and +0.321 volts vs. N.H.E. for an acetate medium in which $UO_2(Ac)_2$ exists. The sluggishness of the electrode reactions at platinum have been attributed to the small rate constants of the disproportionation-formation reactions of U_5. E'_{oh} at pH 7.0 is about -0.05 volts.

A polarographic method has been used to determine the number of complexing anions combined with U_6, U_5, and U_4 ionic species. These numbers are designated as p, q, and r, respectively. For the acetate complex at a concentration of 0.0001 molar uranium, p, q, and r were found to be 3, 1 and 2, respectively above 0.05 molar sodium acetate.

Calculations have been extended so that the dissociation constants of the acetate complexes of U_6, U_5 and U_4 could be evaluated. These were found to be:

$$UO_2(Ac)_3^- = 3Ac^- + UO_2^{++} \qquad K = 5.5 \times 10^{-7}$$
$$UO_2(Ac)_2 = 2Ac^- + UO_2^{++} \qquad K = 2.2 \times 10^{-5}$$
$$UO_2(Ac)_3^- = Ac^- + UO_2(Ac)_2 \qquad K = 2.6 \times 10^{-2}$$
$$UO_2(Ac)_1 = Ac^- + UO_2^{+} \qquad K = 2.6 \times 10^{-2}$$
$$UO(Ac)_2 = 2Ac^- + UO^{++} \qquad K = 2.4 \times 10^{-6}$$

The dismutation constant K for the dismutation of U_5 has been calculated in complexing and non-complexing media.

1019227

[redacted]

[redacted]

PROJECT NO. 14 CHRONIC TOXICITY OF TO_2F_2 FOR DOGS

Current Status: One dog is fed .01 g./kg./day of TO_2F_2. This experiment was begun May 21, 1945 and is to continue for twelve months.

Tests Completed:

a) Two dogs were fed 5 g./kg./day and 0.5 g./kg./day, respectively. Four dogs were fed 0.1, 0.02, 0.005 and 0.00k g./kg./day, respectively.

b) Two dogs were fed .0025, .001 and .0002 g./kg./day of TO_2F_2, respectively.

Tests Projected: None

Personnel: Mr. Maynard

22 January 1946

[redacted]

SECRET

PROJECT NO. 15 CHRONIC TOXICITY OF TF_4 FOR DOGS

Current Status: No work current.

Tests Completed: Thirty day feeding experiment. One dog was fed 20 g./kg./day, one was fed 10 g./kg./day and one was fed 5 g./kg./day.

Tests Projected: One-year feeding tests in which three dogs are fed at each of three levels.

Personnel: None

22 January 1946

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PROJECT NO. 118 CHRONIC TOXICITY OF HIGH GRADE T ORE FOR DOGS

Current Status: No work current

TESTS COMPLETED: One dog was fed 10 g./kg./day, one was fed 5 g./kg./day and one was fed .5 g./kg./day.

Tests Projected: None

Personnel: None

22 January 1946

1019230

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[redacted]

PROJECT NO. 129

THE TOLERANCE TO AN ACUTE DOSE OF T INDUCED BY REPEATED ADMINISTRATION OF SMALL DOSES OF T.

Current Status:

a. Preparing summary report.

b. Testing TO_2F_2 on male and female adult rats by doubling the dose every 14 days.

c. Citric acid excretion and urinary T excretion in rats developing tolerance.

Experiments Planned;

a. Attempt to find a dose small enough to fail to produce tolerance.

b. Colchicine as an indicator of regeneration in the kidneys of tolerant rats.

Personnel:

Frances Haven
Challis Randall

21 January 1946

[redacted]

1019231

~~SECRET~~

PROJECT NO. 132 DISTRIBUTION, STORAGE AND EXCRETION OF T ADMINISTERED BY VARIOUS ROUTES, CHRONIC AND ACUTE

Current Status

Excretion and distribution of an acute dose (2.5 mg.T/kg.) of TNO_3 given intravenously to rats have been studied in time periods varying from 45 minutes to 40 days.

A similar study has been completed employing TCl_4.

Currently, the excretion and distribution of TNO_3 by rats previously made tolerant are being measured using radioactive isotope.

Personnel

Wm. Neuman
E. Mulryan
T. Carlson
M. O'Leary
P. O'Connell

Tests Planned

Similar studies on dogs.

5 February 1946

~~SECRET~~

1019232

SECRET

PROJECT NO. 148 LIPIDS IN T-POISONING

Current Status: Final Report in Preparation.

Experiments Planned: None

Personnel: Frances Haven
Ruth Crossland

21 January 1946

SECRET

1019233

PROJECT NO. 149

THE USE OF THE RADIOACTIVE ISOTOPE IN THE STUDY OF DISTRIBUTION, STORAGE AND EXCRETION OF T IN THE ANIMAL BODY

Current Status

A technique has been marked out by which samples of tissue ash containing radioactive isotope(s) of T are put through the protein-isolation method and the T then plated out along with inert carrier on foils for counting on the alpha counter.

Radioactive T plus inert T in the total amount of 5 mg/kg has been given to 6 male rats and 6 female rats rendered tolerant by 11 injections of small doses of T. One male and one female animal have been sacrificed at six times points ranging from several hours to 40 days. The samples have been through the protein isolation method and are ready to be plated and counted.

Personnel

William Neuman
Anton Carlson
John O'Leary
Elizabeth Mulryan
Paul O'Connell
Frances Haven
Marian Kaley

23 January 1946

[redacted]

PROJECT NO. 150

THE EFFECT OF VARIOUS AGENTS ON T NITRATE AND TO_2F_2 TOXICITY

Current Status: No current work.

Experiments Planned: None.

Personnel: None

January 21, 1946

[redacted]

[redacted]

CURRENT STATUS

MECHANISM SECTION

Alexander L. Dounce, Chief of Section

15 April 1946

[redacted]

[redacted]

MECHANISM SECTION

Current Status Index

1.	Project No. 31	Micromethod
2.	Project No. 75	To Determine Early Tubular Damage by Detection of Enzymes in Urine
3.	Project No. 131A	*In Vitro* Studies on the Mutual Effects Produced by Interaction of T Compounds with Proteins and Enzymes

[redacted]

[redacted]

PROJECT NO. 31 MICROMETHOD

Current Status — Report being written

Work Completed — Working out a micro-micro method for T to be used with body tissues and fluids.

A development of the Fluorescence method used by Hoffman for use at the 10-15 microgram level. The method as at present under trial consists in making the tissues with nitric acid, then fusing the oxidized residue with sodium fluoride and measuring the fluorescence by total extinction using a colorimeter with dark fluid (ink) in the cups.

Personnel — W. R. Bloor

5 February 1946

[redacted]

[redacted]

PROJECT NO. 75 — TO DETERMINE EARLY TUBULAR DAMAGE BY DETECTION OF ENZYMES IN URINE.

Current Status — Studying catalase and protein in urines of rabbits given T_4 intravenously.

Completed work

A. Studies of catalase excretion in the urine of animals and workmen exposed to T compounds.

The method for preventing the decay of catalase activity in urine improved. The possible contribution of white cells to urinary catalase activity was investigated.

Another survey of urinary catalase values of workmen in a T plant was undertaken, using the new apparatus and testing at the plant.

Warburg determinations of the urinary catalase of several hundred chambered animals were carried out.

B. Studies of urinary phosphatase in animals and workmen exposed to T.

The improved phosphatase method was applied to animals exposed to T.

Work Planned — Catalase excretion in cat with bladder fistula.

Personnel

A. Dounce
D. Rothermel
T. Lan
M. Kaley

5 February 1946

[redacted]

1019239

[redacted]

PROJECT NO. 131A

IN VITRO STUDIES ON THE MUTUAL EFFECTS PRODUCED BY INTERACTION OF T COMPOUNDS WITH PROTEINS AND ENZYMES.

Current Status

Studying possible development of method for determining albumin to globulin ratio in plasma using T acetate.

Work Done

The precipitating action of TCl_4 neutralized to pH 5.5 with sodium acetate on proteins was studied, as well as methods to remove T_4 from combination with protein.

The action of T_4 on phosphoglucomutase was studied.

Personnel

A. Dounce
D. Rothermel

5 February 1946

[redacted]

1019240

[redacted]

CURRENT RESULTS

TOXICOLOGY SECTION

Herbert E. Stokinger, Chief of Section

TOXI

15 April 1946

CURRENT RESULTS

[redacted]

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION OF TO_2

Special Characteristics - insoluble
Mean Particle Size - .87μ ± 2.3

CONCENTRATION Compound mg/m³	CONCENTRATION Element mg/m³	Duration of Experiment Hours	Duration of Experiment Days	Criterion of Toxicity	SPECIES Dog	Rabbit	G. Pig	Rat	Mouse
9.3 ± 1.6	8.4	130	29	Mortality	0/6	1/24	1/17	0/29	1/90
				Pathology	+	+ ?	0	0	-
				Biochemistry	-	0	-	-	
				Growth	0	0	0	0	
				Renal Function	-	0	-	-	-
2.0 ± 0.7	1.8	130	29	Mortality	-	0/24	0/18	1/30	0/47
				Pathology	-	0	0	0	-
				Biochemistry	-	0	-	-	-
				Growth	-	0	0	0	-
				Renal Function	-	0	-	-	-

Detailed Biochemistry Tabulation

CONCENTRATION Compound mg/m³	CONCENTRATION Element mg/m³	Duration of Exposure Hours	Duration of Exposure Days	Species	URINARY Protein	Amino Acid N	Catalase	Phosphatase	BLOOD RPM
9.3	8.4	130	29	Rabbits	0/8	0/5	0/8	0/8	0/8
2.0	1.8	130	29	Rabbits	0/8	0/5	0/8	0/8	0/8

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1019242

AR/hmd

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO OF_2

I. Mortality data for animals exposed to OF_2 for two 7-hour periods.

Concentration, parts OF_2 per million by vol.	Total Number of Hours required for 100% mortality	MORTALITY			
		Mice	Rats	G. Pigs	Rabbits
10	4.5	15/15	25/25	20/20	6/6
5	7.0	20/20	25/25	15/15	7/7
1	45.0	20/20	20/20	-	-
0.5	162.0	20/20	23/23	-	-
0.5	80.0	20/20	20/40	-	-
0.1		0/20	0/20	-	-

II. Exposure of 30 day's duration to 0.1 ppm.

Criterion of Toxicity	RESULTS				
	Mice	Rats	G. Pig	Rabbits	Dogs
Mortality	0/50	2/70	0/20	0/8	0/2
Urine protein				10/96	
Urine sugar				0/96	
Hematology		neg.		neg.	
Pathology	neg.	neg.	neg.	neg.	neg.

1019243

CLaB
2-20-46

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PROJECT NO. 23 TOXICITY OF T_3O_8 DUST BY INHALATION

Table of Mortalities of Various
Species Exposed Via the Lung
to Several Concentrations
of T_3O_8 in Chamber Air

Compound mg/m^3	Elemental Equivalent mg/m^3	Duration hours	Dog	Cat	Rabbit	Guinea Pig	Rat	Mouse
17	14.2	101	-	-	0/8	3/18	0/9	0/12

Pathology Some kidney and lung damage was observed.

Hematology No significant changes were observed.

5 February 1946

[redacted]

1019244

SECRET

PROJECT NO. 24 TOXICITY OF TO_3 DUST BY INHALATION

Substance TO_3

Special characteristics - insoluble in water, soluble in bicarbonate
Particle size - Mean 0.72 , Standard deviation 2.23.

Concentration Compound mg/m³	Concentration Element mg/m³	Duration of Exposure hours		SPECIES Dog	Cat	Rabbit	G.P.	Rat	Mouse
19.0	7.72	16.5	130	Mortality	1/6	4/4	12/18	2/21	3/31	4/50
				Pathology	-		- -		-	
				Biochemistry	- -	- -	- -			
				Growth	-	0	-	-	-	
				Heamtology	?		0		0	
				Renal Fnctn.						

Detailed Pathology Tabulation

Concentration Compound mg/m³	Concentration Element mg/m³	Duration of Exposure hours	Species	Lung	Liver	Kidney	Bone Marrow
19.0	16.5	130	Dog	+	0	+	
			Rabbit	+ +	+	+ +	
			Rat	+		+	+

Detailed Biochemistry Tabulation

Concentration Compound mg/m³	Concentration Element mg/m³	Duration of Exposure hours	Species	Urine Protein	Urine Sugar	Urine Creatinine	Blood NPN	Blood Urea
19.0	16.5	130	Dogs	3/3	3/3	0/3	3/4	2/4
			Rabbits	10/10	7/10	0/10	3/7	3/7
			Cats	2/2	2/2	0/2	2/2	2/2

5 February 1946

A polarographic method has been devised for the determination of C-216 with a sensitivity of 1 gamma/ml.

C. Diffusion Studies. Diffusion experiments with two different modifications of the Northrop cell have shown no polymerization of T under the experimental conditions exployed - approximately 0.002 molar T with 0.5 molar acetate buffer present. Description of apparatus and other details are given in the May 1945 Progress Report.

28 January 1946

[redacted]

CURRENT RESULTS

(Projects No. 31, 42, 75, 130, 131)

1) Uranium does not appear to act upon the kidney as a specific enzyme poison, but many enzymes of the kidney tubular cells may be poisoned wherever the fall in pH and resorption of free bicarbonate is sufficient to cause breakdown of the bicarbonate complex of U_6 with resulting liberation of the uranyl ion. At body pH particularly in the presence of bicarbonate U_6 does not act as a drastic enzyme poison for any of the enzymes studied by us, and for this reason we believe that most of the changes in tissues other than the kidney which occur in uranium poisoning are secondary to the kidney damage, provided that low doses of uranium are in question. Massive doses may cause general enzyme poisoning.

In addition to carrying out a considerable amount of work on the action of uranium compounds on the activity of a number of enzymes, we have worked out some of the fundamentals of the reactions of uranium compounds with proteins. This work has been applied to the analytical determination of micro amounts of uranium, and to a study of the mechanism of action of uranium on the kidney.

2) The general mechanism of uranium poisoning has been fairly well established. This mechanism states that yl is carried in the plasma chiefly as the bicarbonate complex, which is very slightly dissociated, and that this complex passes harmlessly through the glomerulus by filtration. In the tubule wherever the pH falls below 6.5 approximately, and especiallly in regions where most of the free bicarbonate has been resorbed, the bicarbonate complex of U_6 is broken down, with the result that the liberated uranyl ion attacks the walls of the tubular cells presumably by combining with the protein in them.

The evidence for this mechanism is derived from the following work:

A. Chemical work on the complexes of U_6, especially bicarbonate and protein.

B. Excfetion studies of uranium in the case of acid and alkaline urine, and with bicarbonate perfusion.

C. Staining of kidney sections for U_6 under conditions described in B.

D. Catalasuria work carried out by Dr. Wills under the conditions described in B.

[redacted]

The general mechanism proposed for uranium poisoning of the kidney might be applicable to mercury with some modification of the chemical details, and perhaps to other metals.

