RADIATION INACTIVATION OF HISTAMINE IN AQUEOUS SOLUTION AND IN PLASMA

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Nuclear Agency
Bethesda, Maryland

Approved for public release; distribution unlimited
All aspects of investigative programs involving the use of laboratory animals sponsored by DoD components are conducted according to the principles enunciated in the "Guide for Laboratory Animal Facilities and Care", prepared by the National Academy of Sciences - National Research Council.
RADIATION INACTIVATION OF HISTAMINE
IN AQUEOUS SOLUTION AND IN PLASMA

T. F. DOYLE
S. L. BRADLEY

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Nuclear Agency
Bethesda, Maryland

Approved for public release; distribution unlimited
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>ii</td>
</tr>
<tr>
<td>I. Introduction</td>
<td>1</td>
</tr>
<tr>
<td>II. Methods</td>
<td>1</td>
</tr>
<tr>
<td>III. Results</td>
<td>2</td>
</tr>
<tr>
<td>IV. Discussion</td>
<td>4</td>
</tr>
<tr>
<td>V. Conclusions</td>
<td>4</td>
</tr>
<tr>
<td>References</td>
<td>5</td>
</tr>
</tbody>
</table>

# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1.</td>
<td>Histamine inactivation in water and plasma solutions after mixed gamma-neutron irradiation</td>
<td>3</td>
</tr>
<tr>
<td>Figure 2.</td>
<td>Activity of aqueous histamine solutions after 17,300 rads of mixed gamma-neutron irradiation</td>
<td>3</td>
</tr>
</tbody>
</table>
ABSTRACT

Dilute solutions of histamine in water and plasma were given 140- to 38,000-rad doses of pulsed mixed gamma-neutron radiation. Histamine activity of the solutions was bioassayed using guinea pig ileum. Inactivation of the histamine in water was apparent at doses of 2000 rads or more; 1.5 μg/ml of histamine in water were completely inactivated by 17,300 rads, 3.0 μg/ml required 33,000 rads. Different concentrations of histamine (1.5 to 2.7 μg/ml) receiving the same dose of radiation (17,300 rads) clearly showed an inverse relation between concentration and inactivation. Histamine in plasma showed less than 10 percent inactivation even at the highest dose used, 38,000 rads.
I. INTRODUCTION

The hemodynamic changes experienced by irradiated animals may be attributed in part to the release of histamine.\textsuperscript{3, 6} There is some indication in monkeys, however, that early postirradiation hypotension becomes less pronounced as the dose is increased to very high values (20,000 to 30,000 rads). Some of the possible explanations for this lessened effect are: (1) the labile, nonmast cell histamine is inactivated directly or indirectly by ionizing radiation; (2) histamine receptor sites are markedly altered; and (3) other vasoactive substances are released (or their synthesis induced) which counteract the effects of histamine.

The objective of this experiment was to determine \textit{in vitro} if pulsed mixed gamma-neutron radiation could inactivate histamine to an extent that the less pronounced hemodynamic effects observed in monkeys following very high doses of radiation might be explained.

II. METHODS

Histamine dihydrochloride* concentrations of 1.5 to 3.0 $\mu$g/ml (as the base) in distilled pyrogen-free water or in pig plasma were given 140 to 38,000 rads of mixed gamma-neutron radiation (incident neutron to gamma ratio of 0.4) from the AFRRI-TRIGA reactor in a single pulse of short duration (pulse width at half maximum approximately 25 milliseconds).

The solutions were irradiated in stoppered glass test tubes but were not deaerated. The possibility of the glass adsorbing histamine was tested\textsuperscript{2} and no measurable

\* Fisher Scientific Company, Fair Lawn, New Jersey
adsorption was found; however, to preclude the occurrence of this possible error nonirradiated standards were handled the same as irradiated samples.

Histamine was bioassayed by the method described by Sturde and Heitmann. A 2-cm terminal ileum segment from a male guinea pig was suspended in a bath of oxygenated Tyrode's solution at 37°C. The histamine containing solutions were applied to the ileum segment and resulting contractions were measured by a linear motion transducer* and recorded.†

The sensitivity of each ileum segment was established by recording the contraction intensity following application of 0.1 ml of histamine standard having the same concentration as originally contained in the irradiated solution to be measured. After a few seconds, the strip was washed with Tyrode's solution, 0.1 ml of the irradiated solution was applied, and the resulting contraction intensity recorded. Following measurement of the irradiated sample activity, the histamine standard was again applied to the ileum strip and the contraction recorded. The two responses from histamine standard were averaged and the contraction from the irradiated sample was then expressed as a percentage of the calculated average. Each data point on Figures 1 and 2 represents the mean value of at least three such comparisons of irradiated sample to standard except where no error bar is shown.

