apparent speed. According to this reasoning, even greater reduction should result from exposing observers to a barrage of randomized visual stimulation (extrinsic noise). An electronic device was used to produce a continually changing display of dots on the face of a 14-inch television tube. The resulting pattern may be called visual noise and defined as a changing pattern of dots devoid of redundancies of position or intensity (noisy exposure field). At the opposite extreme from visual noise there is stimulation with minimal temporal variation—a condition that can be produced by exposure to a fixed pattern, called here a hyperstable field because of the absence of even that amount of object-movement found in everyday scenes. To achieve comparability of exposure conditions we used a still photograph of the picture-tube display which showed the set of dots available at one instant (hyperstable exposure field). Such stimulation may suppress intrinsic noise to a degree greater than normal and hence cause an increase in apparent speed.

Finally, the observers were kept alert in total darkness for a comparable period (dark exposure field). Under the latter three test conditions, illumination level and field size (except for the dark exposure field), exposure time, and other controlled variables were equated with those of the first test. The order of presentation was varied for the 12 observers. The resulting changes in apparent speed are shown in Table 1. An analysis of variance showed that the differences among conditions were significant beyond the .001 level.

Thus, a method has been developed for quantifying one consequence of visual deprivation. Tests in which this method was used have yielded results consistent with the following propositions: (i) Simulation and enhancement of an aftereffect of visual deprivation through exposure to a noisy visual field implies that deprivation entails the randomization of sensory-neural activity rather than the diminution or absence of such activity. (ii) Production of an aftereffect opposite to that of deprivation, after exposure to a hyperstable field, implies that typical exposure fields have relevant noise characteristics somewhere between those of the noise used and those of the hyperstable field. (iii) The normal stability of speed perception depends upon continuous exposure to the typical environment.

RICHARD HELD
BURTON WHITE
Department of Psychology, Brandeis University, Waltham, Massachusetts

References and Notes

1. W. Heron, B. K. Doane, T. H. Scott, *Can. J. Psychol.* **10**, 13 (1956).
2. This research was supported by a grant from the National Science Foundation.
3. These tests were made in collaboration with S. J. Freedman, director of isolation studies, Massachusetts Mental Health Center.
4. R. Granit, *Receptors and Sensory Perception* (Yale Univ. Press, New Haven, Conn., 1955).

11 June 1959

Protection by Sulfur Compounds against the Air Pollutants Ozone and Nitrogen Dioxide

Abstract. Two distinct but related pathways of protection against the lethal effects of ozone and nitrogen dioxide are shown by (i) simultaneous inhalation of compounds that furnish —SH or —SS—, or both, and (ii) by injection of thiourea derivatives several days prior to exposure to these oxidant gases. The mechanism of (i) is believed similar to that proposed for the action of radiation-protective compounds; that of (ii) involves the development of a tolerance initiated by the thiourea against the oxidants.

Ozone (O_3) and nitrogen dioxide (NO_2) are potent respiratory irritants which may be injurious when inhaled (*1*, *2*), and evidence exists that the concentration of O_3 in urban air is damaging to plants (*3*). Nitrogen dioxide, in addition to acting as a pulmonary irritant, acts as a precursor of O_3 in oxidant smogs by photochemical dissociation (*4*).

In tests designed to determine the acute toxicologic effects of combinations of either known or suspected air pollutants, we found that certain sulfur compounds were effective in counteracting the toxic action of O_3 and NO_2. Partial protection by ascorbic acid against acute lethal effects of O_3 has been previously reported from our laboratories (*5*) as well as by Mittler (*6*), who also found slight protection by sodium thiosulfate. Mittler's conclusion that "compounds which protect against death by radiation . . . are not effective against ozone poisoning" is not supported by our work, however. Tests involved the inhalation exposure of mice to an approximate LC_{50} of either O_3 or NO_2 simultaneously with one or more sulfur compounds. In some instances the sulfur compounds were administered intraperitoneally prior to inhalation of the oxidant. Mortality resulting from a 4-hour exposure, as compared with the mortality from a control exposure to oxidant alone, reflected enhancement or suppression of O_3 or NO_2 toxicity as influenced by the sulfur compound. Methods of generation and analysis of O_3 and vapor concentrations of sulfur compounds have been described elsewhere (*5*, *7*). Gaseous sulfur compounds and NO_2 were similarly administered from cylinders in metered amounts and diluted to the desired concentration with purified air. The Saltzman method was used for NO_2 analysis (*8*).

The data in Table 1 represent selected results of a series of tests which show the maximal protection found for each sulfur compound. Comparison of mortalities in sulfur-treated versus control groups indicates the degree of protection afforded. Hydrogen sulfide (H_2S) gave significantly greater protection against oxidant exposure, particularly NO_2, than other sulfur compounds. On a molar basis H_2S protected in a ratio of 1/55 moles of NO_2, whereas benzenethiol, next in order of effectiveness, protected in a ratio of 1/5.4. Higher molar ratios of sulfur compounds were required for protection against O_3, however; for benzenethiol 1.5 mole/mole of O_3, and for H_2S, 2 mole/mole of O_3.