3) The action of U_4 has been shown to be of a different nature, since this material is probably transported in combination with plasma protein and possibly also as colloidal U_4 oxide or hydroxide, and cannot pass through the glomerulus to any great extent unless protein also is passing. The fact that U_4 is less toxic to the kidney after intravenous injection than U_6 is in accordance with this idea.

4) The oxidation-reduction potential of the U_6-U_4 system has been established and we have shown that the reduction of U_6 to U_4 within cells of the body should be thermodynamically possible. We have studied the kinetics of the reaction and find that they are slow but easily measurable. However, U_6 does not appear to enter cells in the body appreciably with the possible exception of the kidney tubular cells. Evidence has been accumulated to show that in plasma some oxidation of U_4 may occur.

5) The oxidation-reduction potential of the U_4-U_3 system has been found so negative that U_3 cannot exist in the body.

6) U_5 is so unstable that it could not exist in the body in appreciable concentration.

7) We have shown that the excretion of U_6 can have little to do with the intake of U_6 at a given level, at a given time after exposure, unless certain factors are rigidly controlled. If the urine is acid, much of the uranium will be undoubtedly be retained by the kidney. If the urine is alkaline a much higher fraction of the dose will be excreted. With a given exposure, excretion may be a good sign, and retention a bad sign.

8) We have developed the urinary catalase test for ealy detection of the action of uranium on the kidney, and we have set up a convenient urinary phosphatase test for the same purpose. (The appearance of phosphatase in urine after uranium poisoning was first reported by Furth and coworkers at Cornell Medical School).

9) We have made a detailed study of U_6 complexes and their dissociation which has contributed greatly to our understanding of how uranium functions in the body. This work furnished the basis of our interpretation of the mechanism of uranium action on the kidney, and it has also contributed to the establishment of the protein separation of uranium from interfering substances in the quantitative analytical method for T worked out by Dr. Neuman's group.

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10) We have demonstrated that a sizable fraction of the urinary protein found after uranium poisoning must be plasma albumin. This was done using immunological technique to identify in the urine beef or horse serum albumin injected into rabbits previously poisoned by intravenous injection of uranium.

January 29, 1946

[redacted]

PROJECT NO. 156 EXCRETION, TRANSPORTATION AND RETENTION STUDIES AFTER ADMINISTRATION OF T_6 AND T_4.

Current Results With intravenous bicarbonate infusion, sufficient bicarbonate can be found in the urine to account for the excretion of T as bicarbonate complex. Bicarbonate clearance was determined.

Personnel A. Dounce
H. Wills

5 February 1946

[redacted]

PROJECT no. 4

Inhalation Toxicity Studies of TCl_4 Dust

SUMMARY OF ACUTE TOXICITY STUDIES ON ANIMALS

EXPOSED BY INHALATION TO TCl_4 - DUST

COMPOUND TCl_4 (mg/m^3)	ELEMENTAL EQUIV. (mg/m^3)	DURATION (hours)	RABBIT	G. PIG	RAT	MOUSE
18.16	11.37	180	6/6	1/20	13/20	55/55
3.27	2.05	180	4/6 Total Exp. 1/6 Head Exp. 3/5	0/20	1/20	12/70
0.42	0.26	180			0/20	3/60

Numerator = No. dead
Denominator = No. exposed

CAUSE OF DEATH — Gross examination showed severe lung and kidney damage at the high concentration and only slight damage of the same organs at the lower concentration.

HEMATOLOGY — The rat and rabbit showed blood cellular changes only at 18.16 mg/m^3.

WEIGHT LOSS — was striking in the rabbits at the 18.16 mg level, while the rats and guinea pigs showed a very small gain in weight at the same level. At the 3.27 mg level all the species lost weight after the exposure started but regained it during the fourth and fifth weeks so that a slight overall gain was shown at the termination of the experiment. A gain in weight of all species was noted at the 0.42 mg level.

CHEMICAL ANALYSES — of the blood and urine of the rabbits showed significant changes at all levels.

(kwz)

February 5, 1946

[redacted]

1019251

[redacted]

SUMMARY OF ACUTE TOXICITY STUDIES ON ANIMALS
EXPOSED BY INHALATION TO TCl_4-DUST

Compound TCl_4 (mg/m^3)	Elemental Equiv. (mg/m^3)	Duration of Exposure hours	Animal Species Rabbit	Rat	Mouse
0.16	0.10	180	0/10	0/19	0/47

Weight Response: There was no apparent retardation in growth.

Biochemical Data:

Urine

Catalase - Doubtful increase
Protein - No appearance
Sugar - No appearance
Amino Acid N - Slight increase when expressed in mg %

Blood

NPN - No significant change
Urea N - No significant change
Amino Acid N - No significant change

(kwz)

February 5, 1946

1019252

[redacted]

[redacted]

SUMMARY OF ACUTE TOXICITY STUDIES ON ANIMALS
EXPOSED BY INHALATION TO TCl_4-DUST

Compound TCl_4	Elemental Equiv.	Duration of Exposure	Animal Species		
			Dog	Rabbit	Rat
Mg/m³	Mg/m³	hours			
1.6	1.0	180	0/4	0/6	0/10
					0/10*

* Ten rats were fed daily 50 mg of sodium citrate.

Weight Response: There was no apparent retardation in growth.

Biochemical Data:

Urine

Catalase - Slight increase
Protein - No appearance
Sugar - No appearance

Blood

NPN = No significant change

(kwz)

February 5, 1946

[redacted]

[redacted]

TOXICOLOGY SECTION

Current Results Index

Summary of Toxicological Measures Applied to Animals Serving as Inhalation Controls

[redacted]

[redacted]

Project 79	Comparison of Relative Efficiencies of Filter Papers in Sampling T Dusts
Project 92	C-216 Analysis
Project 93	The Study of the Influence of T Administration by Parenteral and Pulmonary Routes on Intensity of 'Alkaline' Phosphatase Activity.
Project 109	Carbohydrate Metabolism in T and F Poisoned Animals
Project 110	Changes in Blood Potassium and CO_2 in Acute T Poisoning
Project 113	Approximate Inhalation Toxicity Studies
Project 120	Inhalation Toxicity Studies of Tribnol, Chlorthane, 890 and 891
Project 121	Method of Analysis for Gaseous 891 Compounds
Project 137	The Use of Blood Clotting Time as an Early Clinical Index of Toxicity Resulting from T and C-216 Compounds
Project 138	Toxicity of $Na_2T_2O_7 \cdot 4H_2O$ Dust by Inhalation
Project 139	Toxicity of 'Hi-Grade' Ore by Inhalation
Project 140	Toxicity of $TO_4 \cdot 3H_2O$ Dust by Inhalation
Project 141	Toxicity of $(NH_4)_2T_2O_7$ Dust by Inhalation
Project 165	A Filter Procedure Facilitating the Analysis of Uranium Dust Sample Taken by Means of the Filter Paper Dust Sampler

14 April 1946

[redacted]

SECRET [redacted]

SUMMARY OF TOXICOLOGICAL MEASURES APPLIED TO ANIMALS SERVING AS INHALATION CONTROLS

Controls	Duration of Experiment Hours	Days	Criterion of Toxicity	SPECIES Dog	Rabbit	G. Pig	Rat	Mouse
09-1K	-	90	Mortality	0/5	1/10	-	0/10	-
			Pathology	4/5	10/10	-	9/10	-
			Gross Path.	0/5	5/10	-	?/10	-
			Blood NPN	0	0	-	-	-
			Blood Urea	0	0	-	-	-
			Growth	0	0	-	0	-
			Hematology	0/5	0/10	-	0/10	-
09-2K	-	91	Mortality	0/5	0/10	1/20	0/10	3/30
			Pathology	4/5	10/10	-	8/10	-
			Gross Path.	2/5	3/10	-	0/10	-
			Blood NPN	0	0	-	-	-
			Blood Urea	0	0	-	-	-
			Growth	0	0	0	0	0
			Hematology	0	0	-	0	-
21-AC	180	30	Mortality	0/5	6/25	3/20	0/30	0/25
			Pathology	5/5	15/15	18/20*	23/30*	10/25
			Gross Path.	5/5	15/15	13/20	1/30	4/25
			Blood NPN	0	0	-	-	-
			Blood Urea	0	0	-	-	-
			Blood Ca	0	0	-	-	-
			Blood P	0	0	-	-	-
			Growth	0	0	0	0	0
			Hematology	0/5	0/12	-	0/13	-
21-BC	216	36	Mortality	0/5	0/25	0/20	0/20	1/25
			Pathology	5/5	25/25	17/20	9/20	20/24
			Gross Path.	4/5	22/25	13/20	1/20	0/24
			Blood NPN	0	0	-	-	-
			Blood Ca	0	0	-	-	-
			Blood P	0	0	-	-	-
			Growth	0	0	0	0	0
			Hematology	0/5	0/10	-	0/10	-
21-CC	186	30	Mortality	0/12	2/31	0/30	2/175	-
			Pathology	1/2	-	-	13/24	-
			Gross Path.	0/2	2/2	-	?/24	-
			Blood NPN	0	0		-	-
			Blood Urea	0	0		-	-
			Growth	0	0	0	0	0
			Hematology	0/10	-	-	0/15	-

*Estimated from Pathology Report.

Pathology Notes: None of the animals in any of the five groups showed changes compatible with T-poisoning. The numbers indicated in the numerator indicate the number in each species which showed some abnormality, either grossly or histologically. Chronic interstitial nephritis was the most common finding, occuring in 20% of the animals. Majority of guinea pigs show evidence of pneumonia. Majority of rabbits had encysted livers.

[redacted]

[redacted]

Detailed Biochemical Tabulation

Controls	Duration of Exposure Hours	Species	URINE					BLOOD			
			Protein	Amino Acid	Gluta-lase	Phos-phatase	Sugar	NPN	Urea	Ca	P
09-1K	—	Dogs	-	-	-	-	-	0/5	0/5	-	-
		Rabbits	-	-	-	-	-	0/10	0/10	-	-
09-2K	—	Dogs	-	-	-	-	-	0/5	0/5	-	-
		Rabbits	-	-	-	-	-	0/10	0/10	-	-
21-A6	180	Dogs	0/5	-	-	-	0/5	0/5	0/5	0/5	0/5
		Rabbits	0/7	-	0/7	-	0/7	0/12	0/12	0/12	0/12
21-B6	216	Dogs	0/5	-	-	-	0/5	0/5	-	0/5	0/5
		Rabbits	0/10	0/10	0/10	0/7	0/10	0/10	-	0/10	0/10
21-C6	156	Dogs	0/10	0/10	-	-	-	0/12	0/12	-	-
		Rabbits	0/10	0/10	-	-	-	0/10	0/10	-	-

[redacted]

1019257

GFS/hmd

2-20-46

[redacted]

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS
EXPOSED BY INHALATION TO C-616

PROJECT 16
SUBSTANCE - TF_6

Special characteristics - extremely hygroscopic, hydrolyzing on contact with air to TO_2F_2 and HF.
Particle Size - 0.5μ, standard deviation of 2.2μ.

CONCENTRATION		Duration of Experiment	Criterion of Toxicity	SPECIES					
Compound mg/m³	Element mg/m³			Dog	Rabbit	Guinea Pig	Rat	Mouse	Hamster
2284	1540	10 min.	Mortality	-	-	6/15	15/20	19/20	-
			Pathology	-	-	-	+	-	-
1083	730	10 min.	Mortality	-	-	3/15	6/20	14/20	-
942	636	10 min.	Mortality	-	-	2/15	2/20	4/20	-
23	15.5	0.5 hrs.	Mortality	-	-	-	-	19/20	-
		1.0 hrs.	Mortality	-	-	-	-	20/20	-
		2.0 hrs.	Mortality	-	-	-	-	17/20	-
20	13.5	180 hrs.	Mortality	2/5	10/10	9/20	15/20	20/20	-
			Pathology	+	+	-	+	-	-
			Gross. Path.	+	+	+	+	+	-
			Blood NPN	+	+	-	-	-	-
			Blood Urea	+	+	-	-	-	-
			Growth	+	+	+	+	-	-
			Hematology	?	-	+	-	-	-
*	*	132* hrs.	Mortality	-	-	-	3/20	-	-
*	*	104.5 hrs.	Mortality	-	9/10	-	-	-	-
			Urine Cat.	-	+	-	-	-	-
			Urine Prot.	-	+	-	-	-	-
2.9	2.0	177 hrs.	Mortality	1/5	8/10	1/20	0/20	23/25	1/18
			Pathology						
			Blood NPN	+	+	-	-	-	-
			Blood Urea	+	+	-	-	-	-
			Blood Ca	-	-	-	0	-	-
			Growth	+	+	+	+	-	0
			Hematology						
0.3	0.2	(175 hrs.?)	Mortality	0/5	0/10	0/20	1/19	1/19	0/18
			Pathology						
			Urine Cat.	-	?	-	-	-	-
			Urine Prot.	-	?	-	-	-	-
			Growth	0	0	0	0	-	0

Numerator - No. of deaths or positive values.
Denominator - No. of animals studied.

0 - Normal
+ - Slight change
* - Previously exposed to "flood" concentration

(kwz) 1019258 February 5, 1946

[redacted]

[redacted]

MORTALITIES OF VARIOUS SPECIES EXPOSED VIA THE LUNG
TO 3 MG C-616/m^3

Compound	Elemental Equiv.	Duration	MORTALITY RATIO Dog	Rabbit	G. Pig	Rat	Hamster	Mouse
mg/m^3	mg/m^3	hours						
3	2	177	1/5	8/10	1/20	0/20	2/19	
		143						23/25

numerator = number dead
denominator = number exposed

CAUSE OF DEATH - in rabbits and mice appeared to be due to renal injury typical of T-toxicity. In all other species, death was due to natural causes or of doubtful origin.

WEIGHT LOSS - was not so pronounced at the 3 mg/m^3 level as at the 20 mg/m^3 concentration.

(kwz)

February 5, 1946

1019259

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[redacted] 16

SECRET

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS
EXPOSED BY INHALATION TO TF_6

(First 30 days of Chronic Studies)

Special Characteristics - Extremely hygroscopic, hydrolysing on contact with air to TO_2F_2 and HF.
Particle Size - Mean below 0.4 μ.

CONCENTRATION		Duration of Experiment		Criterion of Toxicity	SPECIES	
Compound mg/m³	Element mg/m³	Hours	Days		Dog	Rat
0.30	0.20	150	32	Mortality	0/19	1/175
				Pathology	-	-
				Hematology	-	-
				Weights	0/19	+
				Blood NPN	0/19	-
				Amino Acids/Creatinine	0/19	-
				Urinary Protein	+	-
				Liver Function	+ +	+ +
0.075	0.050	156	32	Mortality	0/15	0/165
				Pathology	-	-
				Hematology	-	-
				Weights	0/15	+
				Blood NPN	0/15	-
				Amino Acids/Creatinine	0/15	-
				Urinary Protein	+	-
				Liver Function	-	-

Numerator - No. of deaths or positive values.
Denominator - No. of animals studied.