III. RESULTS

Aqueous solutions of histamine in concentrations of 1.5 to 3.0 μg/ml were inactivated by mixed gamma-neutron irradiation. Inactivation became apparent at

---

* Phipps and Bird, Inc., Richmond, Virginia
† Oscillo-riter, Texas Instruments Company, Houston, Texas
about 2000 rads; the 1.5 μg/ml solution was completely inactivated by 17,300 rads, and the 3.0 μg/ml solution by 33,000 rads (Figure 1).

Histamine concentrations of 1.5, 1.8, 2.1, 2.4 and 2.7 μg/ml in water receiving 17,300 rads clearly showed an inverse relationship between concentration and inactivation (Figure 2).

Figure 1. Histamine inactivation in water and plasma solutions after mixed gamma-neutron irradiation

Figure 2. Activity of aqueous histamine solutions after 17,300 rads of mixed gamma-neutron irradiation
Histamine in plasma solution showed less than 10 percent inactivation even at the highest dose used, 38,000 rads.

IV. DISCUSSION

Sturde and Heitmann found that dried or frozen histamine was insensitive to inactivation by irradiation and concluded that the inactivation of histamine in aqueous solution was due to endogenously formed, radiation-derived hydroxyl radicals.

Since the aqueous solutions used in this study were very dilute, the primary effect of the absorbed energy was decomposition of water in a radical yielding process

\[ \text{HOH} \rightarrow \text{H}^* + \text{OH}^* \]

and to a lesser extent to the forward or molecular process

\[ 2 \text{HOH} \rightarrow 2\text{H}^* + \text{H}_2\text{O}_2 . \]

Generally the radicals and molecules formed react preferentially with organic substrate, in this instance, histamine. Histamine inactivation reflected the concentration of free radicals which increased as the dose of ionizing radiation was increased.

The concentration of other organic solutes in plasma far exceeds that of histamine and since the rate of reaction is a function of concentration, the histamine remained relatively unaffected.

V. CONCLUSIONS

Although it is evident by this and other studies that histamine in dilute aqueous solutions is inactivated by ionizing radiation, the lack of inactivation in plasma solutions weakens any conclusion that might be drawn concerning histamine inactivation in vivo playing a role in hemodynamic effects from very high doses of radiation.
REFERENCES


DISTRIBUTION LIST

AIR FORCE

Executive Officer, Director of Professional Services, Office of the Surgeon General, USAF (AFMSM) T-8, Washington, D. C. 20333 (1)
Headquarters, USAF (AFMSPAB), Washington, D. C. 20333 (1)
Chief, Weapons and Weapons Effects Division, HQ, RTD (RTTW), Bolling AFB, Washington, D. C. 20332 (1)
Office of the Command Surgeon (ADC5G), HQ ADC, USAF, Ent AFB, Colorado 80912 (1)
Commander, 6571st Aeromedical Research Laboratory, Holloman AFB, New Mexico 88330 (2)
Air Force Weapons Laboratory, ATTN: WRLD-2 (1), Kirtland AFB, New Mexico 87117 (2)
Chief, Nuclear Medicine Department, P. O. Box 5088, USAF Hospital, Wright-Patterson AFB, Ohio 45433 (1)
USAFSAM (SMBR), ATTN: Chief, Radiobiology Branch, Brooks AFB, Texas 78235 (1)

ARMY

The Surgeon General, U. S. Department of the Army, Washington, D. C. 20315 (1)
USACDC CSSG, Doctrine Division, Fort Lee, Virginia 23801 (1)
Commanding Officer, USAACDC CB Agency, Fort McClellan, Alabama 36201 (1)
Commanding Officer, U. S. Army Combat Developments Command, Institute of Nuclear Studies, Fort Bliss, Texas 79316 (1)
CG, USCONARC, ATTN: ATUTR-TNG (NBC), Fort Monroe, Virginia 23351 (1)
Commanding Officer, U. S. Army Medical Research Laboratory, Fort Knox, Kentucky 40121 (1)
Commanding Officer, USA  Nuclear Medical Research Detachment, Europe, APO New York, N. Y. 09180 (2)
Chief of Research and Development, ATTN: Nuclear, Chemical and Biological Division, U. S. Department of the Army, Washington, D. C. 20310 (1)
Army Research Office, ATTN: Chief, Scientific Analysis Branch, Life Sciences Division, 3045 Columbia Pike, Arlington, Virginia 22204 (1)
Division of Nuclear Medicine, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. 20011 (5)
Commanding Officer, U. S. Army Environmental Hygiene Agency, ATTN: USAEHA-RP, Edgewood Arsenal, Maryland 21010 (1)
Commandant, U. S. Army Medical Field Service School, ATTN: MEDEW-ZNW, Fort Sam Houston, Texas 78234 (1)

