

UNCLASSIFIED

AD NUMBER	
AD061556	
CLASSIFICATION CHANGES	
TO:	UNCLASSIFIED
FROM:	CONFIDENTIAL
LIMITATION CHANGES	
TO: Approved for public release; distribution is unlimited.	
FROM: Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; MAR 1955. Other requests shall be referred to Army Chemical Corps, Army Chemical Center, Medical Laboratory, Aberdeen Proving Ground, MD 21005.	
AUTHORITY	
csl, d/a ltr, 16 mar 1981; csl, d/a ltr, 16 mar 1981	

THIS PAGE IS UNCLASSIFIED

AD- 061556

SECURITY REMARKING REQUIREMENTS

DOD 5200.1-R, DEC 78

REVIEW ON 28 MAR 75

THIS REPORT HAS BEEN DELIMITED
AND CLEARED FOR PUBLIC RELEASE
UNDER DOD DIRECTIVE 5200.20 AND
NO RESTRICTIONS ARE IMPOSED UPON
ITS USE AND DISCLOSURE.

DISTRIBUTION STATEMENT A

APPROVED FOR PUBLIC RELEASE;
DISTRIBUTION UNLIMITED.

UNCLASSIFIED

AD

61556

CLASSIFICATION CHANGED
TO: UNCLASSIFIED
FROM CONFIDENTIAL
AUTHORITY:

- CSL, DA
- Ltr, 16 MAR 81



UNCLASSIFIED

FC

CHEMICAL CORPS MEDICAL LABORATORIES RESEARCH REPORT

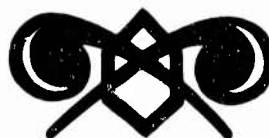
61556

• MLRR No. 350

MUSTARD, LEWISITE, AND PHOSGENE OXIME BURNS ON
THE DEPILATED SKIN OF A HEIFER TO DETERMINE
THE ANIMAL'S VESICATING POTENTIAL

by

J. M. Maas, Captain, M.C.
A. J. McAdams, Captain, M.C.
W. P. McShane



March 1955

Not for Publication

This report, nor any portion thereof, may not be reproduced,
without permission of the Chemical Corps Medical Laboratories.

ARMY CHEMICAL CENTER, MARYLAND

ML 2-79-(55)

CHEMICAL CORPS
MEDICAL LABORATORIES
ARMY CHEMICAL CENTER
MARYLAND

CMLRE-ML-52

Medical Laboratories Research Report No. 350

MUSTARD, LEWISITE, AND PHOSGENE OXIME BURNS ON THE DEPILATED SKIN
OF A HEIFER TO DETERMINE THE ANIMAL'S VESICATING POTENTIAL

by

J. M. Maas, Capt., M.C.
A. J. McAdams, Capt., M.C.
W. P. McShane

March 1955

Publication Control No. 5030-350

ML 2-79-(55)

Medical Laboratories Research Report No. 350

Mustard, Lewisite, and Phosgene Oxime Burns on the Depilated Skin
of a Heifer to Determine the Animal's Vesicating Potential

ABSTRACT

Predictable vesication does not occur in the bovine species following exposure to mustard, lewisite, and phosgene oxime.

Lesions resulting from lewisite are more severe and heal more slowly than mustard lesions in the bovine species.

Medical Laboratories Research Report No. 350

Mustard, Lewisite, and Phosgene Oxime Burns on the Depilated Skin
of a Heifer to Determine the Animal's Vesicating Potential

I. INTRODUCTION.

A. Object.

To determine the vesicating potential of the depilated skin
of the heifer.

B. Authority.

Authorized by the Chief Chemical Officer under Cml C Project
No. 4-59-12-007, Clinical Investigation and Treatment of CW Casualties
in Man, Cml C Research and Development Program for fiscal year 1954.

II. HISTORICAL.

Extensive investigations (1-14) to determine the vesicating pro-
ducing potential of vesicants on various species of animals indicate the
condition cannot be precisely duplicated in the manner observed in human
subjects. Pseudo-vesication manifesting itself as a somewhat greater
accumulation of fluid in the corium has been observed in the skin of the
bird and frog following exposure to a vesicant. Lactating bitches ex-
posed to vesicants developed blisters on and in the area immediately ad-
jacent to the teats. Very young (suckling) pigs demonstrate lesions
superficially resembling vesication in man when mustard or lewisite is
applied percutaneously. The inferences are clear, however, that in many
of the experiments reported in the literature, predictable responses
proved to be the rare exception. Furthermore, the pseudo-vesication ob-
served in frogs and birds differs sufficiently from true vesication noted
in human subjects, so that such animals cannot be utilized for certain
definitive test projects where precisely comparable pathological condi-
tions should exist.

III. EXPERIMENTAL.

A. Methods and Materials.

To the best of our knowledge, the bovine species has hereto-
fore not been investigated for vesicant-producing potentiality following
exposure to mustard or lewisite. As a prelude to a project to select
the most desirable test animal for use in screening certain new decon-
taminants and protective agents against established preparations, it was
speculated that a young calf might be ideal for the purpose. This con-
sideration was based on the premise that heifers and all cloven-footed
animals exhibit typical vesication in the development of cowpox lesions.

A study was therefore proposed to apply mustard, lewisite, and phosgene oxime in liquid and vapor states to the depilated skin of a heifer to determine whether vesication would occur.

Two test sites were decided upon to permit application of the vesicants in vapor and liquid form. The Edgewood Vapor Cup developed at these laboratories was selected for application of the three agents in gaseous states. Simple cotton-tipped orange-stick swabs were decided upon to apply each agent in its liquid form.

A Holstein heifer approximately six months old was used for the experiment. Three days before the test application, the ventral surface of the abdomen just anterior to the udder was bilaterally depilated with strontium sulfate. This procedure provoked cutaneous irritation characterized by erythema, and, subsequently, pin-point areas of bleeding. Photographs 1 and 2 depict the test sites 72 hours post depilation. It is possible that the irritated areas may have been increasingly susceptible to the subsequent action of the vesicants.

Laboratory "pure" sulfur mustard, lewisite, and phosgene oxime were procured from Cal C Chemical & Radiological Laboratories. Orange sticks tipped with a minute amount of cotton were dipped in the individual solutions, and excesses carefully removed by gentle pressure. Vapor cups were prepared by applying one drop of solution to blotter paper affixed in the base of the cup.