0 - Normal Values
+ - Slight Change
+ + - Moderate Change

[redacted]

1019260

CJS/hnd
2-18-46

[redacted] TOXICITY OF TO_2F_2 BY INHALATION

PROJECT 17
SUBSTANCE - TO_2F_2

Special Characteristics - water soluble, somewhat hygroscopic
Particle Size - bulk dust; Mean 0.65 , standard deviation 2.1
within exposure chamber; Mean 1.3 , standard deviation 4.0

Concentration		Duration of	Criterion of	SPECIES					
Compound mg/m³	Element mg/m³	Experiment hours	Toxicity	Dog	Cat	Rabbit	G. Pig	Rat	Mouse
Run 1			Mortality	2/2	2/2	20/20	11/20	0/20	20/20
			Pathology	++	++	+++	+	+	++
12.2 ±5.7	9.4	102	Biochemistry	++	++	++	—	—	—
			Growth	++	++	o	+	o	—
			Hematology	—	—	o	+	+	—
			Renal function						
Run 2			Mortality	0/6	0/4	3/24	1/30	0/30	11/42
			Pathology		—		—		—
2.8 ±1.4	2.1	160	Biochemistry	—	—	++	—	—	—
			Growth	o	o	++	+	o	—
			Hematology	o	—	o	—	o	—
			Renal Clearances	—	—	++	—	—	—
Run 3			Mortality	—	—	1/24*	—	0/10	7/51
			Pathology	—	—		—		—
.65 ± .23	.50	168	Biochemistry	—	—	+	—	—	—
			Growth	—	—	+	—	o	—
			Hematology	—	—	—	—	—	—
			Renal Clearances	—	—	+	—	—	—
Run 4			Mortality	0/6	—	3/23**	—	0/10	2/41
			Pathology						
.19 ± .08	.14	165	Biochemistry	o	—	0	—	—	—
			Growth	o	—	0	—	o	—
			Hematology	—	—	—	—	—	—
			Renal function	—	—	0	—	—	—

Numerator - No. of deaths or positive values
Denominator - No. of animals studied

o Normal
+ Slight change
++ Marked change
+++ Extreme change

* One additional rabbit died because of an intestinal obstruction.
** There is some doubt that these animals died of T-poisoning. Histological examination (in progress) will clear up the point.

(kwz) 101926 [redacted] February 5, 1946

[redacted]

TO_2F_2

Detailed Pathology Tabulation

Concentration Comp.	Element	Duration of Exposure	Species	Tissues Lung	Liver	Kidney
mg/m³		hours				
			Dog	+ +	+	+ + +
			Rabbit	+ +	+	+ + +
12.2	9.4	102	Cat	+ +	+	+ +
			G. Pig	+		
			Rat	+	0	+
2.8	2.1	160	Dog Rabbit Rat			
.65	.50	168	Dog Rabbit Rat			

Detailed Biochemistry Tabulation

Concentration Comp.	Element	Duration of Exposure	Species	Urine Protein	Amino Acid	Catalase	Phosphatase	Sugar	Blood NPN	Urea	CO_2
mg/m³		hours									
			Dogs					0/1	2/2		
12.2	9.4	102	Cats					1/2	2/2		
			Rabbits					0/4	5/5		
2.8	2.1	160	Rabbits	10/10	10/10	—	—		8/10	—	5/10
.65	.50	168	Rabbits	3/10	7/10	4/10	0/10		3/10	3/10	—
.19	.14	165	Rabbits	0/13	1/6	?	—		0/15		
			Dogs	0/3	0/3	—	—		0/3		

1019262

(kwz)

February 5, 1946

[redacted]

Summary Table of Mortalities of Various Species Exposed
Via the Lung to Several Concentrations of
T-Nitrate Dust in Chamber Air

TNO_3 (mg/m^3)	T metal Equiv. (mg/m^3)	Duration (Hrs.)	Dog	Cat	Rabbit	G.Pig	Rat	Mouse
20	10.6	111	-	-	8/10	2/20	2/30	1/40
		158				14/20	given oats alone	
4.5	2.4	158	0/5	4/4	16/20	0/20	0/60	
		185				10/10	given oats alone	
2	1	185				4/10	given oats plus ascorbic acid	
		180					0/22	
		121	0/4					
		14			4/6			
0.5	0.26	178	-	-	6/30	-	2/43	2/50

Numerator equals number dead
Denominator " " exposed

(kwz)

February 5, 1946

[redacted]

MORTALITIES OF VARIOUS SPECIES EXPOSED VIA THE LUNG
TO SEVERAL CONCENTRATIONS OF T-NITRATE
IN CHAMBER-AIR

Compound mg/m³	Elemental Equiv. (approx.) mg/m³	Duration of Exposure hours	Dog	Cat	Rabbit	G. Pig	Rat	Mouse
A 20	10	111	---	---	8/10	2/20	2/30	1/40
B 20	10	152	3/4	---	---	---	2/20	---
4.5	2.3	158	0/5	4/4	16/20	0/20	0/60	6/100
						14/20 (oats alone)		
2.6	1.3	185	---	---	---	10/10 (oats alone)	---	---
						4/10 (oats + vit. C)		
		180	---	---	---	---	0/22	---
1.2 (median)	0.6	99	0/4	---	---	---	---	---
0.5	0.25	178	---	---	6/30	---	2/43	2/50

(kwz) 1019264

February 5, 1946

[redacted]

[redacted]

DETAILED BIOCHEMISTRY TABULATION

T-nitrate

Compound mg/m³	Elemental Equivalent mg/m³	Species	Blood Chemistry NPN	Blood Chemistry Urea N	Blood Chemistry CO_2	Urine Chemistry Protein	Urine Chemistry Sugar	Urine Chemistry Catalase	Remarks
20	10	Dog Rabbit Rat	+ + +	+ + +	+ 0 -	+ 0 o	+ o o	+ o o	
4.5	2.3	Dog Rabbit	+ +	+ +	o o	o o	o o	o o	
1.2	0.6	Dog	o	o	o	+	+	o	Some abnormalities in glucose tolerance
0.5	0.25	Rabbit	+	+	o	+	o	+	

o = not done
- = negative results
+ = positive results

A special study on rabbits showed that exposure to approximately 1 mg/m³ of T-nitrate for short periods of time was sufficient to produce urinary excretion of catalase and protein and marked renal damage.

On histological examination all the species studied showed renal damage at the levels studied with the exception of rats at 0.5 mg T-nitrate/m³.

The rats exhibited an elevation in blood NPN, but no significant change in total blood CO_2 was observed.

[redacted]

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO T-NITRATE, UNIT 5

(First 30 days of Chronic Studies)

CONCENTRATION		Duration of Experiment		Criterion of Toxicity	S P E C I E S			
Compound mg/m³	Element mg/m³	Hours	Days		Dog	Rabbit	G. Pig	Rat
0.30	0.15	133	30	Mortality	1/20*	2/30	1/30	0/153
				Pathology	Slight +	+	+	0
				Gross Path.	+	+	+	+
				Blood NPN	0	0	x	x
				Blood Urea	x	x	x	x
				Growth	0	0	0	0
				Hematology	0	x	x	0
				Renal Cl.	+	x	x	x
				Liver Func.	+	x	x	0
2.0	1.0	133	30	Mortality	0/20	7/30	2/30	0/147
				Pathology	+	+	+	+
				Blood NPN	0	x	x	x
				Blood Urea	x	x	x	x
				Blood CO_2	+	x	x	x
				Growth	0	+	0	0
				Hematology	0	x	x	0

* From biopsy

Concentration		Duration of Exposure	Species	URINE				BLOOD			
Compound mg/m³	Element mg/m³	Hours		Protein	Amino Acid	Catalase	Phospha-tase	Sugar	NPN	Urea	CO_2
0.30	0.15	133	Dog	+	x	x	x	+	+	x	0
			Rabbit	+	x	+	x	+	+	x	x
2.0	1.0	133	Dog	+	x	x	x	x	0	x	+

x - not done
* - data not available yet.
0 - normal
+ - abnormal change

[redacted]

1019266

ER/hmd
2-218-46

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SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS
EXPOSED BY INHALATION TO 2-NITRAZA, UNIT 5

(First 30 days of Chronic Studies)

Special Characteristics - Fairly hygroscopic, changing on contact with air from $2Z_2(NO_3)_2 \cdot 4H_2O \rightarrow 2Z_2(NO_3)_2 \cdot 6H_2O$

Particle-Size on 0.05 mg/m^3 = 7.0 microns, standard deviation 2.9.
on 0.45 mg/m^3 = 9.8 microns, standard deviation 2.3.

CONCENTRATION		Duration of Experiment		Criterion of Toxicity	[illegible]	
Compound mg/m^3	Element mg/m^3	Hours	Days		Dog	Rat
0.10	0.05	133.2	30	Mortality	0/19	0/150
				Blood HPH	0	-
				Growth	0	0
				Hematology	0	0
				Tissue Analysis	+ +	+ +
				Urinary Protein	0	-
0.90	0.45	134.7	30	Mortality	0/19	0/150
				Blood HPH	0	-
				Growth	0	0
				Hematology	0	0
				Tissue Analysis	+ +	+ +
				Urinary Protein	+	-
				Liver Function	+ +	+ +

Numerator - No. of deaths or positive values.
Denominator - No. of animals studied.
0 - Normal
+ + - Slight Change
+ - Very slight change

Detailed Biochemistry Tabulation

CONCENTRATION		Duration of Exposure	Species	Urinary Protein	Blood HPH
Compound mg/m^3	Element mg/m^3	Hours			
0.10	0.05	133.2	Dogs	0/12	0/12
0.90	0.45	134.7	Dogs	0/12	1/12

1019267

~~SECRET~~

UCP/hmd
2/19/65

[redacted]

PROJECT NO. 19 TOXICITY OF TF_4 BY INHALATION

Table of Mortalities of Various Species
Exposed via the Lung to Several
Concentrations of TF_4 in Chamber-Air

Compound (mg/m^3)	Elemental Equivalent (mg/m^3)	Duration (hours)	Dog	Cat	Rabbit	G.Pig	Rat	Mouse
22	17.2	170	1/1	3/3	1/3	3/20	6/19	0/100

Cause of Death was apparently kidney damage.

Pathology Lung as well as kidney damage was present in these animals.

Hematology No significant changes.

(kwz) February 5, 1946

1019268

[redacted]

~~SECRET~~ 19

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO TF_4

(First 30 Days of Chronic Studies)

Special Characteristics - Slightly soluble, green material with amorphous particles.
Particle-Size (circulating dust) - 0.5 - 0.6; σ_g 2.3. Weight size 2.2 - 2.1; σ_g 2.0 - 2.5.

CONCENTRATION		Duration of Exposure		Criterion of Toxicity	SPECIES				
Compound mg/m³	Element mg/m³	Days			Rabbit	Rat	G. Pig	Mouse	Dog
0.7	0.5	166.5	32	Mortality	0/10	1/30	0/20	0/40	
				Pathology	no T dam.	no T dam.	no T dam.	no T dam.	
				Gross Path.	"	"	"	"	
				Blood HFW	normal	-	-	-	
				Urinary Protein	normal	-	-	-	
				Urinary Catalase	rise	-	-	-	
				Urinary Phospha.	rise	-	-	-	
				Growth	normal	retarded	retarded	normal	2 dogs at this level.
5.0	3.8	166.5	35	Mortality	10 rabbits at this level.	1/30	0/20	0/40	0/4
				Pathology		no T dam.	no T dam.	no T dam.	normal inj.
				Gross Path.		"	"	"	no T dam.
				Growth		retarded	normal	normal	loss
				Hematology		rbc blur 5 reticulocytes	-	-	no changes

Detailed Biochemistry Tabulation

CONCENTRATION		Duration of Exposure		Urine				
Compound mg/m³	Element mg/m³	Days	Species	Protein	Catalase	Phosphatase	Blood	
0.7	0.5	35	10 Rabbits	no change	rise on 17th day of exposure, sharp rise on 32nd day	rise on 32 day of exposure	no change	

~~SECRET~~

1019269

RPB/and
2-19-46

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO UF_6

Special Characteristics - insoluble, tetravalent.
Particle Size - mass median 2.8 microns, standard deviation of 1.2 microns.

CONCENTRATION		Duration of Exposure		Criterion of Toxicity	EFFECTS			
Compound mg/m³	Element mg/m³	Hours	Days		Dog	Rat	Rabbit	G. Pig
3.86 (Dogs and Rats)	2.90	154.3	35	Mortality	0/12	1/110*	0/15	0/20
				Pathology	+	0		-
				Biochemistry	0	-	+	-
3.65 (Rabbits and Guinea Pigs)	2.75	140.9	35	Growth	0	0	0	0
				Hematology				
0.78	0.53	160.5	35	Mortality	0/12	0/106	-	-
				Pathology	0	0	-	-
				Biochemistry	0	-	-	-
				Growth	0	0	-	-
				Hematology			-	-

* Histological findings on these rats showed no F-damage. The cause of death in each case was Salmonellosis.

Pat[redacted] Biochemistry Tabu[redacted]

CONCENTRATION		Exposure Hours	Species	URINE		BLOOD
Compound mg/m³	Element mg/m³			Protein	Amino Acid Crystalline	NPN
3.86	2.90	154.3	Dogs	1/10	0/10	0/10
3.65	2.74	140.9	Rabbits	0/10	6/10	0/10
0.78	0.58	160.5	Dogs	0/10	-	0/10

[redacted]

1019270

AB/hmd
2-19-46

SECRET

PROJECT NO. 21 TOXICITY OF TO_2 DUST BY INHALATION

Table of Mortalities of Various Species
Exposed to Several Concentrations via the Lung
of TO_2 in Chamber Air

Compound mg/m³	Elemental Equivalent mg/m³	Duration hours	Dog	Cat	Rabbit	Guinea Pig	Rat	Mouse
22	19.4	140	-	-	6/10	1/20	0/15	0/40
10	8.5	165	0/6	-	1/24*	1/18**	0/44	1/45
2	1.8	165	-	-	0/24	0/18	1/44	0/45

Cause of death appeared to be kidney damage.

Pathology some lung damage was noted.

Hematology leukocytes, erythrocytes and hemoglobin showed a rise. Neutriphiles evidenced a rise and lymphocytes a fall. Platetets rose in the rabbit.