Table 1. Effect of sulfur compounds on the toxicity of nitrogen dioxide and ozone for mice. Mortality at 24 and 72 hours is indicated by deaths/number of mice tested.

Sulfur compound	Av. concn. (ppm)	Av. concn. of oxidant (ppm)		Mortality			
				S treated		Oxidant alone	
		NO_2	O_3	24 hr	72 hr	24 hr	72 hr
1–Hexanethiol	145	78		0/20	1/20	10/20	11/20
1–Hexanethiol	115		4.1	1/20	2/20	10/20	10/20
Methanethiol	65		4.8	2/15	2/15	9/15	9/15
Dimethyl disulfide	45	83		5/20	5/20	10/20	11/20
Dimethyl disulfide	21 mg/kg*	80		4/20	4/20	13/20	13/20
Dimethyl disulfide	21 mg/kg*		4.6	2/20	2/20	10/20	12/20
Hydrogen polysulfide	20 mg/kg*	105		8/25	8/25	16/25	18/25
Di-*tert*-butyl disulfide	24	84		4/15		9/15	
Benzenethiol	14	76		1/20	1/20	10/20	10/20
Benzenethiol	9		6.1	1/20	3/20	11/20	12/20
Hydrogen sulfide†	11		4.9	7/35	7/35	17/35	18/35
Hydrogen sulfide†	1.5	82		1/20	2/20	10/20	10/20
Thiophene	180	85		9/15		8/15	
Dimethyl sulfide	195		4.6	14/30		14/30	

* Administered by intraperitoneal injection. † An aged technical grade.

Certain —SS— compounds also gave protection against oxidant toxicity; both dimethyl disulfide and hydrogen polysulfide significantly protected intraperitoneally injected mice, and dimethyl disulfide and *tert*-butyl disulfide protected via inhalation. It is noted that purified H_2S provided less protection than that shown in Table 1 for a technical grade. This difference in protective ability is attributed on infrared evidence to the presence of —SS—, possibly hydrogen polysulfide, in the technical H_2S, and inasmuch as addition of —SS— to purified H_2S reinforced its protective ability.

The antagonism of oxidant toxicity by sulfur compounds is physiologic and not the result of chemical combination prior to inhalation to form less active compounds. Analyses of chamber atmosphere for oxidant gas showed essentially no change upon addition of sulfur compounds. Moreover, protection was conferred by the injected compounds. Histologic examination of pulmonary tissue showed degrees of tissue change that paralleled the protective effect. Pulmonary edema and cellular infiltration, characteristic responses of oxidant exposure, were markedly inhibited in the protected groups.

The mechanisms involved in the protection are, as yet, unknown. The functional unit appears to be —SH or —SS—, or both, but not —S—; dimethyl-sulfide and thiophene were ineffective. Significantly, —SH and —SS— are characteristic of compounds conferring protection against ionizing radiation (*9*). Brinkman and Lamberts (*10*) have called attention to the possible radiomimetic properties of O_3 by showing that O_3 and irradiation produced the same defect in oxygen consumption of the skin of the finger; also cysteamine was equally protective against the effects of both agents. Likewise, Fetner (*11*) has shown a similar capacity of O_3 and x-rays to produce chromosomal aberrations in *Vicia faba*. The action was presumably mediated through the OH and HO_2 radicals formed from the aqueous decomposition of O_3; the separate effects of O_3 plus irradiation were fully additive.

Single injections of MEG (2-mercaptoethylguanidine-HBr), highly protective against radiation at 200 mg/kg, gave modest protection against NO_2 (mortality: 8/20 S treated, versus 12/20 for NO_2 alone) and O_3 (13/20 versus 19/20). When given in a series of three injections (100 mg/kg on each of 3 days), however, MEG provided greater protection (2/20 versus 10/20 for NO_2 alone). Similarly, 0.04 mg/kg of BAL (2,3-dimercaptopropanol) provided some protection to mice exposed to NO_2 (6/22 versus 12/22 for NO_2 alone) but did not decrease O_3 toxicity (13/25 versus 12/25 for O_3 alone). Thus, there is similarity of action of protective compounds which favors the view that the mechanism of action of the oxidants O_3 and NO_2 may be in part similar to that of x-irradiation.