B. Results.

The test was instituted at 1000 hours, 24 August 1953. Atmospheric conditions prevailing were: Temperature, 74°F.; relative humidity, 65%. The animal was roped, thrown, and then constrained. The right abdomen was tested initially. Lewisite (98.3%) was applied to the skin by swab and permitted to remain in place one minute. Phosgene oxime (70%) was then similarly applied to a site approximately 5 inches caudad and laterally. Finally, a swab containing mustard (95%) was placed in contact with the denuded skin, approximately 6 inches caudad and laterally to the phosgene oxime site.

A vapor cup containing lewisite was placed on a pre-selected point of the denuded test area on the left abdominal wall. Air currents within the cup were induced by means of rotating a paper "fan" attached to an orange stick protruding from the hollow stem of the cup. Phosgene oxime and mustard applications were carried out in a similar manner with each test site located approximately 5 inches caudad and lateral to the previously tested area. In each instance the vapor cup was kept in place for a five minute period. The application of phosgene oxime apparently was accompanied by extreme discomfort inasmuch as the animal bellowed lustily when this agent was applied.

Photographs 3 (right) and 4 (left) taken one hour after completion of the applications are not revealing. The cup margins of the

lewisite exposure (photograph 4) are demarcated by a pale halo. Other exposed areas are not readily discernible. Six hours after exposure, the lewisite lesion on the right revealed a pustular area 3 cm. in diameter. An area of edema 10 by 30 cm. radiated outward from the core of the lesion. The phosgene oxime wound was circumscribed, white, 3 cm. in diameter, with slight erythema extending beyond. The mustard lesion was characterized by a slightly erythematous area 4 to 5 cm. in diameter. The lesions on the left side were essentially similar to those on the right with the exception that the cup edges on the lewisite lesion were demarcated by a pale ring (photograph 4) and the edematous area was somewhat smaller (8 by 25 cm.). Daily observations were made and recorded. To avoid needless repetition, only those pertinent changes appearing chronologically will be described. Dates of individual observations will show number of days elapsed since exposure.

25 August 1953 - 24 hours post exposure

1. Right Side.

a. Lewisite: The general area of the test has an appearance of marked subcutaneous edema. In an area which corresponds to the limits of the swab used to apply the agent, the skin has a yellowish-gray appearance representing coagulation necrosis. The area just described is surrounded to a distance of 2 cm. by a reddish-purple discoloration believed to be hemorrhagic congestion. It seems at this point that the agent has spread to and involves the erythematous area of depilation where there is evidence of irregular, dark brownish-purple discoloration.

b. Phosgene oxime: The involved area corresponds in size to the original test site. There is a dark yellowish-brown discoloration probably representing necrosis. No other obvious reaction apparent.

c. Mustard: The lesion is grey in color and corresponds in size to the initial test area of the swab site. Extending slightly beyond the wound is an irregular, marginal erythema, purple in color.

2. Left Side.

a. Lewisite: The cup margin is clearly demarcated by a pale rim of necrotic tissue. The inner area of the cup site further shows hemorrhagic discoloration without slough. A similar area of discoloration surrounds the primary lesion for a distance of 6 cm. The extensive subcutaneous edema present 6 hours after the exposure, persists and involves the phosgene oxime lesion as well.

b. Phosgene oxime: The lesion is purplish-black and corresponds to the size of the cup used to produce it. Obvious breakdown of tissue is not apparent.

c. Mustard: The lesion is represented only as an erythematous area corresponding to the size of the vapor cup. There is no evidence of subcutaneous edema.

3. Photographs.

a. Right Side, no. 5, 24 hours post exposure.

b. Left Side, no. 6, 24 hours post exposure.

4. Thirty hours post exposure. A large, pendulous sac, 8 by 10 cm. in diameter, and 8 cm. deep, is present in the midline of the abdomen. It is speculated that this sac represents edematous fluid having drained from the lesion sites, particularly from the lewisite areas.

26 August 1953 - 48 hours post exposure

1. Right Side.

a. Lewisite: The original area of necrosis is essentially as seen at 24 hours. At this point there are now irregular extensions of greyish discoloration which are believed to represent necrotic changes. The hemorrhagic erythema areas are darker and browner in color; and more firm in consistency. There appears to be somewhat less edema.

b. Phosgene oxime: The lesion is unchanged in size but darker in color. It is firm in consistency.

c. Mustard: The mustard area is unchanged in size, but definitely browner in color, and with an increase in consistency. Localized edema, not previously present, is now evident.

2. Left Side.

a. Lewisite: The area maintains the same dimensions as previously described. The rim area of necrosis is somewhat more sharply demarcated. The hemorrhagic, necrotic area has taken on a deep brown color, but with some evidence of redness still remaining. Edema has subsided considerably and is less pronounced than on the right side.

b. Phosgene oxime: The area is the same in size as previously noted. The site has acquired a deep brown color.

c. Mustard: The area is unchanged in size. It is only barely distinguishable by a faint erythema.

3. Photographs.

a. Right Side, no. 7, 48 hours post exposure.

b. Left Side, no. 8, 46 hours post exposure.

4. Edema. The bulk of the edema of both areas has shifted to a midline position. Inherent weight and gravity predisposes to a midline sacculation.

27 August 1953 - 72 hours post exposure

1. Right Side.

a. Lewisite: The swab area shows in addition to the greyish-yellow coagulation site, certain areas of blotchy, brown discoloration. The margins of the central swab area are no longer as distinct as previously. The peripheral zone of the previous hemorrhagic erythema has become very dark reddish-brown in color. There is suggestive evidence of newly forming subcutaneous edema.

b. Phosgene oxime: This area has acquired a deep brown color. Its contour is slightly depressed and somewhat concave.

c. Mustard: The swab area is dark brown in color. Definite evidence of subcutaneous edema exists.

2. Left Side.

a. Lewisite: The rim area of coagulation necrosis shows slight brownish discoloration. The cuff area and border of the rim are almost black. There is no change in extent of edema.

b. Phosgene oxime: The area is somewhat darker in color but otherwise unchanged.

c. Mustard: The area can no longer be discerned.