* Death?
** Death not dt. T

5 February 1946

1019271

SECRET

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO TO_2

(Initial 30 Days of Chronic Studies)

Special Characteristics - insoluble, dark-brown material with amorphous particles.
Median Particle Weight Size - 10 mg level - 1.9 - 2.2μ; σ_g 1.3 - 1.5
1 mg level - 1.5 - 2.2μ; σ_g 1.3 - 1.7

CONCENTRATION		Duration of Experiment		Criterion of Toxicity	SPECIES			
Comp. mg/m³	[redacted] mg/m³	Hours	Days		Dog	Rabbit	G. Pig	Rat
11.3	10	130	30	Mortality	0/18*	2/18	0/30	0/150
				Pathology	no T changes	-	-	no T changes
				Gross Path.	no T changes	no T changes	-	no T changes
				Blood NPN	?**	?	-	-
				Blood Urea	?	?	-	-
				Urinary Protein	normal	normal	-	-
				Growth	retarded	normal	normal	normal
				Hematology	no changes	-	-	no changes
1.13	1	130	30	Mortality	0/18	No Rabbits at this level.	No Guinea Pigs at this level.	0/150
				Pathology	no T changes			no T changes
				Gross Path.	no T changes			no T changes
				Blood NPN	?**			-
				Blood Urea	?			-
				Urinary Protein	normal			-
				Growth	normal			normal
				Hematology	no changes			no changes

* numerator - No. of deaths or positive values.
denominator - No. of animals studied.

** All values within normal range. Dogs at both levels showed drop of about 15 mg % in N.P.N. at 20th week. Two weeks later nitrogenous constituents regained previous concentration.

[redacted]

1019272

HPD/hnd
2-20-46

SECRET

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION OF TO_2

Special Characteristics - insoluble
Mean Particle-Size - .8μ ± 2.3

CONCENTRATION Compound mg/m³	CONCENTRATION Element mg/m³	Duration of Experiment Hours	Duration of Experiment Days	Criterion of Toxicity	SPECIES Dog	Rabbit	G. Pig	Rat	Mouse
9.3 ± 1.6	8.4	130	29	Mortality	0/6	1/24	1/17	0/29	1/50
				Pathology	+	+ ?	0	0	-
				Biochemistry	-	0	-	-	
				Growth	0	0	0	0	
				Renal Function	-	0	-	-	-
2.0 ± 0.7	1.8	130	29	Mortality	-	0/24	0/18	1/30	0/47
				Pathology	-	0	0	0	-
				Biochemistry	-	0	-	-	-
				Growth	-	0	0	0	-
				Renal Function	-	0	-	-	-

Detailed Biochemistry Tabulation

CONCENTRATION Compound mg/m³	CONCENTRATION Element mg/m³	Duration of Exposure Hours	Duration of Exposure Days	Species	URINARY Protein	Amino Acid N	Catalase	Phosphatase	BLOOD NPN
9.3	8.4	130	29	Rabbits	0/8	0/5	0/8	0/8	0/8
2.0	1.8	130	29	Rabbits	0/8	0/5	0/8	0/8	0/8

SECRET

1019273

AR/hnd
2-20-46

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO OF_2

I. Mortality data for animals exposed to OF_2 for two 7-hour periods.

Concentration, parts OF_2 per million by vol.	Total Number of Hours required for 100% mortality	MORTALITY			
		Mice	Rats	G. Pigs	Rabbits
10	4.5	15/15	25/25	20/20	8/8
5	7.0	20/20	25/25	15/15	7/7
1	45.0	20/20	20/20	-	-
0.5	162.0	20/20	23/23	-	-
0.5	80.0	20/20	20/40	-	-
0.1		0/20	0/20	-	-

II. Exposure of 30 day's duration to 0.1 ppm.

Criterion of Toxicity	RESULTS				
	Mice	Rats	G. Pig	Rabbits	Dogs
Mortality	0/50	2/70	0/20	0/8	0/2
Urine protein				10/96	
Urine sugar				0/96	
Hemetology		neg.		neg.	
Pathology	neg.	neg.	neg.	neg.	neg.

[redacted]

1019274

CLaB
2-20-46

SECRET

SUMMARY OF TOXICOLOGICAL RESULTS OF [redacted] EXPOSED BY INHALATION TO TCl_4

(First 30 days of Chronic Studies)

Special Characteristics - Extremely hygroscopic, hydrolyzing on contact with air to HCl and TO_2Cl_2.
Average Particle-Size Weight Distribution - 3.45 μ

CONCENTRATION		Duration of Experiment		Criterion of Toxicity	[redacted]	[redacted]
Compound mg/m³	Element mg/m³	Hours	Days		Rat	Rat
0.32	0.20	180	30	Mortality	0/19	2/150*
				Pathology	0	0
				Gross Pathology	0	0
				Blood HPN	0	-
				Urinary Protein	0	-
				Percent of Original Wt.	95.6%	180%
				Hematology	0	0
				Liver Function	0	0
				Mean Concentration	.032 mg T/m³	0.19 mg T/m³
0.05	0.05	180	30	Mortality	1/19**	1/150*
				Pathology	0	0
				Gross Pathology	0	0
				Blood HPN	0	-
				Urinary Protein	0	-
				Percent of Original Wt.	90.4%	180%
				Hematology	0	0
				Mean Concentration	.06 mg T/m³	.06 mg T/m³

* Salmonellosis
** This dog died five days following the renal biopsy performed after 10 exposure-days. Extensive pulmonary hemorrhage and necrosis was found.

Detailed Biochemistry Tabulation

CONCENTRATION		Duration of Exposure		URINE		BLOOD
Compound mg/m³	Element mg/m³	Hours	Species	Protein	Sugar	HPN
0.32	0.20	180	Dog	0/10		0/10
0.05	0.05	180	Dog	1/10*		0/10

* This dog showed protein in the urine at almost every collection during the pre-exposure and exposure periods.

[redacted]

[redacted]

PROJECT NUMBER 28 INHALATION TOXICITY STUDIES OF C-216

SUMMARY OF MORTALITY STUDIES ON ANIMALS EXPOSED

BY INHALATION TO HIGH CONCENTRATIONS OF

C-216

Concentration	Duration of Exposure	(Total Mortality 14 Days After Exposure) Rabbit	Guinea Pig	Rat	Mouse
10,000 ppm	5 minutes	8/8	20/20	45/45	45/45
1,000	30 minutes	8/8	20/20	45/45	45/45
500	1 hour	8/8	20/20	50/50	50/50
200	3 hours	8/8	18/20	45/45	50/50
100	7 hours	7/8	0/20	27/50	43/45

Death in all cases appeared to be due to respiratory failure. Kidney damage became evident only in those animals which survived for several days or more after the exposure.

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019276

[redacted]

SUMMARY OF ACUTE TOXICITY STUDIES ON ANIMALS
EXPOSED BY INHALATION TO C-216

Concentration		Duration		Rabbit		Guinea Pig				
ppm.	mg/m³	(hours)	Dog	Full exp.	Head exp.	Full exp.	Head exp.	Hamster	Rat	Mouse
25	39	95	5/5	18/18	9/9	15/30	4/12		12/12	49/49
8.5	13	160	5/5	19/19	9/10	7/26	2/12	0/30 (136 hrs. exposure)	4/38	10/50
4	6	176	0/5	2/10	3/10	1/12	0/12		1/21	
0.5	0.8	124 (in progress)	0/5	0/10	1/12	1/12	1/12		0/10	

Cause of death appeared to be respiratory failure.

Pathology - In surviving animals kidney damage was more prevalent than lung damage as concentration was reduced.

Growth - At the higher concentrations growth was definitely retarded in all species; at 4 ppm only the full exposure rabbits lost weight. At 0.5 ppm all species are gaining weight.

Numerator = number dead

Denominator = number exposed

February 5, 1946

1019277

[redacted]

SUMMARY OF TOXICOLOGICAL RESULTS OF ANIMALS EXPOSED BY INHALATION TO HYDROGEN FLUORIDE VAPOR

Introduced into Exposure-Unit as HF-Monomer at 100 C.

Concentration of Compound		Duration of Experiment		Criterion of Toxicity	SPECIES				
mg/m³	p.p.m.	Hours	Days		Rat	Mouse	Guinea Pig	Rabbit	Dog
25	31	166	29	Mortality	29/29	18/18	0/20	0/18	0/4
				Pathology	20/20+	-	-	4/10+	4/4+
				Gross Path.	-	-	0/20	1/10+	4/4+
				Blood Ca.	-	-	-	0/10	0/4
				Blood Phosphatase	-	-	-	-	0/4
				Growth	Severe Loss	Severe Loss	+12%	-8%	+3%
				Hematology	±/10	-	-	0/10	0/4
				Blood Coag. Tests	-	-	-	+	+
				Urine, Prot., CBD	-	-	-	0/10	-
7	8.6	166	30	Mortality	0/15	0/20	0/10	2/22*	0/5
				Pathology	-	-	-	-	1/5
				Gross Path.	0/10	0/5	0/5	0/10	1/5
				Growth	22 %	+ 9%	+31%	+17%	+ 4%
				Urinary F	-	-	-	Increase	-
				Blood Coag.	0/4	-	-	-	-
				F-Storage	Increase	-	-	-	Increase

* Two Head-exposed rabbits died early in the experiment apparently from accidental injury.

25 mg level

Pathology in dogs confined to degenerative changes in testes, hemorrhage in lungs. Pulmonary and renal damage in rats.

Blood coagulation tests showed hypercoagulability, hyperprothrombin time and elevated fibrinogen levels in dogs and rabbits.

[redacted]

1019278

HBS/hnd
2-18-46

PROJECT NO. 30 TESTS OF RESPIRATORY PROTECTIVE DEVICES

Current Results

Respirator filters and canisters showed different degrees of efficiency against 8 T compounds.

Of 14 respirators tests

1. Mine Safety Appliances Respirator BM 2133 showed the greatest efficiency in all tests.

2. CESCO Healthguard, Willson 750-L and Chemical Warfare Assault 'Aerosol' masks were likewise acceptable in a limited number of tests.

3. All of 8 respirators were acceptable for use with $TO_4 \cdot 3H_2O$; 9 of 12 respirators were acceptable for use with 'Hi-Grade' Ore. Against the remainder of the compounds a certain variable number of respirators were acceptable.

4. The Mine Safety Appliances AllService Canister Model S, BM 1434, showed the greatest efficiency in this group.

5. None of 4 respiratory protective devices was acceptable against TCl_4.

6. A standard group of respiratory protective devices was selected and will be the basis for future tests.

Respirator tests against 890.

The Willson University Canister, BM 1433, and the Mine Safety Appliance All Service Model S Canister, BM 1434, offer a high degree of protection against atmospheres containing 0.01% of 890 for at least 6 hours. Decisions as to their acceptability must await further toxicity data.

Pharmacology Report No. 314

District File No. M-1676

11 April 1946

1019279

[redacted]

PROJECT NO. 48 GLUTAMIC ACID

Current Results

I. Administration of glutamic acid to rats given U Acetate intraperitoneally had no protective effect.

II. Rabbits inhaling $(NH_4)_2U_2O_7$ dust following injections of glutamic acid failed to show protective action judged by mortality and blood NPN values.

Personnel Stokinger, Roberts

I.

II. District Filed No. M-1563

Pharmacology Report No. 35

7 March 1946

1019280

[redacted]

SECRET

PROJECT NO. 49 URINARY PROTEIN

Current Results — Protein of rat urine following intraperitoneal administration of U nitrate showed an electrophoretic pattern like rat plasma except the absence of the fibrinogen peak and the albumin had a higher mobility than in plasma.

Personnel — Roberts, Alling

District File No. M-1632

Pharmacology Report No. 266

7 March 1946

1019281

SECRET

[redacted]

PROJECTS 50 AND 75

DETERMINATION OF EARLY TUBULAR DAMAGE. URINARY 'ALKALINE' PHOSPHATASE ACTIVITY AS A SENSITIVE AND EARLY INDEX OF T POISONING.

Current Results

Rats, rabbits, dogs, and cats excreted catalase and phosphatase in the urine following injection or inhalation of U compounds.

A large body of data shows catalase activity in urine to be a very sensitive test of U poisoning.

Personnel

Roberts, Dounce, Wills, Lan, Kaley, O'Connell, Rothermel and Robinson

30 March 1946

[redacted]

[redacted]

PROJECT NO. 52 RIBOFLAVIN

Current Results

Riboflavin as given by mouth does not alleviate any of the symptoms of T poisoning resulting from injection of T acetate.

Personnel

Rothstein

No Report

30 March 1946

[redacted]

[redacted]

PROJECT NO. 58 THE MECHANISM OF BICARBONATE ACTION IN T POISONED RATS

Current Results

A study of the previously observed beneficial action of bicarbonate in rats poisoned by injection of soluble T compounds has been made to determine whether bicarbonate acts by diminishing intra-renal precipitation of proteins and by preventing kidney damage. The hypothesis that bicarbonate may cause a more rapid excretion of T from the kidneys was also tested. The progression of renal injury and regeneration was studied in a serial manner.

Eighty rats were employed comprising four experimental groups of 18 animals each and a control group of 8 rats. Determinations were made of urinary volume, pH, creatinine, urea, and protein, and of blood non-protein nitrogen, urea nitrogen, and creatinine.

The usual effects of T poisoning were noted in all of the animals whether or not they received bicarbonate after the injection of 0.3 mg. yl acetate per 100 grams of body weight. In each case a marked rise in urinary protein occurred and was followed by a sharp fall in the creatinine excretion. At the time that the blood non-protein nitrogen and urea attained maximal values the creatinine reached a minimum. In each case, the urine volume rose on the first day after injection and reached a maximum a short time after the blood non-protein nitrogen began to fall. The animals receiving bicarbonate after the injection exhibited a greater total output of urine than did the other groups although bicarbonate administered to uninjected rats exerted no influence on urine volume. In the case of the group which received bicarbonate after the injection the protein excretion rose to significantly higher levels than that of the other group, while the blood non-protein nitrogen of the latter group reached a higher level than that of the former. At no time were there any significant pathological differences observed between the animals which did or did not receive bicarbonate. Bicarbonate also had no influence on the removal of T from the kidney after injection.

These data are consistent with the hypothesis that $NaHCO_3$ decreases the toxicity of yl salts administered to rats by injection by aiding the alimination of protein in the urine. It is concluded that $NaHCO_3$ does not prevent the kidney damage caused by T poisoning but aids the recovery of the poisoned animals by alleviating secondary effedts such as acidosis and precipitation of proteins in the kidney.

Personnel Roberts, Spiegl

Pharmacology Report No. No. 266
District File No. M-1632

1019284

[redacted]

[redacted]

PROJECT NO. 59 MORTALITY OF MICE EXPOSED TO TO_2F_2.

