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# MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

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## SPECIAL REPORT

on

## THE EFFECT OF TETRAMETHYL-ORTHO-SILICATE ON THE EYES

Carbide and Carbon Chemicals Corporation Industrial Fellowship No. 274-1

Because of four lost-time accidents resulting from the industrial manipulation of Tetramethyl-Ortho-Silicate (known here as TMOS for brevity), a study has been made of the effects of this compound on the eyes, using 22 albino rabbits for subjects. It must be remembered that the findings strictly speaking apply only to the eyes of rabbits, although there is good reason to believe that the same facts are true of human eyes, with perhaps some quantitative differences.

Experimental details have been included in the weekly reports and will be repeated here only when necessary for clarity.

### Summary of Experimental Work

1. As little as 0.001 ml. TMOS (measured in a specially made and calibrated pipette, with 0.001 ml. equal to 2.1 millimeters on the scale) introduced into the eye as a fluid will produce a chemical burn identical in appearance with the burns suffered by humans as the result of ill-defined exposure. The burn at its height consists of inflamed eyelids, edema of the mucous membrane resulting in the lids being swollen shut, cornea dull or opaque, and revealing upon staining with fluorescein solution a sharply defined central area of necrosis over the iris in the form illustrated in Figure I, 1 to 5. The extent of this necrosis varies somewhat

with a given volume of TMOS, sometimes being as large as Figure 1, 6; sometimes being as small as Figure 1, 7.

2. Fifteen minutes after introducing fluid TMOS into the eye, the lids become congested, and the inner conjunctival folds begin to swell. Probably at this time the eye smarts somewhat, but not so much that it could not be easily overlooked. About two and one-half hours after introducing the fluid, the cornea starts to grow cloudy, but necrosis of the cornea is not evident upon staining until about six hours after introducing the fluid. From the histories of the affected workmen, there is reason to believe that the progress of the reaction is slower in human eyes.

3. Healing of the burn proceeds from the margin of the necrosis inwards, there being always a sharply defined edge to the necrosed area, as illustrated in Figure I, 7 to 9. The healing of the mucous membrane proceeds more rapidly than that of the cornea, and any small areas of necrosis on the inner surface of the lower lid vanish much more rapidly than does the necrosis of the cornea. Within 5 to 12 days, and without treatment, the corneas of burned rabbits return to normal without any evident opacities remaining. Daily washing of burned eyes with Milk of Magnesia does not appear to hasten healing.

4. TMOS diluted with an equal volume of water, and within one minute placed in the eye in amounts equivalent to 0.01 ml. of undiluted ester, does not burn the eye at all. The heat of dilution is dissipated by the cool measuring pipette, so that cool ester enters the eye. This volume of undiluted ester produces a severe burn.

5. TMOS manufactured by the Niagara Smelting Corporation produced identical burns in identical amounts, showing that the product of the donor is

not unique. TMOS carefully redistilled for purification, and of low acidity, produced identical burns in identical amounts, showing that an impurity is not to blame.

6. Flushing the eye with one per cent sodium bicarbonate, then washing well with Milk of Magnesia, within one minute after placing 0.01 ml. of TMOS in the eye, does not prevent or lessen the burn.

7. Flushing the eye with one per cent sodium bicarbonate, or washing well with Milk of Magnesia, one minute before placing 0.01 ml. TMOS in the eye, does not prevent or lessen the burn, provided the TMOS is placed directly on the cornea, not in the accumulated secretion and washing on the lower lid.

8. TMOS introduced into an eye which has recovered from a burn, produces a second burn at least as severe as the first burn. Recovery from this second burn appears to be a little delayed.

9. TMOS will produce severe inflamation, edema, surface necrosis, and pain upon mucous membranes other than those of the eye. This was determined by placing 0.1 ml. of TMOS high up in the vagina of a rabbit. The resulting burn swelled the mucous membrane to at least ten times its normal size.

10. TMOS does not materially injure unbroken skin during one-half hour of contact, although the skin is slightly reddened. This was determined using corked glass cells, cemented onto clipped rabbit skin, after the method described by Etchells and Fabian, J. Ind. Hyg. 17, 298-9, 1935. In a simultaneous test, Dimethyl Sulphate produced necrosis of the skin, with marked oozing of serum.

11. Acetic Anhydride and Dimethyl Sulphate introduced into the eyes as fluids in amounts of 0.01 ml. produced similar, but more severe eye injuries. The form of the necrosed area resembled Figure 1, 6, but the mucous membranes were much more edematous, and recovery was slower than with TMOS.