NAVY

Chief, Bureau of Medicine and Surgery, U. S. Navy Department, Washington, D. C. 20390 (1)
Commanding Officer, Naval Aerospace Medical Institute, Naval Aviation Medical Center, ATTN: Director of Research, Pensacola, Florida 32512 (3)
Commanding Officer, Nuclear Weapons Training Center, Atlantic, Nuclear Warfare Department, Norfolk, Virginia 23511 (1)
Commanding Officer, Nuclear Weapons Training Center, Pacific, U. S. Naval Air Station, North Point, San Diego, California 92135 (1)
Director, Biological Sciences Division, Office of Naval Research, Washington, D. C. 20360 (1)
Commanding Officer, U. S. Naval Hospital, ATTN: Director, REEL, National Naval Medical Center, Bethesda, Maryland 20014 (1)
Head, Animal Behavioral Sciences Branch, Naval Aerospace Medical Institute, Naval Aviation Medical Center, ATTN: Dr. John S. Thach, Jr., Pensacola, Florida 32512 (1)
Commanding Officer, Naval Submarine Medical Center, Naval Submarine Base, NJ, ATTN: Medical Library, Groton, Connecticut 06340 (1)
Commanding Officer, Naval Submarine Medical Center, Naval Submarine Base, NJ, ATTN: Code 53, Nuclear Medicine Training Division, Groton, Connecticut 06340 (1)

D. O. D.

Director, Defense Atomic Support Agency, Washington, D. C. 20305 (1)
Director, Defense Atomic Support Agency, ATTN: DDBT, Washington, D. C. 20305 (1)
Director, Defense Atomic Support Agency, ATTN: Chief, Medical Directorate, Washington, D. C. 20305 (4)
Director, Defense Atomic Support Agency, ATTN: Chief, Radiation Directorate, Washington, D. C. 20305 (1)
D. O. D. (continued)

Commanding Officer, Harry Diamond Laboratories, ATTN: Nuclear Vulnerability Branch, Washington, D. C. 20438 (1)
Commander, Field Command, Defense Atomic Support Agency, ATTN: FC Technical Library, Sandia Base, Albuquerque, New Mexico 87115 (1)
Commander, Headquarters Field Command, Defense Atomic Support Agency, ATTN: FCTG8, Sandia Base, Albuquerque, New Mexico 87115 (2)
Director, Armed Forces Institute of Pathology, Washington, D. C. 20305 (1)
Administrator, Defense Documentation Center, Cameron Station, Bldg. 5, Alexandria, Virginia 22314 (20)

OTHER GOVERNMENT

U. S. Atomic Energy Commission, Headquarters Library, Reports Section, Mail Station G-17, Washington, D. C. 20545 (1)
U. S. Atomic Energy Commission, Division of Biology and Medicine, Washington, D. C. 20545 (1)
U. S. Atomic Energy Commission, Bethesda Technical Library, 7920 Norfolk Avenue, Bethesda, Maryland 20014 (1)
National Aeronautics and Space Administration, ATTN: Lt. Col. Charles M. Barnes, USAF, DB-3, MSC, Houston, Texas 77058 (1)
National Aeronautics and Space Administration, Manned Spacecraft Center, ATTN: Dr. B. D. Newsom, Mail Code DA, Houston, Texas 77058 (1)
National Bureau of Standards, ATTN: Chief, Radiation Physics Division, Washington, D. C. 20234 (1)
U. S. Public Health Service, Bureau of Radiological Health, Division of Biological Effects, 12720 Twinbrook Parkway, Rockville, Maryland 20852 (1)
U. S. Public Health Service, Bureau of Radiological Health, Library, 12720 Twinbrook Parkway, Rockville, Maryland 20852 (1)
U. S. Public Health Service, Northeastern Radiological Health Laboratory, 109 Holton Street, Winchester, Massachusetts 01890 (1)
U. S. Public Health Service, Southeastern Radiological Health Laboratory, P. O. Box 61, Montgomery, Alabama 36103 (1)
U. S. Public Health Service, Southwestern Radiological Health Laboratory, P. O. Box 15027, Las Vegas, Nevada 89114 (1)