Current Results

PERCENTAGE MORTALITY OF MICE EXPOSED TO TO_2F_2

Days After First Exposure / Hours of Exposure	1	2	3	4	5	6	7	8	9	10-14
	Per Cent Mortality of Mice on Fox Chow Diet N = 50									
2	0	0	0	10	30	40	50	60	70	80
4	0	0	0	0	40	80	80	80	90	90
6	0	0	0	0	60	80	90	90	90	90
8	0	0	0	0	55	55	65	75	80	80
	Per Cent Mortality of Mice On Fox Chow + 0.5% $NaHCO_3$ N= 49									
2	0	0	0	10	40	50	50	50	50	50
4	0	0	0	20	60	60	60	60	70	70
6	0	0	0	30	60	60	80	80	80	80
8	0	0	0	5	42	47	58	68	84	84

Personnel Stokinger, Roberts

Pharmacology Report No. 13

District File No. M-1602

12 April 1946

[redacted]

1019285

[redacted]

PROJECT NO. 60 VITAMIN C METABOLISM IN U TOXICITY

Current Results

1. Rats injected intraperitoneally with 0.3 mg. Y1 acetate per 100 g. of rat showed a pronounced lateration in ascorbic acid metabolism. Animals maintaining a low urinary level of the vitamin were stimulated by T injection to a daily excretion as high as 8 times the control rate. When 1% of sodium bicarbonate was included in the diet, an amount which significantly reduced the mortality of the T poisoned animals, somewhat smaller amounts of vitamin C were excreted. The injection of 0.3 mg. Y1 acetate per 100 g. of rat caused a greater vitamin excretion than did the injection of the larger dose of 0.6 mg. Y1 acetate per 100 g. of rat.

Animals stimulated by sodium phenobarbital to produce large amounts of vitamin C exhibited a marked decrease in urinary ascorbic acid after injection of T. The excretion after administration of the Y1 acetate was approximately half of that prior to injection.

2. One per cent sodium bicarbonate in the diet of T poisoned rats reduced the mortality from 50% to 0% but did not prevent renal damage. Neigher excess vitamin C nor sodium phenobarbital had any significant effect on mortality rates.

3. The period 6 to 8 days after injection was critical for the poisoned animals. Most of the deaths occurred at this time. Appetite, urine volumes, vitamin C excretion, and growth curves all showed minima during this period.

4. The T poisoned animals showed infiltration of the perivascular spaces of the lungs and tubular necrosis in the kidneys. Spectrochemical studies showed that T had almost disappeared from the kidneys within two weeks after injection of the Y1 acetate.

In conclusion, this experiment demonstrates that T toxicity induces a significant alteration in the vitamin C metabolism of the rat but that excess vitamin C has little effect on mortality. Sodium bicarbonate in the diet can reduce the rate of mortality, but does not prevent tissue damage.

Personnel	Spiegl, Roberts
Pharmacology Report No.	274
District File No.	M-1652

12 April 1946

[redacted]

1019286

[redacted]

PROJECT NO. 79 COMPARISON OF RELATIVE EFFICIENCIES OF FILTER PAPERS IN SAMPLING T DUSTS

Current Results

1. Comparative test of filter papers Whatman No. 41, H-17, H-18 and Waterman No. 50 showed that Whatman No. 41 was the most efficient paper when air was sampled at 0.5 or 1.0 cubic foot per minute against TO_2 of mean particle size 0.4, (thermal precipitator) and at concentrations of from 14.0 to 20.3 mg. per cubic meter.

2. H-17, H-18 were each 89 per cent as efficient as Whatman No. 41 when sampling was done at 1.0 cubic foot per minute, but were approximately as efficient as Whatman No. 41 when tested at 0.5 cubic foot per minute.

3. Waterman No. 50 was 46.5 per cent as efficient (range 45-48 per cent) as Whatman No. 41 at a sampling rate of 0.5 cubic foot per minute.

4. Resistance of Waterman No. 50 was sufficient to allow a sampling rate of only 0.5 cubic foot per minute.

5. Analytical difficulties encountered in the use of H-17 and H-18 indicate that a gravimetric procedure is the most feasible method of determining filter paper load with thesepapers.

Personnel Dygert, Oberg, Stokinger

Pharmacology Report No. 3

District File No. M-1553

12 April 1946

[redacted]

1019287

[redacted]

PROJECT NO. 92 C-216 ANALYSIS

Current Results

1. A method for the quantitative determination of C-216 ion has been developed, the basis of which is the inhibition of hog-liver esterase activity by C-216.

2. The useful range for the determination of C-216 concentrations was 0-0.5 ppm C-216 (by weight) with an estimated error of ± 5%. This range could be extended to 10 ppm C-216 by the addition of 174 ppm zirconium ($ZrOCl_2 \cdot 8H_2O$).

3. The method yielded valid results in the presence of T compounds and NaCl.

4. Carbonate or other buffering ions interfered.

Personnel: Max Schlamowitz

District File: M-1718

Pharmacology Report No. 361

24 January 1946

[redacted]

[redacted]

PROJECT NO. 93

THE STUDY OF INFLUENCE OF T ADMINISTRATION BY PARENTERAL AND PULMONARY ROUTES ON INTENSITY OF 'ALKALINE' PHOSPHATASE ACTIVITY

Current Results

In administration of U salts by both parenteral and pulmonary means a reduction in the alkaline phosphatase activity of the kidney but not in the intestines occurs.

Personnel

Roberts, Anders, Spiegl

Pharmacology Report No.

433 and 444

District File No.

M-1846 (No. 444 is still in rough draft form)

Also See Pathology Files

11 April 1946

[redacted]

[redacted]

PROJECT NO. 109

CARBOHYDRATE METABOLISM IN T AND F POISONED ANIMALS.

Current Results

Exposure to uranium and HF decreased the ability of rats to return blood sugar to normal levels after the injection of a standard dose. The ability to form liver glycogen was unaffected but the rate of formation of muscle glycogen was decreased. The glucose tolerance of dogs exposed to U nitrate and HF was significantly decreased. Alloxin treated rats were found deficient (markedly) in the criteria studied while the control group of rats gave the results expected from normal animals.

Personnel

Roberts, Bishop

Report

Being written in form of thesis by Bishop.

11 April 1946

[redacted]

[redacted]

PROJECT NO. 110

Changes in blood potassium and CO_2 in Acute T Poisoning.

Current Results

To date severe U poisoning either by pulmonary or parental routes has been found to cause reduction in total blood CO_2 but little or no change in the level of blood potassium.

Personnel

Roberts

District File No. M-1846
Pharmacology Report No. 433

10 April 1946

[redacted]

1019291

[redacted]

PROJECT NUMBER 113

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF P-539 IN CHAMBER AIR

METERED CONCENTRATION ppm	DURATION (hours)	RAT	MOUSE	GUINEA PIG	DOG	RABBIT
12850	0.16	0/10	0/10	5/10		
1000	14	10/10	6/10	10/10		
500	14	1/10	0/10	10/10		
	8				0/1	
	7					0/3
100	14	0/10	0/10	0/10		
50	14	0/10	0/10	0/10		

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

PROJECT NUMBER 113 APPROXIMATE INHALATION TOXICITY STUDIES

MORTALITY OF MICE EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF T-1

CONCENTRATION ppm	DURATION hours	MOUSE
55,787	1	9/10
21,482	1	9/10
4,735	4	0/10
2,148	3.3	0/10

Death appeared to be due to respiratory difficulty.

No damage found on gross pathological examination.

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019293

[redacted]

PROJECT NUMBER 120 INHALATION TOXICITY STUDIES OF TRIBNOL, CHLORTHANE, 890, and 891.

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG

TO TWO CONCENTRATIONS OF 890 IN CHAMBER AIR

Metered Concentration 890 (ppm)	Duration hours	Dog	Cat	Rabbit	Guinea Pig	Rat	Mouse	Hamster
50	206	0/5	2/6	0/12	23/30	16/99	89/89	-
20	211.5	0/5	0/6	0/12	2/29	6/100	9/47	2/6

Cause of Death - appeared due to respiratory failure.

Pathology - No reports received. Probably lung hemorrhage.

Weight Loss - Apparent only in cats, guinea pigs and mice at 50 ppm level.

Hematology - No significant blood cellular changes.

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS
TO SEVERAL CONCENTRATIONS OF C-816-CRUDE IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
500	552	6.5	10/10	10/10	10/10
250	225	14	8/10	10/10	2/9
100	55	14	0/10	10/10	0/10
50	0-150	14	0/10	2/10	0/10
50	80	14	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF C-816-FORESHOT IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
500	624	9	10/10	10/10	10/10
100	325	14	4/10	10/10	9/10
100	0-130	14	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019296

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS
TO SEVERAL CONCENTRATIONS OF C-716-2 IN CHAMBER AIR

CONCENTRATION, ppm Metered	Analyzed	DURATION Hours	RAT	MOUSE	GUINEA PIG
5000	4596	4.7	0/10	0/10	0/10
1000	746	14	0/10	1/9	0/10
500	129	14	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019297

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF C-716-FORESHOT IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
500	496	7	10/10	9/9	9/10
250	230	14	5/9	10/10	7/10
100	82	14	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS
TO SEVERAL CONCENTRATIONS OF C-716-CRUDE IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
1000	977	9.5	0/10	10/10	5/10
500	512	14	0/10	10/10	0/10
250	281	14	0/10	1/10	0/10
100	114	14	0/10	6/9	0/9

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019299

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS
TO SEVERAL CONCENTRATIONS OF C-816-1 IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
1000		7	10/10	10/10	10/10
1000	880	3	2/10	5/10	8/10
500	820	14	10/10	10/10	10/10
500	524	14	8/10	10/10	8/10
230	272	14	0/10	1/10	0/10
100	110	14	0/10	1/10	0/10

Numerator = number dead

Denominator = number exposed

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS
TO C-816-1 IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
500	372	14	0/10	5/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF C-816-2 IN CHAMBER AIR

CONCENTRATION, ppm		DURATION	RAT	MOUSE	GUINEA PIG
Metered	Analyzed	Hours			
1000		14	0/10	0/10	0/10
500	665	14	0/10	0/8	0/10
500	309	14	0/10	0/10	0/10
250		14	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF CHLORTHANE IN CHAMBER AIR

METERED CONCENTRATION	DURATION Hours	RAT	MOUSE	G. PIG	CONDITION OF CAGES
ppm					
85	14	3/10	10/10	0/10	wet with decomposition products
50	14	10/10	10/10	0/10	wet with decomposition products
20	7	10/10	10/10	0/10	wet with decomposition products
100	14	0/10	14/15	0/10	dry, changed every hour
50	14	0/10	0/15	0/10	dry, changed every two hours
20	14	0/10	0/10	0/10	dry, changed every two hours

Death appeared due to lung hemorrhage

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019302

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG

TO SEVERAL CONCENTRATIONS OF TRIBNOL IN CHAMBER AIR

Meter Concentration, Tribnol ppm.	Duration Hours	Dog	Cat	Rabbit	G.Pig	Rat	Mouse
100 *	187.8	0/5	0/6	0/12	1/26	1/97	50/28
100	202.5	5/5	6/6	12/12	40/40	100/100	101/101
20	60	0/5	0/6	0/12	25/30 **	1/100	36/99

* Faulty method of metering

** Unexplained accident killed 25 of 30 guinea pigs on 9th day of exposure. Experiment terminated.

Cause of Death - appeared due to respiratory failure.

Pathology - Lung hemorrhage

Weight Loss - Striking only at second 100 ppm level.

Hematology - No significant blood cellular changes.

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019303

S E C R E T [redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG TO SEVERAL CONCENTRATIONS OF TRIBNOL IN CHAMBER AIR

METERED CONCENTRATION, TRIBNOL, ppm	DURATION	DOG	CAT	RABBIT	GUINEA PIG	RAT	MOUSE
15	195.5	0/5	0/6 *	0/12	1/30	2/100	18/93

* One sacrificed. Liver very fatty: damage not due to Tribnol.

February 5, 1946

[redacted]

1019304

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS TO SEVERAL CONCENTRATIONS OF TRIBNOL IN CHAMBER AIR

METERED CONCENTRATION, TRIBNOL ppm	DURATION Hours	RAT	MOUSE	GUINEA PIG
750	6.5	1/10	1/10	10/10
350	1.5			7/10
135	11.0	0/10	0/10	0/10

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF MICE EXPOSED VIA THE LUNG

TO 72 mg 891 PER CUBIC METER

OF CHAMBER AIR

METERED CONCENTRATION mg/cubic meter	DURATION	MOUSE
72	197.8	0/15

No apparent damage

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

[redacted]

MORTALITY OF ANIMALS EXPOSED VIA THE LUNG FOR SHORT PERIODS

TO SEVERAL CONCENTRATIONS OF 890 IN CHAMBER AIR

Concentration ppm.	Duration (hours)	Rat	Mouse	Guinea Pig	Concentration ppm.	Duration (hours)	Rat	Mouse	Guinea Pig
4582	6.5	4/4			548	14.0	1/4		
3452	9.5	4/4			485	14.0	1/4		
3135	0.8			3/3	404	0.3			2/2
3113	0.8			1/2	381	7.0		10/10	
2577	3.5	2/4			344	14.0	0/4		
1997	0.3			2/2	265	14.0	0/4		
1290	14.0	1/4			223	14.0		10/10	
1106	0.3			2/2	223	0.8			2/2
880	5.6		3/6		156	14.0		0/10	
849	14.0	3/4			108	2.3			1/2
694	2.8			3/3	97	14.0		0/10	
569	0.9			2/2	52	3.8			1/2
					38	14.0			0/2

Numerator = number dead

Denominator = number exposed

February 5, 1946

[redacted]

1019307

[redacted]

PROJECT NO. 121 METHOD OF ANALYSIS FOR GASEOUS 891 COMPOUNDS

Current Result

A semiquantitative method has been developed that is both simple and rapid for the determination of boron fluoride, boron fluoride dimethyl ether, or boron chloride in a concentration range of 10 to 200 ppm in air. Boron halide-air samples are drawn for a counted number of strokes through a small hand pump containing a filter paper impregnated with turmeric. The color developed after 10 minutes is matched with a standard and the concentration of boron halide is read from a table. The method is most accurate in the range 12 to 30 ppm and from 160-220 ppm boron halide. Vapors of hydrochloric and nitric acid and of fluoride mixtures do not interfere. Color is produced by ammonia in the absence of boron halides but this color fades before the 10-minute period required for matching elapses. UF_6 does not affect the dry paper. A number of other metallic ions may interfere but these are not ordinarily present in boron halide atmospheres. In the case that interfering ions are suspected, a simple confirmatory test for boron halides may be performed. This is described herein.

Personnel: C. A. Horton
C. S. Weil
H. Wilson

District File No.: M-1798

Pharmacology Report No. 410

24 January 1946

[redacted]

1019308

PROJECT NO. 137

THE USE OF BLOOD CLOTTING TIME AS AN EARLY CLINICAL INDEX OF TOXICITY RESULTING FROM T AND C-216 COMPOUNDS

Current Results.

1. Rabbits exposed to C-216 (3 mg/m^3) for only 16-22 hours, evidence striking increases in plasma prothrombin and fibrinogen.

2. No significant alterations observed. Dogs and mice exposed to 5 mg/m^3 of high grade ore after 4-5 weeks.

3. Dogs and rabbits exposed to 1.6 mg/m^3 TCl_4 for 66 hours. Prothrombin levels significantly elevated. Fibrinogen levels depressed. The bromsulphalein retention values in the dogs indicated progressive hepatic dysfunction which was restored simultaneously with a return to normal of plasma prothrombin fibrinogen after 180 hours exposure.