12. Ethylene Glycol Silicate, Ethyl Silicate, or a mixture of Ethyl Silicate with "Synosol" placed in the eye in amounts of about 1 ml. did not produce any burn, but did give a brief pain and a transitory inflammation. The Glycol ester is more water soluble than is TMOS, but hydrolyzes considerably slower. The Ethyl Silicate is of low water solubility, and hydrolyzes even more slowly than the Glycol ester. Ethyl Silicate in "Synosol" is water soluble.

13. Exposure of one minute to a saturated mixture of droplet-free TMOS vapor in air (about 0.6% by volume) produces a typical burn, but less severe than that from 0.01 ml. of fluid TMOS in the eye. Apparently one minute exposure does not injure the lung. However, 10 to 30 minutes exposure produces a very severe eye burn of the same type, as well as a toxic pneumonia in which the lungs are hemorrhagic and edematous in large areas, and the exposed animal is probably fatally injured.

14. Thirty minutes exposure to air saturated with TMOS and with water vapor at the same time, produces practically as severe a lung injury as when humidity is normal, but the eye burn is less than that from the same exposure at normal humidity.

15. To injure eye tissues, TMOS must enter the eye directly as a fluid or vapor; inhalation of vapors with the eye completely protected will not produce the typical burn, even when the animal's lungs have been fatally

injured by the exposure. This was determined by making a 30 minute vapor exposure of a rabbit with one eye sealed shut with collodion.

## Gaps in the Study

Microscopic pathology of injured eyes is not reported here, although a pathologist is making a study of this now. It is thought that this phase is of limited interest to most of those who wish a prompt report on the experimental work.

Treatment of injured eyes has not been studied, because of the belief that no such treatment will entirely eliminate the lost time from a burn, and if any lost time is inevitable, the wisdom of manufacturing the compound is questionable.

No evidence has been obtained on the effect of long continued exposure to vapors not sufficiently concentrated to burn the eyes. It is inferred from two of the human accidents that such exposure causes the eyes to be more sensitive to an accidental overdose, and materially increases the burn resulting from such an overdose.

The question of possible systemic action of the material has not been considered. It is expected that some indication of the ability of the material to produce silicosis will be obtained within the next few months, but no other investigation of possible systemic effects is being attempted.

## Conclusions

It is concluded that TMOS acts upon the eye tissues as a methylating agent, not primarily as a silicate. Being apparently a less active methylating agent than Dimethyl Sulphate, it does not injure unbroken skin beyond a slight irritation.

There is no doubt that TMOS itself, not some impurity, could have caused the human burns mentioned in opening this report, and in all probability did cause them. The author is at a loss to explain the lack of eye burns reported by others who have manufactured and handled the material, but in view of the results reported here is forced to believe this is due to happy chance alone.

It would appear that workmen can be protected with completely vapor-tight goggles, worn at all times when there is the least chance of vapor or splashing of TMOS. This precaution is of course cumbersome and inconvenient. If goggles are worn, care must be taken in removing and replacing them to avoid all possibility of wiping fluid TMOS from the frames into the eyes. In view of the uncertainty of the effects of long continued exposure to traces of vapors on the eyes, it is to be doubted if it is possible to make this material safely save in a completely isolated installation where no unprotected man can possibly be exposed to any vapors whatever.

Apparently no treatment of the eyes before or after exposure to TMOS vapors or splashing will reduce the severity of a burn.

It would seem that the hazards of this material are similar to, although not quite so severe, as the hazards of Dimethyl Sulphate as far as mucous membrane injury is concerned.

## Recommendation

The Fellow recommends that the donor does not manufacture TMOS in the future, unless probable demand justifies the construction of an isolated unit as vapor- and leak-tight as that used elsewhere for the manufacture of highly hazardous materials.

It is further recommended that an attempt be made to substitute other water soluble organic silicates, such as Ethylene Glycol Silicate, for the present uses of TMOS. These silicates can be manufactured from Ethyl Silicate, which does not cause eye burns, and apparently can be handled quite safely, as far as present evidence goes.