OTHER

Argonne National Laboratory, Library Services Department, Report Section Bldg. 203, RM-CE-125, 9700 South Cass Avenue, Argonne, Illinois 60440 (1)
Dr. Donald G. Baker, Radiobiology Department, Zellerbach Saroni Tumor Institute, 1600 Divisadero Street, San Francisco, California 94115 (1)
Dr. J. T. Brennan, Radiology Department, University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 (1)
Brookhaven National Laboratory, Information Division, ATTN: Research Library, Upton, Long Island, New York 11973 (2)
Dr. J. S. Burkle, Director of Nuclear Medicine, York Hospital, York, Pennsylvania 17403 (1)
S. C. Bushong, Department of Radiology, Baylor University College of Medicine, Houston, Texas 77024 (1)
University of California, Lawrence Radiation Laboratory, Library, Bldg. 50, Room 134, Berkeley, California 94720 (1)
Director, Radiobiology Laboratory, University of California, Davis, California 95616 (1)
University of California, Laboratory of Nuclear Medicine and Radiation Biology, Technical Information Division Library L-3, P. O. Box 808, Livermore, California 94551 (2)
University of California, Laboratory of Nuclear Medicine and Radiation Biology, Library, 900 Veteran Avenue, Los Angeles, California 90024 (1)
Dr. C. Jelleff Carr, Director, Life Sciences Research Office, Federation of American Societies for Experimental Biology, 9550 Rockville Pike, Bethesda, Maryland 20014 (1)
Cdr. William H. Chapman, USN (Ret.), Bio-Medical Division L-523, Lawrence Radiation Laboratory, University of California, P. O. Box 808, Livermore, California 94551 (1)
Director, Collaborative Radiological Health Laboratory, Colorado State University, Fort Collins, Colorado 80521 (1)
Dr. L. W. Davis, Radiology Department, University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104 (1)
Professor Merrill Eisenbud, New York University, Tuxedo, New York 10987 (1)
Dr. T. C. Evans, Radiation Research Laboratory, College of Medicine, University of Iowa, Iowa City, Iowa 52240 (1)
OTHER (continued)

Dr. Arnold Feldman, Institute of Radiology, School of Medicine, Washington University, 510 South Kingshighway, St. Louis, Missouri 63110 (1)

Mr. Orin Gelderloos, Division of Literature, University of Michigan, Dearborn Campus, Dearborn, Michigan 48124 (1)

General Dynamics/Fort Worth, ATTN: Librarian, P. O. Box 748, Fort Worth, Texas 76101 (1)

Gulf General Atomic Incorporated, ATTN: Library, P. O. Box 608, San Diego, California 92112 (1)

Dr. James E. Huff, Department of Pharmacology and Toxicology, School of Medicine and Dentistry, University of Rochester, 260 Crittenden Blvd., Rochester, New York 14620 (1)

IIT Research Institute, ATTN: Document Library, 10 West 35th Street, Chicago, Illinois 60616 (1)

Johns Hopkins University, Applied Physics Laboratory, ATTN: Document Library, 8621 Georgia Avenue, Silver Spring, Maryland 20910 (1)

Dr. R. F. Kallman, Department of Radiology, Stanford University, Palo Alto, California 94305 (1)

Dr. L. S. Kelly, Donner Laboratory, University of California at Berkeley, Berkeley, California 94720 (1)

Dr. Robert Landolt, Bionucleonics Department, Purdue University, Lafayette, Indiana 47907 (1)

Los Alamos Scientific Laboratory, ATTN: Report Librarian, P. O. Box 1663, Los Alamos, New Mexico 87544 (1)

Director, Nuclear Science Center, Louisiana State University, Baton Rouge, Louisiana 70803 (2)

Lovelace Foundation for Medical Education and Research, Document Library, 5200 Gibson Blvd., S. E., Albuquerque, New Mexico 87108 (1)

Dr. Ross A. McFarland, Guggenheim Professor of Aerospace Health and Safety, Harvard School of Public Health, 665 Huntington Avenue, Boston, Massachusetts 02115 (1)

Dr. J. I. Marcum, Rand Corporation, 1700 Main Street, Santa Monica, California 90401 (1)

Massachusetts Institute of Technology, M.I.T. Libraries, Technical Reports, Room 14 E-210, Cambridge, Massachusetts 02139 (1)

Dr. Charles W. Mays, Physics Group Leader, Radiobiology Division, University of Utah, Salt Lake City, Utah 84112 (1)

Ohio State University, Nuclear Reactor Laboratory, 1298 Kinnear Road, Columbus, Ohio 43212 (1)

Dr. Harvey M. Patt, Laboratory of Radiobiology, University of California, San Francisco Medical Center, San Francisco, California 94122 (1)