4. Dogs and rabbits exposed to 25 mg/m^3 of HC-216 showed marked hyper prothrombinemia and elevated fibrinogen levels after only 6 hours. With continued exposure values increased to 200-300 per cent above normal.

5. Rabbits exposed for 6 hours to 3 mg/m^3 of TF_6 showed elevated prothrombin fibrinogen levels. Fibrinogen values continued to increase in subsequent 10 days without further exposure to to 200% above normal. Restoration to pre-test normals required 14-22 days.

Personnel — John Field

10 April 1946

[redacted]

PROJECT NO. 138 TOXICITY OF $Na_2T_2O_7 \cdot 4H_2O$ DUST BY INHALATION

Substance $Na_2T_2O_7$

Special Characteristics -
Particle Size - Mean 0.65

Concentration Compound mg/m3	Concentration Element mg/m3	Duration of Exposure hours		Species Dog	Cat	Rabbit	G. Pig	Rat	Mouse
20.3±3.2	15.1		Mortality	0/6	0/4	10/23	4/30	0/30	19/50
			Pathology						
			Biochemistry			+ +			
			Growth	+	+	+ +	+	+	
			Hematology	0		0		0	
			Renal Function						

Detailed Pathology Tabulation

Concentration Comp. mg/m3	Concentration Element mg/m3	Duration of Exposure hours	Species	Tissues
20.3	15.1		Cats Dogs Rabbits Rats	

Detailed Biochemistry Tabulation

Concentration Comp. mg/m3	Concentration Element mg/m3	Duration of Exposure	Species	Creatinine	Creatine	Lactic Acid	NH_3	Protein	NPN	Urea	Lactic Acid	CO_2
20.3	15.1		Rabbit	0/13	6/13	5/13	14/14	12/13	12/17	12/17	0/18	10/18

February 5, 1946

[redacted]

1019310

[redacted]

PROJECT NO. 139 TOXICITY OF 'HI-GRADE' ORE BY INHALATION

Current Results Inhalation of 'Hi-Grade' Ore dust at 22 mg/m^3 U was moderately toxic to rabbits, mildly so to rats, guinea pigs and to mice.

Personnel Dygert, Oberg, Sanford

Pharmacology Report No. 453

District File No. Not available as yet. Report in rough draft form.

11 April 1946

[redacted]

[redacted]

PROJECT NO. 139 TOXICITY OF 'HI-GRADE' T ORE BY INHALATION

Table of Mortalities of Various Species
Exposed via the Lung to Several Concentrations
of 'Hi-Grade' Ore in Chamber-Air

Compound (mg/m^3)	Elemental Equivalent (mg/m^3)	Duration (hours)	Dog	Cat	Rabbit*	Guinea Pig	Rat	Mouse
20	12.0	132	-	-	6/10	3/20	1/15	2/40

* Coccidiosis broke out in the rabbit colony after start of experiment.

Cause of Death - appeared to be kidney damage.

Pathology - Showed some lung as well as kidney damage.

Table of Mortalities of Various Species
Exposed via the Lung to Two Concentrations
of 'Hi-Grade' Ore in Chamber-Air

Compound (mg/m^3)	Elemental Equivalent (mg/m^3)	Duration (hours)	Dog	Rabbit	Guinea Pig	Rat	Mouse
5	3	171	0/5	1/15	1/20	0/45	10/45
1	0.6	171	0/5	0/15	1/20	0/45	7/50

Numerator = number dead

Denominator = number exposed

[redacted]

February 5, 1946

[redacted]

PROJECT NO. 140 TOXICITY OF $TO_4.3H_2O$ DUST BY INHALATION

TABLE OF MORTALITIES OF VARIOUS SPECIES EXPOSED VIA THE LUNG
SEVERAL CONCENTRATIONS OF $TO_4.3H_2O$ IN CHAMBER-AIR

Compound (mg/m^3)	Elemental Equivalent (mg/m^3)	Duration (hours)	Dog	Cat	Rabbit	Guinea Pig	Rat	Mouse
20	13.3	103	-	4/4	4/5	6/20	2/20	25/40 (21-29 gm) 8/30 (16-19 gm)

Cause of Death - was apparently kidney damage

Pathology - Lung as well as kidney damage was observed

Hematology - There were no significant changes.

February 5, 1946

[redacted]

[redacted]

PROJECT NO. 141 TOXICITY OF $(NH_4)_2T_2O_7$ DUST BY INHALATION

Table of Mortalities of Various Species
Exposed via the Lung to Several Concentrations
of $(NH_4)_2T_2O_7$ in Chamber-Air

Compound (mg/m³)	Elemental Equivalent (mg/m³)	Duration (hours)	Dog	Cat	Rabbit	Guinea Pig	Rat	Mouse
20	14.2	153	-	-	9/10	4/20	0/30	21/40

Cause of Death - (Pathology report has not been submitted)

Hematology - Fall in leukocytes, erythrocytes and hemoglobin. Rise in eosinophils.

February 15, 1946

S[redacted]

1019314

[redacted]

PROJECT NO. 165

A FILTER PROCEDURE FACILITATING THE ANALYSIS OF URANIUM DUST SAMPLES TAKEN BY MEANS OF THE FILTER PAPER DUST SAMPLER

Current Result

An all-glass filter apparatus which employs a fritted disc allows dust samples of certain uranium compounds taken by absorption on filter paper to be extracted and analyzed directly in a receiver by the ferrocyanide procedure with a resulting saving in time and increased accuracy. Compounds other than those of uranium may also be analyzed by means of this apparatus.

Personnel: Cohenour
Davis

District File No.

Pharmacology Report No. 451

24 January 1946

[redacted]

[redacted]

[redacted]

CURRENT RESULTS

PHARMACOLOGY SECTION

Frances L. Haven, Chief of Section

PHARM

15 April 1946

[redacted]

PHARMACOLOGY SECTION

Current Results Index

Project 1	Chronic Toxicity of T Nitrate for Rats
Project 2	Data on Feeding of TF_4 to Rats
Project 3	Data on Feeding of TO_3 to Rats
Project 4	Data on Feeding TO_2 to Rats
Project 5	Data on Feeding of T_3O_8 to Rats
Project 7	Data on the Feeding of TO_4 to Rats
Project 8	Data on the Feeding of TCl_4 to Rats
Project 9	Data on the Feeding of TO_2F_2 to Rats
Project 11	Mortality Data on Dogs Fed TO_3 for 30 Days
Project 12	Mortality Data on Dogs Fed TNO_3 for 30 Days
Project 13	Mortality Data on Dogs Fed TCl_4 for 30 Days
Project 14	Mortality Data on Dogs Fed TO_2F_2 for 30 Days
Project 15	Mortality Data on Dogs Fed TF_4 for 30 days
Project 100	Mortality Data on Dogs Fed T_3O_8 for 30 Days
Project 114	Mortality Data on Dogs Fed TO_3 for 30 days
Project 115	Mortality Data on Dogs Fed TO_4 for 30 Days
Project 116 4	Mortality Data on Dogs Fed $Na_2T_2O_7$ for 30 days
Project 117	Mortality Data on Dogs Fed $(NH_4)_2T_2O_7$ for 30 Days
Project 118	Mortality Data on Dogs Fed 'Hi-Grade' Ore for 30 Days
Project 166	Chronic Toxicity of T Nitrate for Rabbits
Project 167	Chronic Toxicity of T Nitrate for Hamsters

[redacted]

Project 33	A Histological Study of the Pancreas in Acute T Poisoning
Project 34	Fatty Acids
Project 38	The Effect of Diet on Acute Toxicity
Project 39	The Effect of Diet on Acute T Toxicity
Project 54	Included in Project 148
Project 55	Use of Digestive Stimulants
Project 56	An Investigation of Methods of Laundering Materials Contaminated with T.
Project 68	Forcing and Restricted Fluids
Project 71	The Localization of Uranium in the Rat Kidney
Project 73	A Study of Phenols in Blood and Urine in T Poisoning
Project 85	Exposure of the Skin to Various Compounds (Rabbits) Exposure of the Eye to Various Compounds
Project 98	The Effect of T Compound on the Turnover of Lipid Phosphorus Fractions
Project 128	The Therapeutic Use and Metabolic Role of Citrates in T Poisoning
Project 148	Lipids in T Poisoning and Study of Cholesterol
Project 150	The Effect of Various Agents on T Nitrate and TO_2F_2 Toxicity

14 April 1946 [redacted]

PROJECT NO. 1 DATA ON THE FEEDING OF TNO_3

The Percentage Mortality and the Average Weights Relative to the Control Average Weights of the Various Groups of Rats (males and females separately) are given.

TNO_3

% in Diet	Males		Females	
	% Mortality	Wt. Vs. Control after 30 days on diet	% Mortality	Wt. Vs. Control after 30 days on diet
3.0			33	-41
2.0	7, 15	-52, -38	16	-30
1.0	10	-20	0 7	-12 -10
0.50	0 0	+3 -10	0	-6
0.10	5 0	-13 -11	5 0	+3 -1
0.05	0	-3	0	-3
0.01	0	-6	0	-3
20.0	100			
10.0	100		86	-92
5.0	67	-115	67	-57

28 January 1946

1019319

SECRET

[redacted]

PROJECT NO. 1

CHRONIC TOXICITY OF T-NITRATE FOR RATS

TWO YEAR TEST

No. of Days	No. of Animals	% of TNO_3 in Diet	Effect	Mortality
730 T*	20 ♂	Controls	----	65%
	20 ♂	0.1%	♂ + 6g	65%
	20 ♂	0.5%	♂ +57g	75%
	20 ♂	1.0%	♂ -27g	65%
	20 ♂	2.0%	♂ -26g	70%
(Completed)				
504	25 ♀	Controls	----	24%
	25 ♀	0.1%	♀ -11g	8%
	25 ♀	0.5%	♀ -19g	16%
	25 ♀	1.0%	♀ -35g	24%
	25 ♀	2.0%	♀ -55g	28%
730 T	15 ♂	Controls	----	67%
	15 ♂	0.01%	♂ +90g	86%
	15 ♂	0.05%	♂ +59g	53%
	15 ♂	0.1%	♂ +12g	79%
730 T	20 ♀	Controls	----	75%
	20 ♀	0.01%	♀ +26g	65%
	20 ♀	0.05%	♀ + 5g	85%
	20 ♀	0.1%	♀ +30g	70%

ONE YEAR TEST

84 T	25 ♂	Controls	----	0%
	25 ♂	0.1%	♂ + 6g	0%
	25 ♂	0.5%	♂ + 2g	0%
	25 ♂	2.0%	♂ -20g	8%
84 T	25 ♀	Controls	----	0%
	25 ♀	0.1%	♀ - 8g	0%
	25 ♀	0.5%	♀ -10g	0%
	25 ♀	2.0%	♀ -79g	40%
301	25 ♂	Controls	----	12%
	25 ♂	0.1%	♂ - 2g	8%
	25 ♂	0.5%	♂ -22g	4%
	25 ♂	2.0%	♂ -92g	12%

* T = Experiment terminated by sacrifice of rats as planned.

[redacted]

[redacted]

PROJECT NO. 1

ONE YEAR TESTS CONTINUED

No. of Days	No. of Animals	% of TNO_3 in Diet	Effect	Mortality
300	25 ♀	Controls	----	8%
	25 ♀	0.1%	C + 2g	12%
	25 ♀	0.5%	C -11g	0%
	25 ♀	2.0%	C -27g	24%
287	25 ♂	Controls	----	0%
	25 ♂	0.1%	C -21g	0%
	25 ♂	0.5%	C -14g	0%
	25 ♂	2.0%	C -78g	36%
287	25 ♀	Controls	----	4%
	25 ♀	0.1%	= C	4%
	25 ♀	0.5%	C - 8g	0%
	25 ♀	2.0%	C -24g	36%
266 T*	25 ♂	Controls	----	4%
	25 ♂	0.1%	C -16g	4%
	25 ♂	0.5%	C -32g	0%
	25 ♂	2.0%	C -79g	48%
266 T	25 ♀	Controls	----	8%
	25 ♀	0.1%	C + 9g	4%
	25 ♀	0.5%	C - 6g	0%
	25 ♀	2.0%	C -26g	24%

No. of Days	No. of Animals	% of TNO_3 in Diet	Effect	# Sacrificed	# Died
238 T	28 ♂	Controls	----	13	0
	28 ♂	0.1%	C -23g	12	2
	28 ♂	0.5%	C -15g	13	0
	28 ♂	2.0%	C -82g	12	2
238 T	28 ♀	Controls	----	11	0
	28 ♀	0.1%	C - 1g	11	1
	28 ♀	0.5%	C - 6g	12	2
	28 ♀	2.0%	C -38g	11	4

* T = Experiment terminated by sacrifice of rats as planned.

1019321

[redacted]

PROJECT NO. 1

ONE YEAR TESTS CONTINUED

No. of Days	No. of Animals	% of TNO_3 in Diet	Effect	Mortality
168 T*	25 ♂	Controls	----	0%
	25 ♂	0.1%	C -12g	0%
	25 ♂	0.5%	C -12g	0%
	25 ♂	2.0%	C -44g	8%
168 T	25 ♀	Controls	----	0%
	25 ♀	0.1%	C + 4g	0%
	25 ♀	0.5%	C + 7g	4%
	25 ♀	2.0%	C -35g	32%

* T = Experiment terminated by sacrifice of rats as planned.

Effect of T Compound on Reproductive Tissues

Group	No. of Rats	Diet
DAA	50 pairs	Control rats - no TNO_3 in Diet
DBB	50 pairs	2.0% TNO_3 in Diet

The above groups of rats were started on experiment August 17, 1944. At the end of 279 days on the diet, a total of 313 litters had been born to control pairs and 178 litters had been born to TNO_3 rats. On February 28, 1945 the rats that had been fed 2.0% TNO_3 for a period of 195 days were shifted to a diet of straight fox-chow meal to determine if there would be any recovery either in number of litters or in body weight. The ratio of litters born while on a diet containing 2.0% TNO_3 was 1:2.07; after removal of TNO_3 from diet the ratio has been 1:1.4. In a period of 83 days following removal of TNO_3 from the diet the experimental rats have had average weight increases greater than the controls: ♀ + 15g. ♂ + 16g.

[redacted]

[redacted]

PROJECT NO. 34 FATTY ACIDS

Current Results

In acute T poisoning the unsaturation of the phospholipid fatty acids of the liver and blood increases whereas there is a simultaneous decrease in that of the kidney.

Personnel

Ruth Crossland

District File No.

Pharmacology Report No. 463

26 February 1946

[redacted]

1019323

PROJECT NO. 38 THE EFFECT OF DIET ON ACUTE TOXICITY

Current Results

1. Addition of 0.5% sodium bicarbonate to the diet reduced the mortality by T poisoning from an average of 80% to 20-30%. (Dose of T nitrate: 5 mgm/kg).