3. Photographs.

a. Right Side, no. 9, 72 hours post exposure.

b. Left Side, no. 10, 72 hours post exposure.

4. Edema. Midline edema has abated to approximately 50% of that previously described.

28 August 1953 - 96 hours

1. Right Side.

a. Lewisite: The swab site is barely distinguishable. The entire area, including the marginal spread, has assumed a relatively uniform, very dark, reddish-brown color. Along the periphery there is evidence of separation which suggests a superficial slough. Edema in the immediate area is unchanged.

b. Phosgene oxime: The entire area is dark brown in color. The upper margin shows signs of separation indicating a superficial slough.

c. Mustard: The area is somewhat more brown in color than previously described. There is evidence of very early separation at the margins. The edema described earlier has abated somewhat.

2. Left Side.

a. Lewisite: The color previously discussed persists in an unchanged condition. Only a small portion of the lesion from the cup rim is discernible. The entire lesion has acquired a definite depressed character. There is evidence of superficial separation at the margin. Edema is more pronounced.

b. Phosgene oxime: The area shows no change from the preceding day.

3. Photographs.

a. Right Side, no. 11, 96 hours post exposure.

b. Left Side, no. 12, 96 hours post exposure.

4. Edema. The edematous sacculation in the midline persists.

5. General Appearance. A slight but definite weight loss is visually perceptible. The discomfort the animal experiences probably precludes appetite, and/or feeding.

1 September 1953 - 8 days

1. Right Side.

a. Lewisite: The lesion is covered by a dirty gray eschar. Edema is subsiding.

b. Phosgene oxime: As for Lewisite.

c. Mustard: As for Lewisite.

2. Left Side.

a. Lewisite: As for lewisite on right side.

b. Phosgene oxime: As for lewisite.

3. Edema. No change in degree or character of midline edema.

3 September 1953 - 10 days

1. Right Side.

a. All lesions similar in appearance to previous description.

2. Left Side.

a. Lewisite: The surface appearance is unchanged. There is definite evidence of resuming edema represented by an area 8 cm. in diameter and 3 cm. thick.

b. Phosgene oxime: The area shows no change from that previously described.

8 September 1953 - 15 days

1. Right Side.

a. Lewisite: No change.

b. Phosgene oxime: The eschar became detached while palpating the wound. The underlying surface is clean, pink, and shows no points of bleeding.

c. Mustard: No change.

2. Left Side.

a. Lewisite: The edema persists.

b. Phosgene oxime: No change in the lesion.

11 September 1953 - 18 days

1. Right Side.

a. All lesions essentially static in character.

2. Left Side.

a. Lewisite: The edema appears to be subsiding. The eschar remains intact.

b. Phosgene oxime: The eschar previously present apparently became detached spontaneously. The base of the wound is clean, pink in color, not tender, and shows no points of bleeding.

21 September 1953 - 28 days

1. Right Side.

a. Lewisite: The eschar is firm, hard, dirty-gray in color. There is no further progression of the detaching process described earlier.

b. Mustard: The eschar remains intact.

2. Left Side.

a. Lewisite: As for right side.

7 October 1953 - 44 days

1. Right Side.

a. Lewisite: The eschar shows evidence of detaching spontaneously. Dark yellow-red purulent exudate exudes from the exposed wound edges.

b. Mustard: The eschar shows early signs of spontaneous detachment.

2. Left Side.

a. Lewisite: The eschar remains intact.

12 October 1953 - 49 days

1. Right Side.

a. Lewisite: The eschar has become detached spontaneously. The surface of the wound shows presence of deep brown, thick, purulent material. The ulcer wall is clearly demarcated. There is evidence of recent bleeding. The crater is estimated to be 3/8 inch deep.

b. Mustard: The eschar has become detached. The base of the underlying wound is pink, clean, not tender, and shows no recent points of bleeding.

2. Left Side.

a. Lewisite: The eschar remains intact.

13 October 1953 - 50 days

1. Right Side.

a. Lewisite: The purulent discharge is still present, but reduced in quantity.

15 October 1953 - 52 days

1. Right Side.

a. Lewisite: The purulent discharge is no longer present. The base of the wound is deep red in color.

2. Left Side.

a. Lewisite: No change from earlier description.

19 October 1953 - 56 days

1. Right Side.

a. Lewisite: The wound is approximately 1 1/8 inches in diameter and about 3/8 inch deep. The edges are well demarcated. The base is clean, and pink in color.

22 October 1953 - 59 days

1. Right Side.

a. Lewisite: A new eschar has formed. The new eschar is thin, about 1/4 inches in diameter and is dirty grey in color.

2. Left Side.

a. Lewisite: No change from previous description.

3 November 1953 - 71 days

1. Right Side.

a. Lewisite: The eschar has again spontaneously detached. The base of the wound is clean, pink in color, dry, and shows no points of bleeding.

2. Left Side.

a. Lewisite: The eschar shows early signs of detachment.

5 November 1953 - 73 days

1. Left Side.

a. Lewisite: The eschar remains attached at one corner only. The crater of the wound is approximately 2 inches in diameter, and 3/8 inch deep. The walls are clearly demarcated. Extensive, deep yellow-brown, thick purulent exudate is present together with a small quantity of almost black, residual blood. The area is not tender to palpation.

9 November 1953 - 77 days

1. Right Side.

a. Lewisite: The wound shows evidence of slow progressive healing. There is no indication of new eschar formation.

2. Left Side.

a. Lewisite: The eschar is completely detached. The area of the ulcer is somewhat smaller and shallower. Exudation is minimal. There is no evidence of new eschar formation.

12 November 1953 - 80 days

1. Right Side.

a. Lewisite: The lesion is completely healed.

2. Left Side.

a. Lewisite: The crater is replaced by granulation tissue. The area is slightly tender and bleeds readily. There is no evidence of exudate or new eschar formation.

16 November 1953 - 84 days

1. Left Side.

a. Lewisite: A thin eschar has again formed on the lesion. The lesion is approximately 1½ inches long, ¼ inch wide. The color is dirty gray.

23 November 1953 - 91 days

1. Left Side.

a. Lewisite: The eschar has become detached. The wound surface is pink, clean, and shows no points of bleeding.

27 November 1953 - 95 days

1. Right Side.

a. All test areas have acquired an appearance comparable to surrounding tissue.