Purdue University, Nuclear Engineering Library, Lafayette, Indiana 47907 (1)

Dr. S. M. Reichard, Director, Division of Radiobiology, Medical College of Georgia, Augusta, Georgia 30902 (1)

Dr. H. H. Rossi, 630 West 168th Street, New York, N. Y. 10032 (1)

Dr. Eugene L. Saenger, Director, Radiisotope Laboratory, Cincinnati General Hospital, Cincinnati, Ohio 45229 (1)

Sandia Corporation Library, P. O. Box 5800, Albuquerque, New Mexico 87115 (1)

Scientific Committee on the Effects of Atomic Radiation, ATTN: Library, United Nations Room 3267, United Nations Plaza, New York, N. Y. 10017 (1)

Scope Publications, Franklin Station, P. O. Box 7407, Washington, D. C. 20004 (1)

Dr. Arthur R. Tamplin, Biophysicist, Information Integration Group, University of California, Lawrence Radiation Laboratory, L-012, Livermore, California 94550 (1)

Texas A and M University, Radiation Biology Laboratory, Texas Engineering Experiment Station, College Station, Texas 77840 (2)

Texas Nuclear Corporation, ATTN: Director of Research, Box 9207 Allandale Station, Austin, Texas 78756 (1)

University of Rochester, Atomic Energy Project Library, P. O. Box 287, Station 3, Rochester, New York 14620 (1)

University of Southern California, Nuclear Physics Laboratory, University Park, Los Angeles, California 90007 (1)

Western Reserve University, Department of Radiology, Division of Radiation Biology, Cleveland, Ohio 44106 (1)

Mr. Lionel Zamore, 601 Brightwater Court, Brooklyn, New York 11235 (1)

FOREIGN

International Atomic Energy Agency, Kärntnerring 11, Vienna I. 1010, Austria (1)

European Atomic Energy Community, C. E. E. A., Library, 51 rue Belliard, Brussels 4, Belgium (1)

Dr. L. G. Lajtha, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester, England (1)

Dr. L. F. Lamerton, Biophysics Department, Institute of Cancer Research, Surrey Branch, Belmont, Sutton, Surrey, England (1)

National Lending Library for Science and Technology, Boston Spa, Yorkshire, England (1)

Directorate of Medical and Health Services, FAF (Federal Armed Forces), Bonn, Ermekellstrasse 27, West Germany (1)

Abteilung für Strahlenbiologie im Institut für Biophysik der Universität Bonn, 53 Bonn-Venusberg, Annaberger Weg 15, Federal Republic of Germany (2)

Prof. Dr. H. Langendorff, Direktor des Radiologischen Instituts der Universität, 78 Freiburg im Breisgau, Albertstrasse 23, Germany (1)
FOREIGN (continued)

Priv.-Doz. Dr. O. Messerschmidt, Radiologisches Institut der Universität, 78 Freiburg im Breisgau, Albertstrasse 23, Germany (1)
Dr. Helmut Mitschrich, Akademie des Sanitäts- und Gesundheitswesens der Bundeswehr, Spezialstab ATV, 8 München, Schwere Reiterstrasse 4, Germany (2)
Prof. Dr. F. Wachsmann, Gesellschaft für Strahlenforschung m.b.H., 8042 Neuherberg bei München, Institut für Strahlenschutz, Ingolstädter Landstrasse 1, München, Germany (1)
Dr. M. Feldman, Section of Cell Biology, The Weizmann Institute of Science, Rehovoth, Israel (1)
Dr. G. W. Barendsen, Radiobiological Institute TNO, Rijswijk, Netherlands (1)
Dr. L. M. van Putten, Radiobiological Institute TNO, 151 Lance Kleiweg, Rijswijk 2 H, Netherlands (1)
Puerto Rico Nuclear Center, ATTN: Reading Room, College Station, Mayaguez, Puerto Rico 00708 (2)
Dr. H. Cottier, Pathological Institut der Universität, Bern, Switzerland (1)
Dilute solutions of histamine in water and plasma were given 140- to 38,000-rad doses of pulsed mixed gamma-neutron radiation. Histamine activity of the solutions was bioassayed using guinea pig ileum. Inactivation of the histamine in water was apparent at doses of 2000 rads or more; 1.5 µg/ml of histamine in water were completely inactivated by 17,300 rads, 3.0 µg/ml required 33,000 rads. Different concentrations of histamine (1.5 to 2.7 µg/ml) receiving the same dose of radiation (17,300 rads) clearly showed an inverse relation between concentration and inactivation. Histamine in plasma showed less than 10 percent inactivation even at the highest dose used, 38,000 rads.