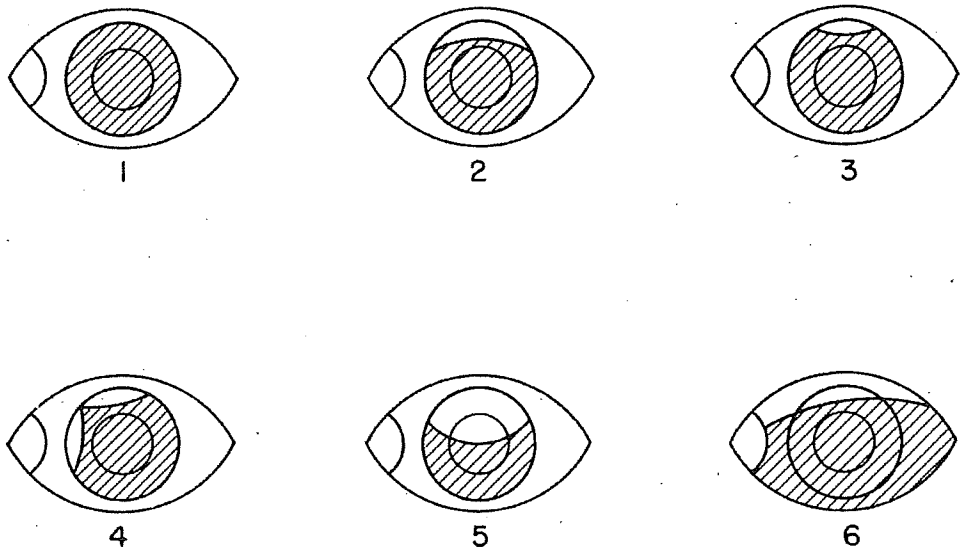
Henry F. Smyth, Jr.

INDUSTRIAL FELLOW

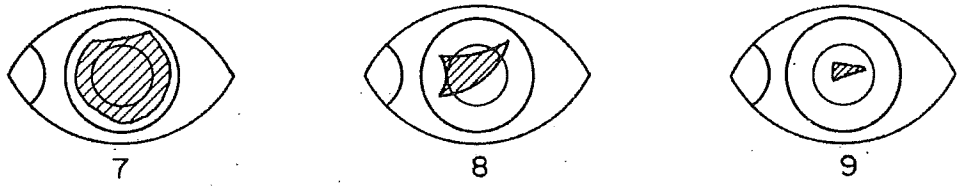
February 2, 1938-mah

Figure I TYPICAL NECROSIS FROM TMOS IN THE EYE

(Fluorescein stained necrosis shown cross-hatched; right eye of rabbit, tear duct and transverse lid to the left.)




1–6 initial necrosis; 12 to 18 hrs. after TMOS




7–9 typical healing., 1 to 2 days between drawings

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## SPECIAL REPORT

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4 Copies given to Dr. Smyth.

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INDUSTRIAL FELLOW

February 25, 1936:KJ

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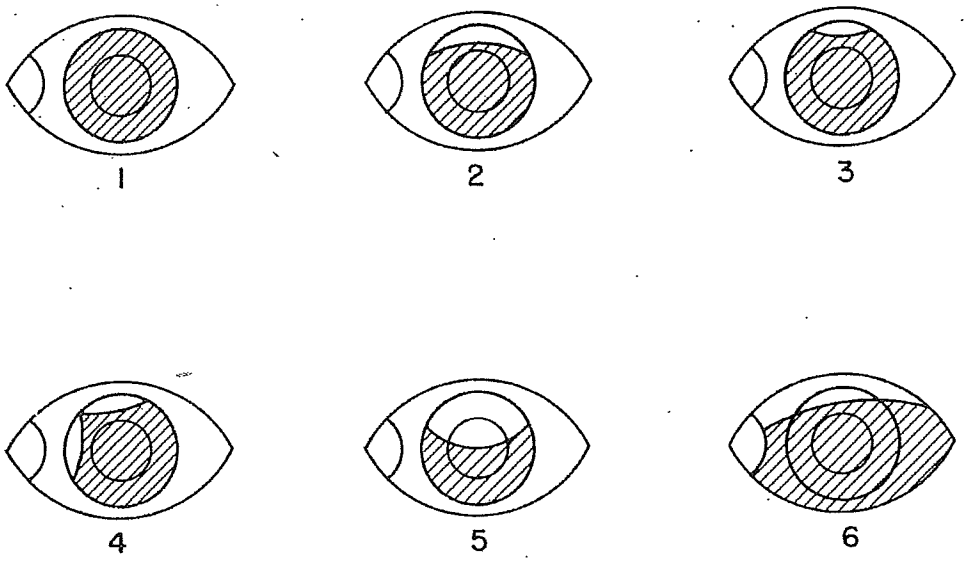


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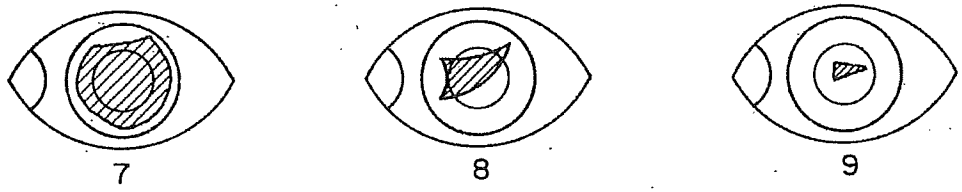


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