2. Left Side.

a. As above.

IV. CONCLUSIONS.

1. Heifers do not predictably develop blisters following application of vesicants.
2. Lewisite was found to produce lesions of far greater severity and which healed far more slowly than mustard or phosgene oxime in at least this single test animal of the bovine species.
3. Application of phosgene oxime to the depilated skin of the test animal was accompanied by immediate intense pain.
4. Because of difficulty in handling, the bovine species is not an ideal animal to employ for test purposes such as this experiment consisted of.

V. BIBLIOGRAPHY.

1. Renshaw, Birdsey. 1946. Mechanisms in production of cutaneous injuries by sulfur and nitrogen mustards. OSRD. Summary Technical Report of Division 9, NDRC. 1(364): Chapter 23.
2. McMaster, P.D., G.H. Hogeboom, M.B. Sulzberger, R.L. Baer, and A. Kanof. 1945. The development of methods for testing the abilities of agents to combat the effects of mustard gas, H, and other vesicants upon skin. OSRD 4853. The Rockefeller Institute for Medical Research.
3. Geiling, E.M.K. 1942. Inf. Month. Prog. Reports on Toxicity of Chemical Warfare Agents (NDRC B4-A and 9:4:1) Div 9-125-M2, OSRD Inf. Rep., Contract NDCrc-132, Univ of Chicago Toxicity Lab., Report of 20 July.
4. Mirsky, A. 1942. Studies with Vesicant Agents, Contract OEMcmr-97-98. May Institute for Medical Research (Cincinnati), Div. 9-362-M1.
5. Barr, D.P. and M.B. Sulzberger. 1942. Contract OEMcmr-103, Report of 1 September. Cornell Medical College, Div. 9-500-M1.
6. U. S. Army Cml Warfare Service. 1939. Pathology of heat and mustard burns: a comparison. EATR 292.
7. U. S. Army Cml Warfare Service. 1942. The production of vesicles on the plantar surfaces of the feet of white rats. Development of a method for applying liquid chemical warfare agents and therapeutic treatment together with illustrations. W (EA) MR 48.
8. U. S. Army Cml Warfare Service. 1944. Med. Div. Inf. Month. Prog. Report, October.
9. U. S. Army Cml Warfare Service. 1943-1944. MRL (EA) Inf. Month. Prog. Reports. October, December 1943; April, May 1944.

10. U. S. Public Health Service. 1943. Toxic action of B₂B¹-Dichloroethyl Sulfide (Mustard Gas). National Cancer Institute Report (Carl Voegtlin), National Institute of Health, received by NDRC 30 August.

11. Dixon, M. and A. Wormald. British Reports, Extramural Research. Cambridge Biochemical Laboratory.

a. Danielli, J. F. and M. Danielli. 1941. Studies on the mechanism of blister formation. Dixon Report No. 8 (V. 10548) Chemical Board.

b. Danielli, J. F. and M. Danielli. 1941. The use of frogs in testing for vesicant activity. Dixon Report No. 9 (V. 17203).

12. W. 257. Compilation of Reports by Four Extramural Teams. Miscellaneous Extramural British Reports.

a. Fell, H.B., C.B. Allsopp, and J.F. Danielli. 1942. Provisional interim report on some physiological properties of S.

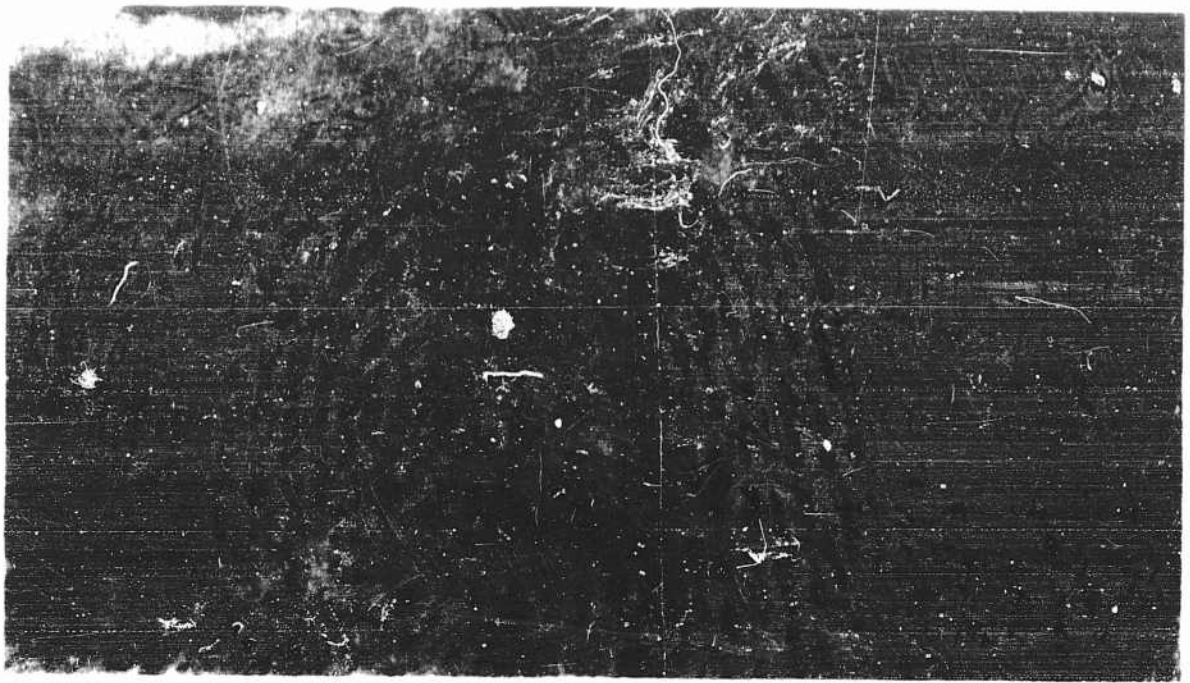
b. Needham, D.M., R. Hill, R. van Heymingen, J. Mackworth, J.F. Danielli, J. Morgan and M. Dixon. Preliminary Report on the Biochemical Effects of S.

c. Peters, R.A. 1942. Provisional Note Upon T. 1024.

d. Kilby, M. to L. T. D. Williams. 1942. Note on the toxicity of S, containing data in addition to those reported on 23 March and 28 March 1942.