2. Alkali administration is of less benefit if given 1 day after injection of T. This would indicate that the alkali effect is not due to the symptomatic relief of the acidosis of the uremia caused by poisoning but rather due to a prevention of kidney damage.

3. Feeding the sodium salts of various acids which can be metabolized (i.e., citrate, malate, lactate) or injection of these compounds in quantities equivalent to a dietary level of 0.5% sodium bicarbonate gives about the same protection as does bicarbonate.

4. The administration of acid (as ammonium chloride) increased the mortality from 80 to 95%.

Personnel

Wm. Neuman
E. Mulryan

District File: M-1691

Pharmacology Report No. 316

[redacted]

PROJECT NO. 39 THE EFFECT OF DIET ON ACUTE T TOXICITY

Current Results

Environmental temperatures of 76–80° are optimal for survival of rats given acute (5 mg/kg) doses of TNO_3 intraperitoneally. Temperatures above or below this range gave larger mortalities.

Usually the rectal temperature fell to less than 35° C. in the period 24 to 48 hours before death.

Personnel

Wm. Neuman
E. Mulryan

District File No. M-1691

Pharmacology Report No. 316

2 February 1946

1019325 [redacted]

[redacted]

PROJECT NO. 55 USE OF DIGESTED STIMULANTS

Current Results

Daily injections in rats of sodium glycocholate and of doryl, did not reduce the mortality following the intraperitoneal administration of an acute dose (5 mg./kg.) of T nitrate.

Personnel

Wm. Neuman
E. Mulryan

Not reported as yet.

5 February 1946

[redacted]

[redacted]

PROJECT NO. 56

AN INVESTIGATION OF METHODS OF LAUNDERING MATERIALS CONTAMINATED WITH T

Current Results

In this laboratory, chemical tests revealed that special methods of laundering are necessary for removal of T from contaminated fabric.

Of all the substances tested, the most suitable washing agent for general use from the standpoint of both cost and effectiveness was sodium bicarbonate. However, no general procedure or agent can be recommended for the removal of any and all T compounds.

In our studies, bicarbonate proved to be an excellent washing agent for all of the soluble hexavalent T salts. For some of the tetravalent salts, bicarbonate together with an oxidizing agent (presumably to convert the T to the hexavalent state) was quite effective. The stable oxides and ore samples were extremely difficult to extract from cloth. No truly satisfactory means was discovered for the removal of these inert compounds.

From the standpoint of toxicology, bicarbonate or bicarbonate with added peroxide renders contaminated fabric practically free of all toxic T compounds. Compounds of T which are not removed by this treatment are relatively non-toxic.

Personnel

Wm. Neuman
A. Carlson

District File No. M-1692

Pharmacology Report No. 301

5 February 1946

1019327

[redacted]

[redacted]

PROJECT NO. 68 FORCING AND RESTRICTED FLUIDS

Current Results

Restricting the fluid intake increase mortality; forcing fluids (stomach tube) reduced mortality following the administration of an acute dose (5 mg./kg.) of TNO_3 in rats.

Personnel

Wm. Neuman
E. Mulryah

5 February 1946

1019328

[redacted]

[redacted]

PROJECT NO. 71 THE LOCALIZATION OF URANIUM IN THE RAT KIDNEY

Current Results

There is a low concentration of uranium throughout the kidney and superimposed on this background there are scattered areas of comparatively high concentration. The latter fact indicates that even a fatal dose of uranyl salt does not affect all nephroi of the kidney to the same extent, but leaves some relatively unaffected. With smaller doses, the proportion of unaffected nephroi in respect to the total probably becomes greater the less the dose. Thus, survival or fatality may depend only indirectly on the dose of poison; they would depend directly on the number of renal units left functioning. There was no evidence of concentration in the glomeruli.

Personnel

Wm. Neuman
H. Wills
D. Adler

District Report No. II 143-4740

Pharmacology Report No. 398

5 February 1946

1019329

[redacted]

[redacted]

PROJECT NO. 73 A STUDY OF PHENOLS IN BLOOD AND URINE IN T POISONING

Current Results

1. A quantitative study of urinary phenol excretion in T poisoned rats has revealed that

   a. A significant rise in free and total phenol excretion occurred after the intraperitoneal injection of TNO_3 in doses of 0.32 to 2.50 mg per kg of body weight.

   b. Such increase in phenol excretion reached a maximum four days following injection of T.

   c. The increase in phenol excretion became greater with increase in T dosage.

   d. The phenol conjugation mechanism appeared to be relatively unaffected by T injection, since no significant change in the per cent of conjugated phenols was observed.

2. A color which appeared at one stage in the application of the phenol method to the urine of T poisoned rats has been shown to consist of colloidal silver formed by the reducing action of light on silver chloride and stabilized by blood protein present in the urine.

Personnel Frances Haven
J. O'Leary
J. O'Leary

District File No. M-1696

Pharmacology Final Report No. 326

2 February 1946

1019330

[redacted]

PROJECT NO. 85 EXPOSURE OF THE SKIN TO VARIOUS COMPOUNDS

A. Approximate Order of Local Toxicity (Rabbit)

Compound	Dose per animal	Length of Exposure	Concentration	Vehicle	Evaluation of Damage	Remarks
890	1.0 cc.	10 min. or longer	100%	none	4+	
	1.0 cc.	5 min.	100%	none	3+	
	1.0 cc.	1 min. or less	100%	none	0 to 1+	
HCPH	0.5 cc.		100%	none	4+	
HCPE	1.0 cc.		100%	none	4+	
C-216	40 lbs. pres.	0.3 sec. or longer			3+	
	40 lbs. pres.	0.2 sec.			1+	
HCP	5.0 cc.		100%	none	2+	very painful
TCl_5	1.0 gm.		100%	none	2+	
TCl_4	2.0 gm.		65%	lanolin	2+	
	0.5 gm.		100%	none	0	
TO_2F_2	1.0 gm.		50%	water	0	
	1.0 gm.		65%	lanolin	0	
	1.0 gm.		65%	lanolin	0	
HCPF	0.5 gc.		100%	none	1+	
$TO_2(NO_3)_2$	1.0 gm.		71%	ether	1+	
TO_3	1.0 gm.		65%	lanolin	0	
$Na_2T_2O_7$	1.0 gm.		65%	lanolin	0	
$(NH_4)_2T_2O_7$	1.0 gm.		65%	lanolin	0	
TO_4	1.0 gm.		65%	lanolin	0	
TF_4	1.0 gm.		65%	lanolin	0	
T_3O_8	1.0 gm.		65%	lanolin	0	
TO_2	1.0 gm.		65%	lanolin	0	
891	1.0 gm.		100%	none	0	

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JAN 28 1946

EXPOSURE OF THE SKIN TO VARIOUS COMPOUNDS

B. Approximate Order of Systemic Toxicity from Percutaneous Absorption (Rabbit)

Compound	Dose in gm/animal	Concentration	Vehicle	Highest Average Urinary Protein in gms. per cent	Mortality	Remarks
$TO_2(NO_3)_2$	1.0	71%	ether		6/6	
TCl_4	2.0	65%	lanolin	2.60	6/6	
	0.5	100%	none	0.15	2/4	
HCPF	0.5	100%	none	0.22	4/5	severe renal necrosis
TCl_5	1.0	100%	none	0.58	5/6	
TO_2F_2	1.0	65%	lanolin	1.50	6/6	
	1.0	50%	water	2.50	5/6	
HCP	5.0 cc.	100%	none	0.06	6/6	
TO_3	1.0	65%	lanolin	0.35	4/6	
$Na_2T_2O_7$	1.0	65%	lanolin	0.23	4/6	
HCPH	0.5	100%	none	0.02	1/6	
HCPE	1.0	100%	none	0.02	0/6	
TO_4	1.0	65%	lanolin	0.08	0/6	
TF_4	1.0	65%	lanolin	0.05	0/6	
T_3O_8	1.0	65%	lanolin	0.05	0/6	
TO_2	1.0	65%	lanolin	0.05	0/6	
890	1.0	100%	none		0/9	
891		100%	none		0/8	
C-216		40 lbs.pres.			0/6	

EXPOSURE OF THE SKIN TO VARIOUS COMPOUNDS

C. Dosage-Mortality Data for $TO_2(NO_3)_2$ and TCl_4

Compound	Dose in gm/kg	Concentration	Vehicle	Mortality	LD50 in gm/kg.	Species
$TO_2(NO_3)_2$		71% 6%	ether		0.125 ± 0.035	rabbit
		71%	ether		4.44 ± 0.61	guinea pig
		71%	ether		1.04 ± 0.55	rat
	13.27	71%	ether	9/20		mouse
TCl_4	1.75	40%	water	5/21		guinea pig
	3.40	40%	water	4/21		guinea pig
	6.70	40%	water	10/21		guinea pig

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10193

28 January 1946

EXPOSURE TO VARIOUS T COMPOUNDS OF THE EYE OF THE RABBIT

A. Approximate Order of Local Toxicity (one eye exposed)

Compound	Dose in gm/animal	Concentration	Vehicle	Evaluation of Damage	Duration of damage	Remarks
TCl_5	0.001	100%	none	4+	long	
HCPE	0.05	100%	none	4+	long	very painful
HCPH	0.05	100%	none	3+	long	very painful
$TO_2(NO_3)_2$	0.350	53%	water	3+	long	
TCl_4	0.250	50%	water	2+	long	
$Na_2T_2O_7$	0.100	100%	none	3+	short	
$(NH_4)_2T_2O_7$	0.100	100%	none	2+	short	
TO_2F_2	0.200	40%	water	3+	short	
TF_4	0.100	100%	none	1+	short	
HCP	0.05	100%	none	1+	short	
HCPF	0.05	100%	none	1+	short	
TO_3	0.100	100%	none	0		
	0.750	65%	lanolin	0		
TO_4	0.025	6%	water	0		
	0.100	100%	none	0		
	0.750	65%	lanolin	0		
T_3O_8	0.100	100%	none	0		
	0.750	65%	lanolin	0		
TO_2	0.100	100%	none	0		
	0.750	65%	lanolin	0		

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1019334

28 January 1946

EXPOSURE OF THE EYE OF THE RABBIT TO VARIOUS T COMPOUNDS

B. Approximate Order of Systemic Toxicity from Conjunctival Absorption

Compound	Dose in gm/animal	Concentration	Vehicle	Mortality
TCl_5	0.001	100%	none	2/4
TO_3	0.100	100%	none	4/4
TF_4	0.100	100%	none	3/6
TO_2F_2	0.200	40%	water	3/4
TCl_4	0.250	50%	water	3/4
$TO_2(NO_3)_2$	0.350	53%	water	3/4
HCPE	0.05	100%	none	1/4
$Na_2T_2O_7$	0.100	100%	none	1/4
$(NH_4)_2T_2O_7$	0.100	100%	none	1/4
HCP	0.05	100%	none	0/3
HCPB	0.05	100%	none	0/4
HCPH	0.05	100%	none	0/4
TO_4	0.025	6%	water	0/4
	0.100	100%	none	0/4
	0.750	65%	lanolin	0/4
TO_3	0.750	65%	lanolin	0/4
T_3O_8	0.100	100%	none	0/4
	0.750	65%	lanolin	0/4
TO_2	0.100	100%	none	0/4
	0.750	65%	lanolin	0/4

28 January 1946

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PROJECT NO. 98 THE EFFECT OF T COMPOUND ON THE TURNOVER OF LIPID PHOSPHORUS FRACTIONS

Current Results No significant changes were found in the turnover of lipid phosphorus fractions from liver and kidney of rats given an acute dose (5 mg./kg.) of TNO_3 intraperitoneally.

Personnel
Wm. Neuman
E. Mulryan
J. O'Leary
P. Fanta

Report being written.

5 February 1946

1019336

[redacted]

[redacted]

PROJECT NO. 128

THE THERAPEUTIC USE AND METABOLIC ROLE OF CITRATES IN T POISONING.

Current Results

Na citrate, Na fumarate and Na succinate are as effective as $NaHCO_3$ (given by stomach tube) in reducing mortality of rats given intraperitoneally 5 mg/kg TNO_3. Citric acid is ineffective.

From metabolism studies, a 3 to 4 fold increase in citric acid excretion has been observed in the period of 1 to 4 days and again in the period of 10 to 20 days following the intraperitoneal administration of 2.5 or 0.5 mg/kg TNO_3 to make rats.

There is no relation between the citric acid content of rat femurs and the T content after an acute dose of TNO_3.

Personnel

Frances Haven
Challis Randall

District File No.

Pharmacology Report No.

2 February 1946

[redacted]

1019337

[redacted]

PROJECT NO. 148 LIPIDS IN T POISONING

including

PROJECT NO. 54 CHOLESTEROL

Current Results

1. Immediately following poisoning of male or female rats with an acute dose of uranium nitrate there was a shift of cholesterol from the plasma to the red blood cells. Later the cholesterol of both red cells and plasma was transferred to the body fluids or tissues (or possibly burned in the case of female animals) resulting in low blood cholesterol values.

2. The blood cholesterol of male or female rats given a sub-acute dose of uranium nitrate decreased on the first day after injection. This decrease was followed by a fluctuating increase.

3. No change in the ratio of free to combined cholesterol of the plasma occurred.

4. Small amounts of cholesterol were found in the urine of rats given an acute dose of uranium nitrate. This probably comes from kidney cell debris.

5. After injection with an acute dose of uranium nitrate the male rat maintained andincreased its total body cholesterol as though it were a normal growing animal. The female maintained but did not increase her total body cholesterol as would a normal growing female.

6. A decrease in total cholesterol, a decrease in free cholesterol and a very slight increase in ester cholesterol was found in the livers of male rats acutely poisoned with uranium nitrate. No change was found in the cholesterol content and ratio of the liver of female rats.

7. An increase in the total cholesterol content of the kidneys of female rats occurred after treatment with an acute dose of uranium nitrate. This could be accounted for by an increase in ester cholesterol. No change in the cholesterol content and ratio of the kidneys of male rats was found.

8. The adrenals of both male and female rats showed a decreased amount of total cholesterol at death from uranium nitrate. The adrenals of normal and experimental male rats contained a greater amount of cholesterol in the free form than normal and experimental female rats.

Personnel Frances Haven
Jean Box

Pharmacology Report No.

District File No.

[redacted]

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PROJECT NO. 150 THE EFFECT OF VARIOUS AGENTS ON T-NITRATE AND TO_2F_2 TOXICITY

Current Results .

1. The mortality after a 5 mg/kg dose of T-nitrate was not decreased in rats on diets containing supplements of

   choline hydrochloride neutralized choline hydrochloride
   disodium hydrogen phosphate
   lactic acid sodium lactate calcium lactate
   essential fatty acids

2. A renal extract prepared from beef kidney and used on rats did not decrease but did delay the mortality from an acute dose of TNO_3. The extract decreased the diuresis following a subacute dose.