Another means of protecting against the lethal effects of NO_2 and O_3 was achieved by still other sulfur compounds, α-naphthylthiourea (ANTU) and phenylthiourea (PTU). Mice exposed to 5.8 ppm of O_3 the day following the last of 3 intraperitoneal injections of ANTU (10 mg/kg every other day) and rats which received 128 ppm of NO_2 18 days after administration of ANTU (8 mg/kg) showed marked tolerance to the oxidants. Comparative mortalities were: mice, 0/15 versus 12/15 for controls; rats, 1/6 versus 6/6 for controls. Similarly, PTU (8 mg/kg) given in four injections every other day and exposed to either O_3 or NO_2 3 days after the last injection produced good protection (4/10 versus 9/10 for O_3 alone, and 4/10 versus 8/10 for NO_2 alone). Although the mechanism presumably still involves reactive sulfur constituents, the pathway is obviously different from that mediated by —SH and —SS— compounds because the tolerance afforded by ANTU and PTU persists, a condition not met by the simple —SH and —SS— compounds. Also, unlike —SH and —SS—, simultaneous treatment with oxidant and ANTU (itself a potent producer of pulmonary edema) produces additive toxicity, instead of protection. It has been demonstrated that rats develop a marked tolerance to ANTU (*12*) and also to O_3 (*1*). The cross tolerance between ANTU and oxidant indicates that the basic mechanisms may be similar. Furthermore, it appears that the tolerance mechanism is related to the edema mechanism, and the latter to sulfur balance, inasmuch as —SH (cysteine) blocks the lethal effects of ANTU (*13*), whereas —SH or —SS—, or both, reduces oxidant toxicity.

It is felt that the antagonism to oxidants displayed by certain sulfur compounds is highly significant for the insight it provides concerning possible mechanisms for protection against air pollutants, and also toward elucidation of the hitherto unexplained toxic action of oxidants (*14*).

EDWARD J. FAIRCHILD II
SHELDON D. MURPHY
HERBERT E. STOKINGER
Occupational Health Program, U.S. Public Health Service, Cincinnati, Ohio

References and Notes

1. H. E. Stokinger, *A.M.A. Arch. Ind. Health* **14**, 181 (1957).
2. W. F. von Oettingen, *U.S. Public Health Service, Public Health Bull. No. 272*, Security Agency, Public Health Service (1941).
3. H. T. Freebairn, *Science* **126**, 303 (1957).
4. A. J. Haagen-Smit, *Proc. 2nd Natl. Air Pollution Symposium, Pasadena, Calif.* (1952).
5. R. N. Matzen, *J. Appl. Physiol.* **11**, 105 (1957).
6. S. Mittler, *Nature* **181**, 1064 (1958).
7. E. J. Fairchild and H. E. Stokinger, *Am. Ind. Hyg. Assoc. J.* **19**, 171 (1958).
8. B. E. Saltzman, *Anal. Chem.* **26**, 1949 (1954).
9. D. G. Doherty, W. T. Burnett, Jr.. R. Shapira, *Radiation Research* **7**, 13 (195 R. Shapira, D. G. Doherty, W. T. Burnett, Jr., *ibid.* **7**, 22 (1957); A. Pihl and L. Eldjarn, *Pharmacol. Revs.* **10**, 437 (1958).
10. R. Brinkman and H. B. Lamberts, *Nature* **181**, 1202 (1958).
11. R. W. Fetner, *ibid.* **181**, 504 (1958).
12. C. P. Richter, *J. Am. Med. Assoc.* **129**, 927 (1945).
13. K. P. DuBois, L. W. Holm, W. L. Doyle, *Proc. Soc. Exptl. Biol. Med.* **61**, 102 (1946).
14. We thank L. D. Scheel of our laboratory for preparing the hydrogen polysulfide, and K. P. DuBois, professor of pharmacology, University of Chicago, for supplying the ANTU.

16 July 1959

Uridine Isomer (5-Ribosyluracil) in Human Urine

Abstract. A substance isolated from human urine by anion exchange absorption and paper chromatography was found to correspond in its ultraviolet absorption spectrum and chromatographic mobilities with a uridine isomer (5-ribosyluracil) recently described as a component of yeast ribonucleic acid.

In 1957 Davis and Allen (*1*) reported the isolation from yeast ribonucleic acid of a new nucleotide ("the fifth nucleotide") and described its physical and chemical properties, notably a characteristic bathochromic shift in the ultraviolet absorption spectrum at alkaline *p*H. The corresponding nucleoside, prepared by the action of intestinal phosphatase, was subjected to hydrazinolysis, and the carbohydrate component was identified as D-ribose. Cohn (*2*) also obtained from yeast ribonucleic acid an "apparently modified uridylic acid" identical with the "fifth nucleotide" of Davis and Allen.

The structure of this new nucleotide proved to be of unusual interest. Recent investigation by Yu and Allen (*3*) revealed that the nitrogenous component is uracil and that the D-ribose, which has the furanose configuration, apparently is attached to the pyrimidine ring at the 5 position. Methylation studies by Scannell, Crestfield, and Allen (*4*) also indicated the structure to be 5-ribosyluracil. Further evidence for this formulation was obtained by Cohn (*5*) by means of periodate oxidation and nuclear magnetic resonance spectra. The C—C ribosyl linkage reported for the uridine isomer is unique thus far for components of nucleic acid, but C—C glycosyls occur in certain natural products (*6*).

A compound identical in spectral and chromatographic properties with this isomer of uridine was encountered in