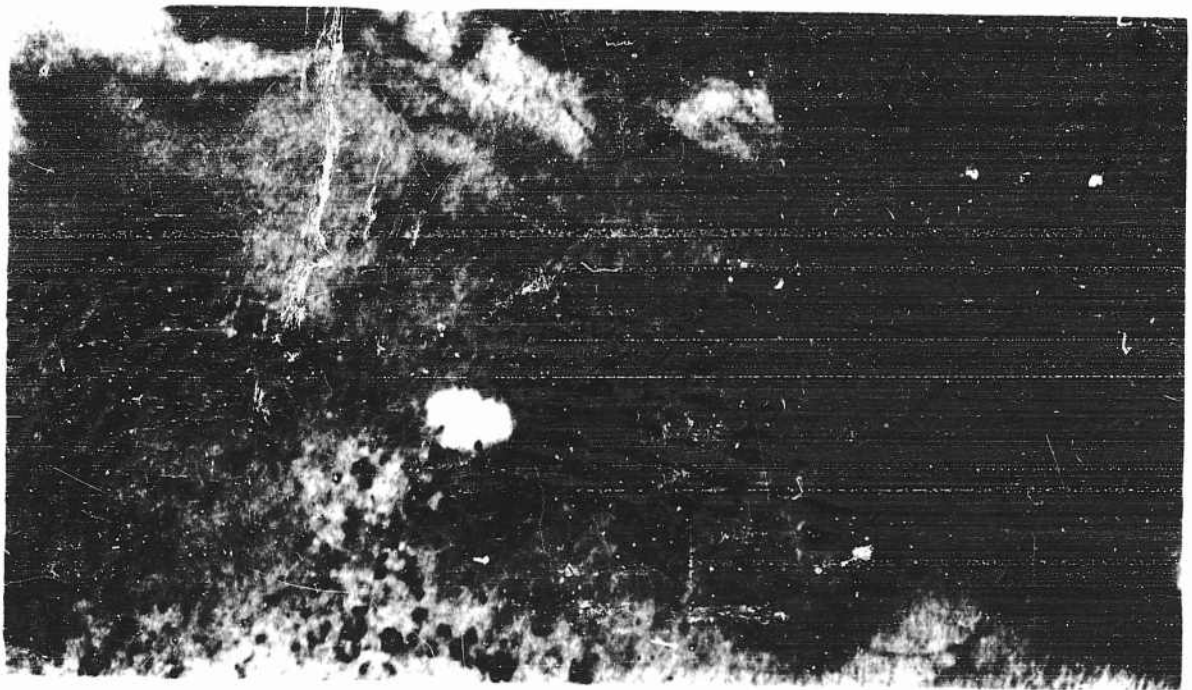
13. Goldschlag, S. 1942. Experiments on the improvement of the treatment of mustard gas lesions of the skin. Med. J. Australia. 1:620-622.

14. Mirsky, I.A. and L. Goldman. 1943. The production of bullae in the skin of the duck. Arch. Dermat. Syph. 48:161-163.



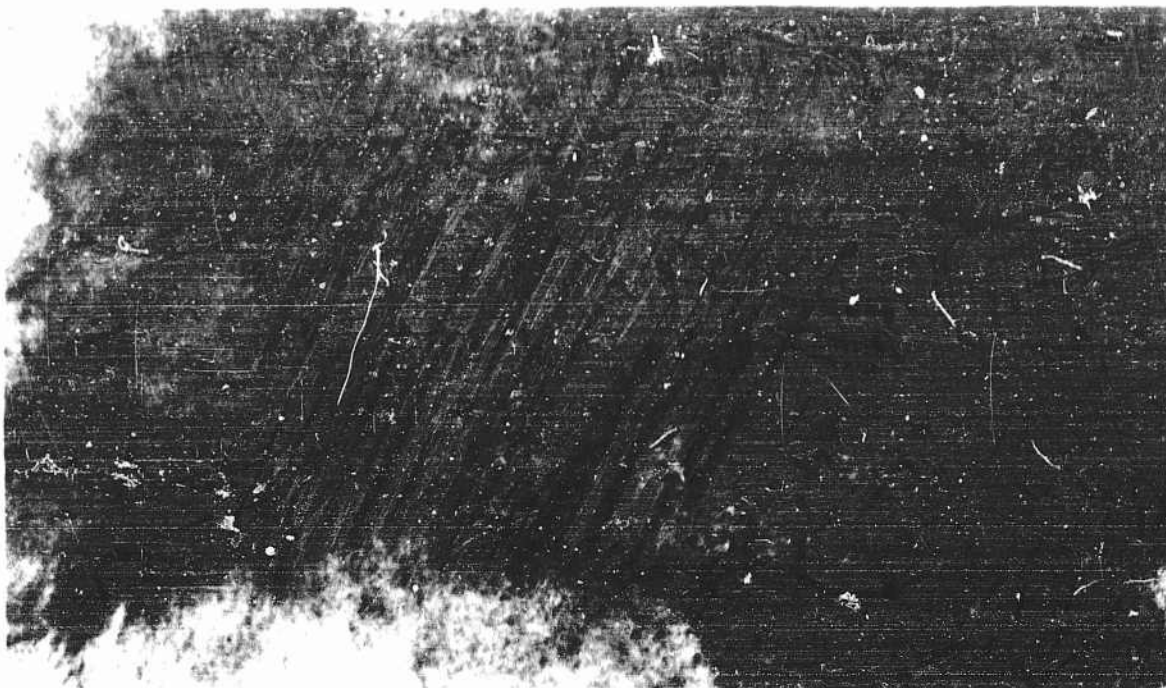
Photograph 1

Test site 72 hours post depilation.