3. Adrenal cortical hormones. Of the four commercial preparations tried, three caused a delay of 24 hours or more in mortality of rats after an acute dose of TNO_3.

4. Sodium bicarbonate and sodium citrate administered in equivalent amounts by stomach tube were equally effective in reducing the mortality in acute TNO_3 poisoning. Citric acid was ineffective. Sodium fumarate and sodium succinate also reduced the mortality in acute T poisoning.

5. Sodium bicarbonate administered by stomach tube to rats caused a highly significant decrease in mortality from 2.5 mg/kg of TO_2F_2

Frances Haven

23 January 1946

1019339

[redacted]

PROJECT NO. 2

DATA ON FEEDING OF TF_4 TO RATS

% in Diet	Males			Females		
	Number	% Mortality	Weight vs. Control	Number	% Mortality	Weight vs. Control
20.0	8	0	-49	7	0	-17
	15	0	-15	15	7	-14
	15	0	-20	15	0	-5
2.0	8	0	+3	7	0	0
	15	0	-1	15	0	+4
	15	0	0	15	0	-2
0.5	8	0	-2	7	0	+3
	15	0	+2	15	0	+4
	15	0	-5	15	0	+1

Feeding the toxic compounds at levels of 20% of the diet frequently killed all the animals in a few days. In fact, 2% of the more toxic compounds in the diet killed most of the rats within a week. Consequently, for a number of compounds additional one month pilot experiments were set up in which various lower levels of dietary intake were used. In these experiments several fractional percentages were tested.

28 January 1946

[redacted]

PROJECT NO. 2

CHRONIC TOXICITY OF TF_4 FOR RATS

No. of Days	No. of Animals	% of TF_4 in Diet	Effect	Mortality
730 T*	15 ♂	Controls	----	73%
	15 ♂	0.5%	----	100%
	15 ♂	2.0%	♂ - 8g	67%
	15 ♂	20.0%	♂ -11g	60%
730 T	15 ♀	Controls	----	53%
	15 ♀	0.5%	♀ -23g	53%
	15 ♀	2.0%	♀ +23g	53%
	15 ♀	20.0%	♀ -32g	60%

* T = Experiment terminated by sacrifice of rats as planned.

[redacted]

[redacted]

PROJECT NO. 3 DATA ON FEEDING OF TO_3 TO RATS

% in Diet	MALES			FEMALES		
	Number	% Mort.	Wt. Vs. Control	Number	% Mort.	Wt. Vs. Control
20.0	15	100	-			
2.0	15	0	-33			
0.5	15	0	-11			

[redacted]

1019342

[redacted]

PROJECT NO. 4 DATA ON FEEDING OF TO_2 TO RATS

% in Diet	Males			Females		
	Number	% Mortality	Weight vs. Control	Number	% Mortality	Weight vs. Control
20.0	10	0	+27	5	0	+4
	15	0	- 3	15	0	+2
2.0	10	0	+ 9	5	0	+6
	15	0	+ 9	15	0	-1
0.5	10	0	+ 2	5	0	+9
	15	0	+ 8	15	0	+3

28 January 1946

[redacted]

1019343

[redacted]

PROJECT NO. 4

CHRONIC TOXICITY OF TO_2 FOR RATS

No. of Days	No. of Animals	% of TO_2 in Diet	Effect	Mortality
730 T*	15 ♂	Controls	----	80%
	15 ♂	0.5%	♂ +58g	40%
	15 ♂	2.0%	♂ +86g	67%
	15 ♂	20.0%	♂ +60g	60%
730 T	15 ♀	Controls	----	67%
	15 ♀	0.5%	♀ + 4g	60%
	15 ♀	2.0%	♀ +37g	40%
	15 ♀	20.0%	♀ +70g	54%

* T = Experiment terminated by sacrifice of rats as planned.

[redacted]

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PROJECT NO. 5 DATA ON FEEDING OF T_3O_8 TO RATS

% in Diet	Males			Females		
	Number	% Mortality	Weight vs. Control	Number	% Mortality	Weight vs. Control
20.0	7	0	-6	8	0	+8
2.0	7	0	-5	8	0	+11
0.5	7	0	+9	8	0	+9

28 January 1946

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1019345

PROJECT NO. 7

DATA ON THE FEEDING OF TO_4

The Percentage Mortality and the Average Weights Relative to the Control Average Weights of the Various Groups of Rats (males and females separately) are given.

% in Diet	TO_4			
	Males		Females	
	% Mortality	Wt. Vs. Control after 30 days on diet	% Mortality	Wt. Vs. Control after 30 days on diet
20.0			100	
2.0	100		47	-47
1.0	27 45	-60 -37	0	-13
0.75				
0.50	7	-36	0	-2
0.25	0	-18	0	-7
0.10	0	-20		

28 January 1946

PROJECT NO. 8

DATA ON THE FEEDING OF TCl_4

The Percentage Mortality and the Average Weights Relative to the Control Average Weights of the Various Groups of Rats (males and females separately) are given.

% In Diet	TCl_4			
	Males		Females	
	% Mortality	Wt. Vs. Control after 30 days on diet	% Mortality	Wt. Vs. Control after 30 days on diet
20.0			100	
3.0	100		70	-89
2.0			7	-40
1.5	60	-68	20	-50
1.0	33	-55	0	-31
	0	-57	0	-18
0.75				
0.50				
0.25				
0.20	0	-19	0	+2

28 January 1946

PROJECT NO. 9

DATA ON THE FEEDING OF TO_2F_2

The Percentage Mortality and the Average Weights Relative to the Control Average Weights of the Various Groups of Rats (males and females separately) are given.

% in Diet	TO_2F_2			
	Males		Females	
	% Mortality	Wt. Vs. Control after 30 days on diet	% Mortality	Wt. Vs. Control after 30 days on diet
20.0	100		100	
5.0	100		100	
2.0	40	-150	40	-77
1.0	100		93	-85
0.75	20	-114	27	-78
0.50	0	-64	0	-18
	0	-32	0	-23
0.25	0	-10	0	-9
	0	-48	0	-11
	0	-20	0	-6
	0	-17	0	-7
0.10	0	-13	0	-2
0.05	0	-16	0	-7
	0	+2	0	-7
0.01	0	-1	0	-8

[redacted]

PROJECT NO. 9

CHRONIC TOXICITY OF TO_2F_2 FOR RATS

No. of Days	No. of Animals	% of TO_2F_2 in Diet	Effect	Mortality
730 T*	15 ♂	Controls	----	67%
	15 ♂	0.25%	♂ -26g	67%
	15 ♂	0.50%	♂ -74g	93%
730 T	15 ♀	Controls	----	60%
	15 ♀	0.25%	♀ -24g	33%
	15 ♀	0.50%	----	100%
644	25 ♂	Controls	----	40%
	25 ♂	0.01%	= ♂	44%
	25 ♂	0.05%	♂ -22g	52%
	25 ♂	0.25%	♂ -23g	60%
644	25 ♀	Controls	----	40%
	25 ♀	0.01%	♀ -11g	16%
	25 ♀	0.05%	♀ -23g	56%
	25 ♀	0.25%	♀ -38g	32%
482	25 ♂	Controls	----	20%
	25 ♂	0.05%	♂ - 8g	4%
	25 ♂	0.10%	♂ -25g	24%
	25 ♂	0.15%	♂ -36g	44%

* T = Experiment terminated by sacrifice of rats as planned.

1019349

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MORTALITY DATA ON DOGS FED VARIOUS T COMPOUNDS FOR 30 DAYS

Project No.	Compound	Dosage in grams per kilogram body weight per day: 20	10	5	2	0.5	0.1	0.02	0.005	.001
11	TO_3	Lived 30 days		Lived 30 days						
12	TNO_3		Dead in 6 days		Dead in 4 days	Dead in 10 days	Lived 30 days			
13	TCl_4			Dead in 4 days		Dead in 11 days	Dead in 22 days	Lived 30 days		
14	TO_2F_2			Dead in 6 days		Dead in 4 days	Dead in 9 days	Dead in 11 days	Dead in 22 days	Dived . 30 days
15	TF_4	Dead in 10 days	Dead in 19 days	Lived 30 days						
100	T_3O_8	Dead in 17 days	30 days Lived							
115	TO_4					Dead in 5 days		Lived 33 days		
116	$Na_2T_2O_7$					Dead in 10 days	Lived 30 days			
117	$(NH_4)_2T_2O_7$					Dead in 17 days	Lived 30 days			
118	Ore, Hi-Grade		Dead in 17 days	Dead in 10 days		Lived 30 days				
114	TO_3					Dead in 10 days	Lived 30 days			

28 January 1946

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PROJECT NO. 12

The dogs were placed on diets containing TNO_3 on January 11th, January 12th, and January 13th, 1945, at levels as follows:

1. Two dogs to receive 0.2 g./kg. body weight daily.
2. Two dogs to receive 0.1 g./kg. body weight daily.
3. Two dogs to receive 0.02 g./kg. body weight daily.
4. Four dogs to receive no TNO_3. (Controls)

One dog at a level of 0.2 g./kg. daily died after 136 days on the diet. At the end of one year the nine surviving dogs were sacrificed for histopathological studies and tissue analyses.

[redacted]

[redacted]

PROJECT NO.14

The dogs were placed on diets containing TO_2F_2 on November 25, 1944, at levels as follows:

1. Two dogs to receive 0.001 g./kg. body weight daily.

2. Two dogs to receive 0.0025 g./kg. body weight daily.

3. Two dogs to receive 0.0002 g./kg. body weight daily.

4. Seven dogs to receive no TO_2F_2. (Controls)

   (at the end of one year, the above dogs were sacrificed for histopathological studies and tissue analyses)

5. One dog was placed on a diet containing 0.01 g./kg. body weight daily, on May 21, 1945, and is in good health at the end of about 8 months.

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PROJECT NO. 166

CHRONIC TOXICITY OF T-NITRATE FOR RABBITS

I. 30 DAY TEST

No. of Days	No. of Animals	% of TNO_3 in Diet	Mortality
30 T*	6	Controls	1/6
30 T	6	0.02%	1/6
30 T	6	0.1%	5/6
10 T	6	0.5%	6/6

II. SUPPLEMENTARY 30 DAY TEST

The following rabbits were fed baked blocks of rabbit chow meal containing the various levels of TNO_3:

No. of Days	No. of Animals	% of TNO_3 in Diet	Mortality
31 T	6	Controls	0/6
31 T	6	0.02%	0/6
31 T	6	0.1%	4/6
10 T	6	0.5%	6/6

* T = Experiment terminated by sacrifice of rabbit as planned.

1019353

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PROJECT NO. 167

CHRONIC TOXICITY OF T-NITRATE FOR HAMSTERS

4 MONTH TEST

No. of Days	No. of Animals	% of TNO_3 in Diet	Mortality
	2	4.0%	0%
128	2	4.0%	0%
142			

1019354

[redacted]

CURRENT RESULTS

ANALYTICAL SECTION

John F. Flagg, Chief of Section

ANALYT

15 April 1946

[redacted]

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ANALYTICAL SECTION

Current Results Index

Summary of Projects Completed Under the General Subject of Methods for Determining Radium, Uranium, and Radon

1. The Determination of Nitrogen Oxides in Air
2. The Determination of Uranium with Isatin Oxime.
3. Analysis of Ore - Cooperative Study
4. Coprecipitation of Radium Sulfate with Lead Sulfate
5. Chromatographic Analysis
6. Semimicro Volumetric Determination of Uranium
7. The Determination of HF in Air

Project 102 To Study Certain Organic Analytical Reagents in Order to Find Reagents Which May Be Used for the Detection and Estimation of T.

Project 124 C-216 Analysis

14 April 1946

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1019356

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SUMMARY OF PROJECTS COMPLETED UNDER THE GENERAL SUBJECT OF METHODS FOR DETERMINING RADIUM, URANIUM, AND RADON.

1. Subject of Report: The Determination of Nitrogen Oxides in Air.

   Findings: Nitrogen oxides in concentrations ranging from 1 to 50 ppm. in air may be determined quantitatively by drawing the air sample through a silica gel absorbent, developing a color on the silica gel with diphenylamine sulfonic acid, and comparing with standards.

2. Subject of Report: Determination of Uranium with Isatin Oxime.

   Findings: The macro and semimicro gravimetric determination of uranium is satisfactory, using isatin oxime, in solutions containing alkali metals or alkaline earths as foreign substances. Most other ions interfere. The reagent is not suited for the colorimetric determination of uranium.

3. Subject of Report: Analysis of Ore - Cooperative Study.

   Findings: Radium was determined in ores and ore concentrates in cooperation with the National Bureau of Standards. Our analyses were used in helping establish a standard radium content for the various materials.

4. Subject of Report: Coprecipitation of Radium Sulfate with Lead Sulfate.

   Findings: Radium sulfate is more or less completely coprecipitated by lead sulfate. Coprecipitation is favored by a high ratio of lead to radium; also by a low concentration of sulfuric acid. Radium is precipitated to approximately the same degree as lead under a given set of conditions.

5. Subject of Report: Chromatographic Analysis.

   Findings: Uranium is separated from other elements on an aluminum oxide absorbent by the chromatographic technique. The bands are indistinct, and do not permit a quantitative separation to be made. Quantities of uranium from 50 micrograms upwards may be identified by this technique.

6. Subject of Report: Semimicro Volumetric Determination of Uranium.

   Findings: Uranium may be determined volumetrically by precipitating with 8-hydroxyquinoline, dissolving the precipitate after filtration and washing, and titrating with potassium bromate. The method is most useful in the range 50 to 500micrograms of uranium.

7. Subject of Report: Determination of HF in Air.

   Findings: A rapid determination of HF in air may be made by drawing the air samples through a solution of ferric salicylate, and measuring the bleaching produced. The bleaching is standardized in terms of known fluoride samples. The method is rapid, and compares in accuracy with other methods that require greater time for completion.

2.7.46 Signed John F. Flagg

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PROJECT NO. 102

TO STUDY CERTAIN ORGANIC ANALYTICAL REAGENTS IN ORDER TO FIND REAGENTS WHICH MAY BE USED FOR THE DETECTION AND ESTIMATION OF T.

Current Result

The following reagents were tested.

A careful literature survey has been made to ascertain what organic reagents combine with uranium ions, and under what conditions. The results of this survey are embodied in Pharmacology Report M-1633 (February 1945).

From the many reagents reported to give reactions with uranium ions, those showing greatest promise of having value for the detection and (or) determination of that element have been selected for more detailed investigation. The results of studies on many of these reagents are contained in this report.

Of the reagents studied, none combines exclusively with uranium. For the colorimetric detection and determination of uranium, chromotropic acid and aluminon seem particularly useful, as these reagents show the greatest sensitivity for the element. Of the reagents that precipitate uranium quantitatively, for subsequent determination either by weighing or ignition of the complex, 8 - hydroxy quinoline seems unexcelled, although far from being an ideal reagent.

Personnel: E. Ware

District File: M-1633, M-1721, M-1769

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