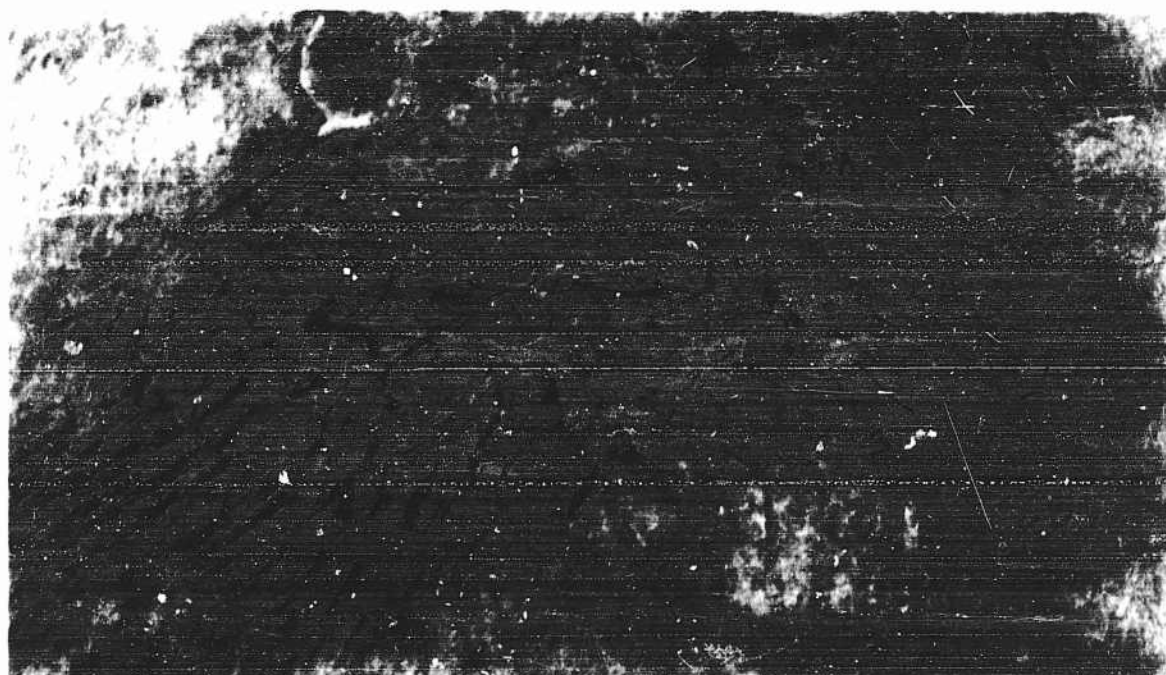
Photograph 2

Test site 72 hours post depilation.



Photograph 3

Right side, one hour post application of vesicant, not revealing.



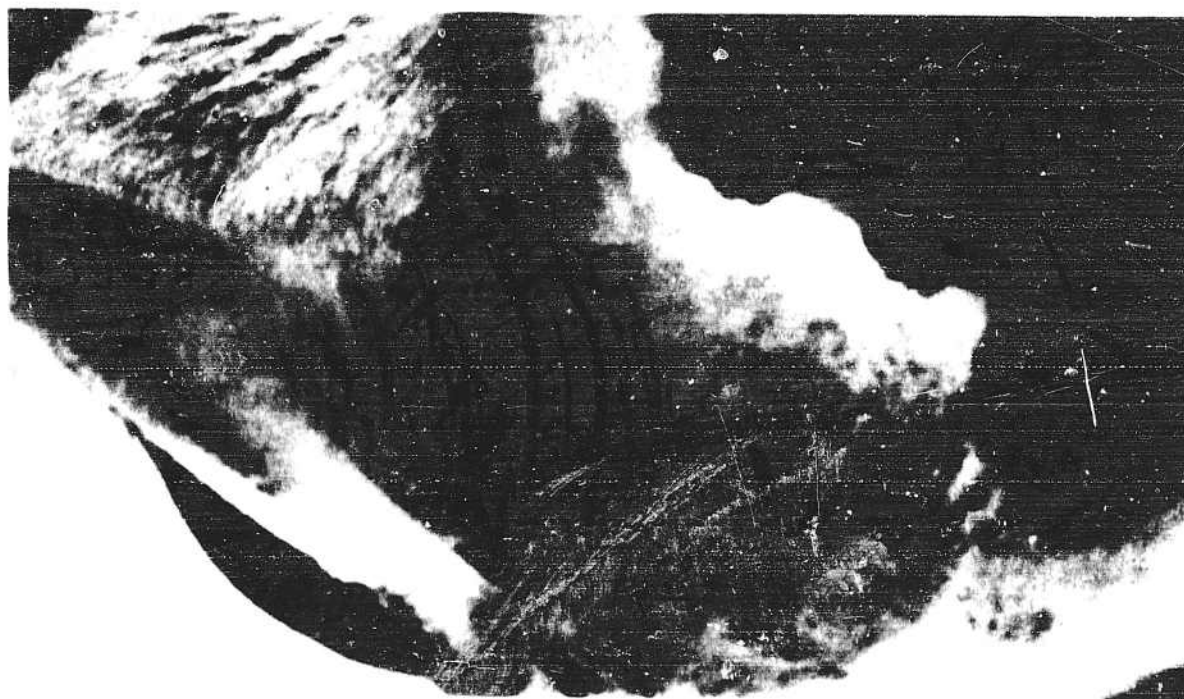
Photograph 4

Left side, one hour post application of vesicant. Cup margins of lewisite exposure are demarcated by a pale halo.



Photograph 5

Right side, 24 hours post exposure.



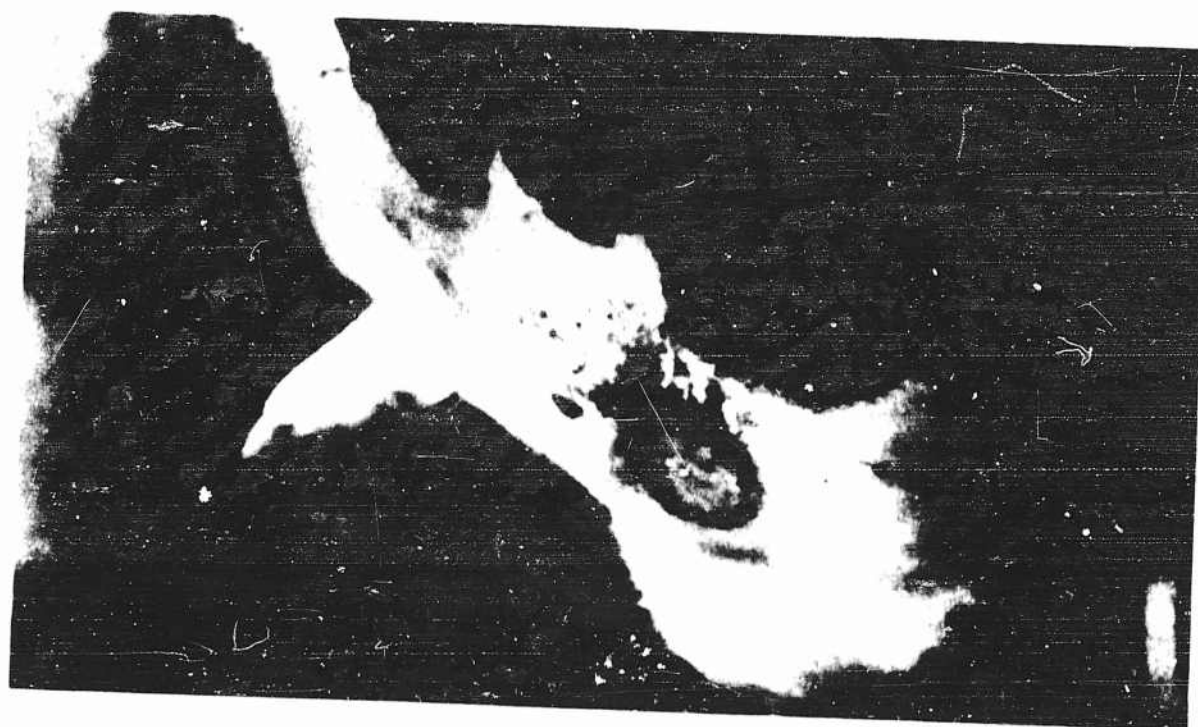
Photograph 6

Left side, 24 hours post exposure.



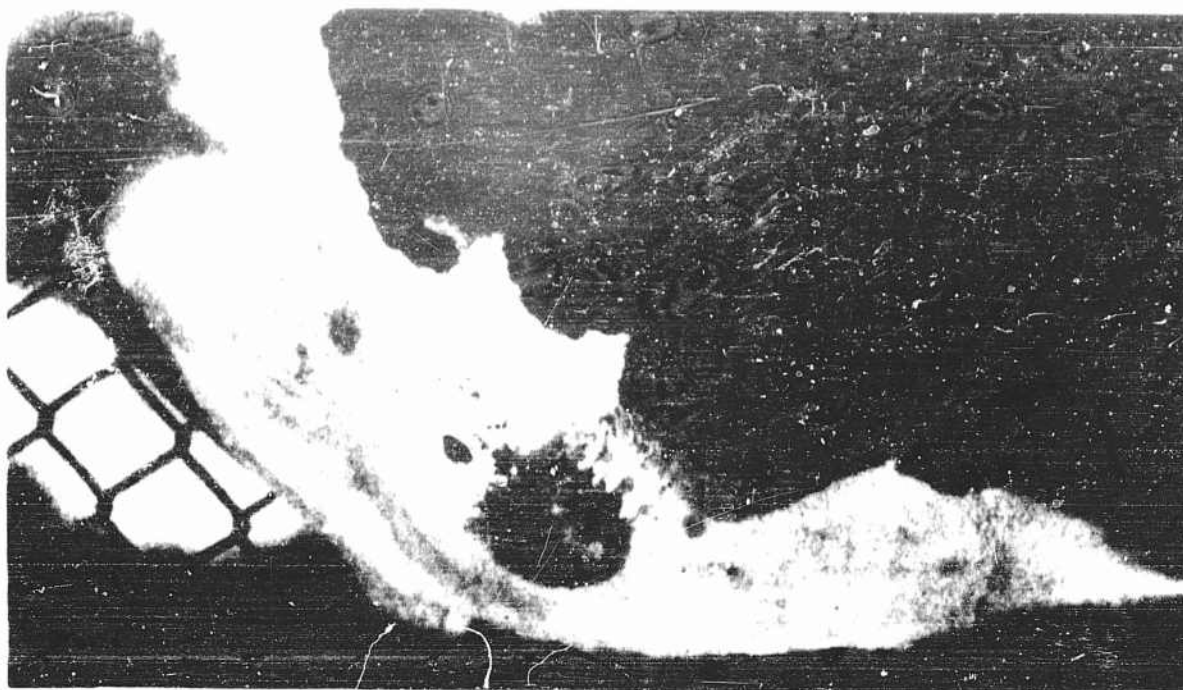
Photograph 7

Right side, 48 hours post exposure.



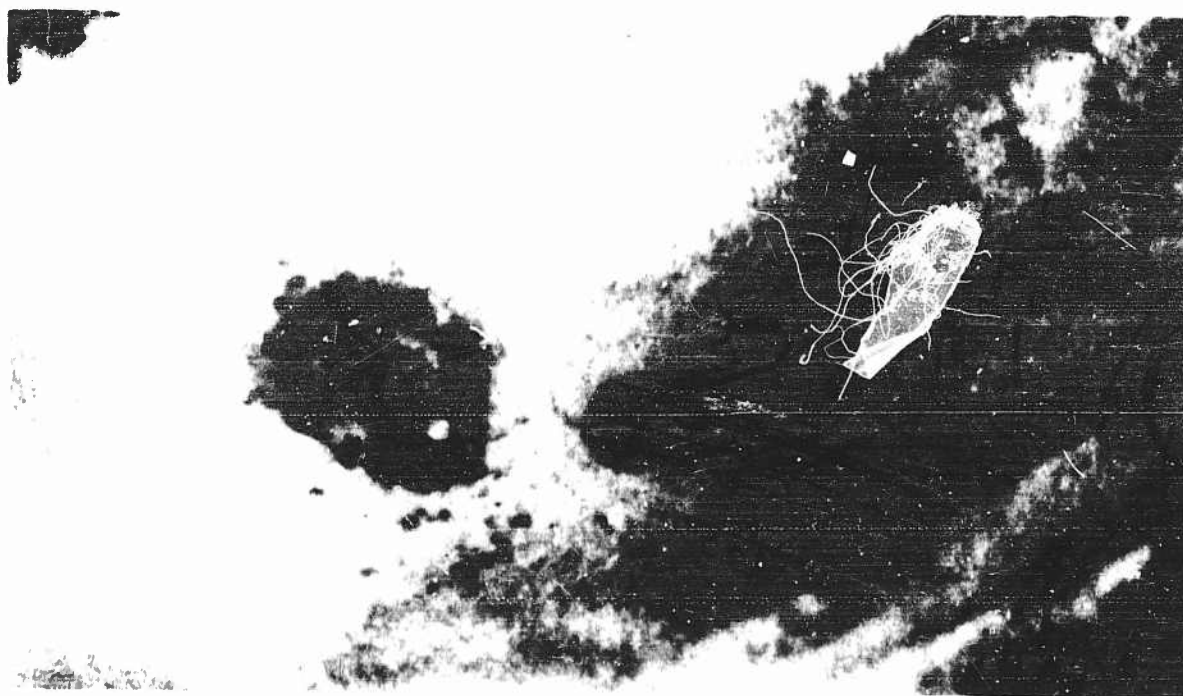
Photograph 8

Left side, 48 hours post exposure.



Photograph 9

Right side, 72 hours post exposure.



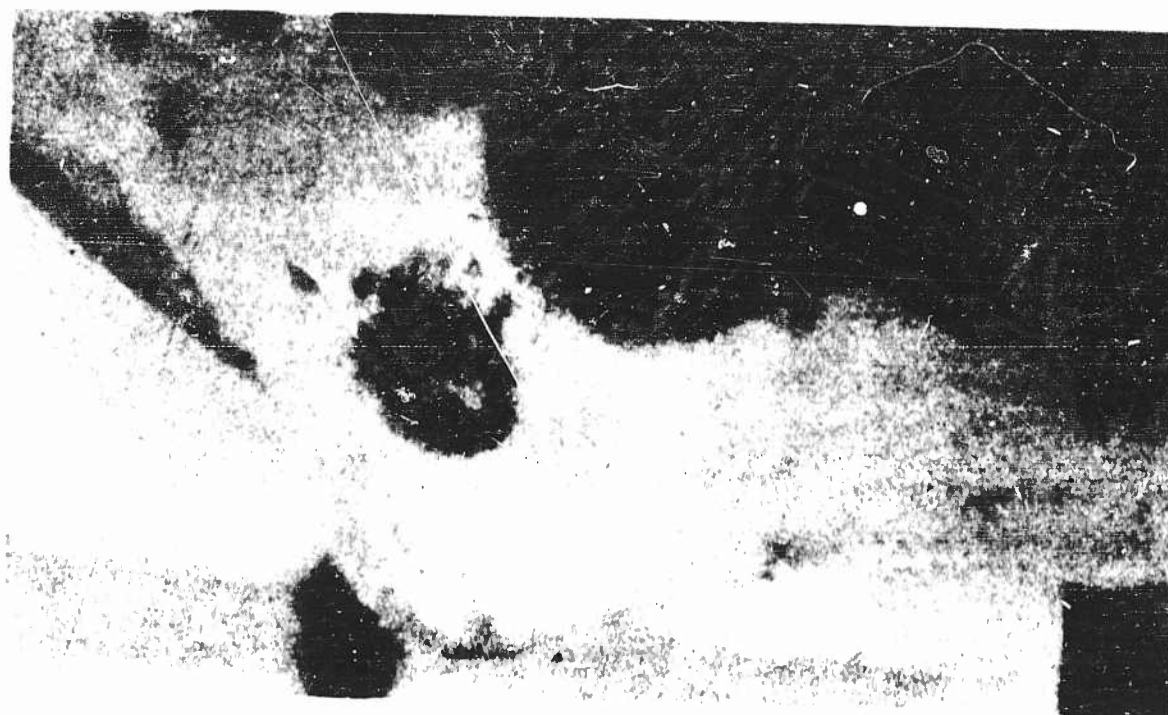
Photograph 10

Left side, 72 hours post exposure.



Photograph 11

Right side, 96 hours post exposure.

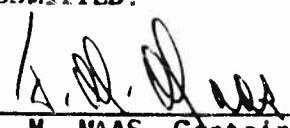


Photograph 12

Left side, 96 hours post exposure.

Medical Laboratories Research Report No. 350
Mustard, Lewisite, and Phosgene Oxime Burns
on the Depilated Skin of a Heifer to
Determine the Animal's Vesicating Potential.

SUBMITTED:


J. M. MAAS, Captain, M.C.*
Clinical Investigation Branch


A. J. McADAMS, Captain, M.C.*
Pathology Branch

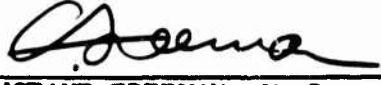

WILLIAM P. McSHANE*
Clinical Investigation Branch

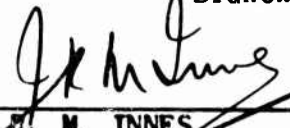
* Authors

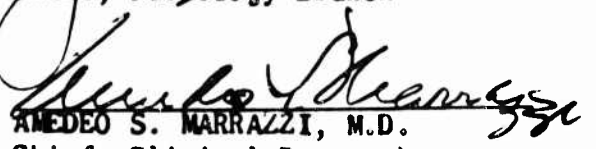
Authority:

Project No. 4-59-12-007

APPROVAL RECOMMENDED:

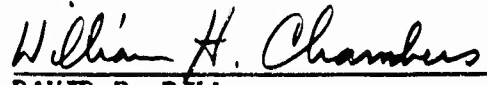

GUSTAVE FREEMAN, M. D.
Chief, Clinical Investigation
Branch

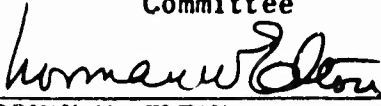

J. H. M. INNES
Chief, Pathology Branch


AMEDEO S. MARRAZZI, M.D.
Chief, Clinical Research
Division

Typed: 17 March 1955
jch

APPROVED:


for DAVID B. DILL
Scientific Director
Chairman, Publications
Committee


NORMAN W. ELTON
Colonel, Medical Corps
Commanding

CMLRE-ML-52
Publication Control No. 5030-350
Distribution (12)

SUGGESTED TOPICS FOR INDEXING MEDICAL LABORATORIES RESEARCH REPORT NO. 350

1. Lewisite, physiol. effects, depilated skin
2. Mustard, physiol. effects, depilated skin
3. Phosgene oxime, physiol. effects, depilated skin