of nitrogen, it will survive longer in the nitrogen than it would if exposed to nitrogen without having been previously decompressed. The reverse is likewise true; i.e., if the housefly is first exposed to nitrogen for 3 min and 10 min later is exposed to decompression, it will survive longer under decompression than if it were only decompressed without being previously exposed to nitrogen. By "survival" we mean the time from the beginning of exposure until the last visible movement of any part of the insect's body or appendage.

We have measured survival to repeated decompression in 5 orders of insects, Diptera, Hymenoptera, Coleoptera, Hemiptera, and Lepidoptera, and have found that each order showed acquired tolerance to anoxia. Larvae of insects as well as adults show acclimatization. All adult species show some tolerance in 10 min time—i.e., with the second decompression. Tolerance to anoxia persists apparently for hours, for we have found that the housefly, *Musca domestica*, still retains some acquired tolerance for as long as 48 hr (Table 1).

Further evidence that the tolerance is produced by anoxia is shown by submerging houseflies under water.

TABLE 1

SURVIVAL TIME IN SECONDS OF 6 *M. domestica** EXPLOSIVELY DECOMPRESSED AT 25° C AT PRESSURES OF 0.2–0.15 MM HG AT INTERVALS OF 0, 10, 20, AND 30 MIN

Fly No.	0 min	10 min	20 min	30 min
1	7	11	27	23
2	6	21	20	33
3	8	31	40	37
4	15	20	27	22
5	4	23	26	24
6	8	27	30	30
Average	8.0	25.5	28.3	28.1

* The housefly is characteristic of other insects in showing developing tolerance to repeated decompressions. These 6 flies represent a random sample, not being chosen for similarity.

If flies are kept submerged for 3 min after all movement has ceased and then removed and dried and allowed to recover, they will survive the first explosive decompression about 3 times as long as will flies not submerged under water. In fact, the average survival time of flies previously submerged for 3 min is 23 sec as contrasted to 7.8 sec for the controls.

Detached legs of insects placed in the decompression chamber occasionally showed slight movements, although these were rarely seen and did not appear to be the same type of movements as those of the intact insect. They were much slower and required a longer period of decompression for their appearance.

The decompression chambers in which the flies were placed were the rounded bottoms of culture tubes cut off at appropriate lengths to accommodate the insects. Through a rubber stopper placed in the open end of the chamber a glass stopcock was connected with a vacuum pump. The stopcock shut off the insect chamber until time for explosive decompression. With the vacuum pump running, the stopcock was quickly opened, causing sudden decompression. With the pump in operation, time was determined to the closest second until the last visible movement was seen.

In spite of investigations of the effects of reduced barometric pressures on insects (*1–6*) it appears that no one has reported the acquisition of tolerance to anoxia. The authors offer no explanation for acquired tolerance in insects. It probably is a cellular adjustment and it appears to be anoxic, as it results from either the anoxic anoxia of nitrogen or explosive decompression. It occurs if the interval between the first and second decompression is only 10 min or several hours.

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The Antihypertensive Influence of Certain Sulfhydryl Compounds[1]

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During an investigation of the effects on blood pressure of various compounds, it was noticed that certain substances containing sulfhydryl groups appeared to exert a specific depression upon the hypertension of rats (*1*). A differential action was observed in that the blood pressure of normotensive rats was not lowered. In addition, the response to a number of natural pressor agents was abolished or markedly diminished.

Rats were made hypertensive by partial constriction of one renal artery, a method which in our hands has been effective in two thirds of animals. Systolic blood pressure was measured in unanesthetized animals by the foot-cuff method (*2*), a photocell being used as an indicator. After hypertension had become established (3 weeks), blood pressure was measured under anesthesia directly with a Hamilton optical manometer while the test substances were injected intravenously (*3*). To evaluate the discriminative effect of a compound, depression of diastolic pressure 12 mm Hg or more 20 min after injection was chosen as the criterion. Table 1 shows the action of various sulfhydryl compounds when tested in this manner. Apparently those with a straight chain of 3 carbon atoms were antihypertensive in the sense that they lowered blood pressure acutely in hypertensive animals but did not in normotensive ones. The maximum effect developed slowly, contrary to the usual rapid action of most depressor drugs, and lasted for the duration of the

[1] Work performed under a grant-in-aid from the National Heart Institute of the National Institutes of Health, USPHS.

TABLE 1

EFFECT OF SULFHYDRYL COMPOUNDS ON DIASTOLIC BLOOD PRESSURE OF NORMOTENSIVE AND HYPERTENSIVE RATS

Compound	Dose (mg)	Normotensive			Hypertensive			Remarks
		No. expt.	Av change (mm Hg)	No. with fall (12 mm Hg)*	No. expt.	Av change (mm Hg)	No. with fall (12 mm Hg)*	
Cysteine	2–5	5	− 1	0	6	−20	4	
β-Mercaptopropionic acid	5–10	5	0	0	8	−18	6	
					5	0	0	With normal B P
Thioglycolic acid	5–10	3	−11	1	5	−40	5	
Mercaptosuccinic acid	5–10	2	− 5	0	2	−28	2	
2-Mercaptothanol	2–20	5	0	2	5	0	1	Unstable
Thiosalicylic acid	5–20	4	− 5	1	4	− 4	1	
1-Methyl 2-mercaptoimidazole	5–20	4	− 4	1	6	− 5	1	
1,2 Mercaptobenzoxazole	5–20	4	− 7	2	5	0	0	In propylene glycol
Sodium 2-mercapto-5 benzothiazole bisulfonate	5–15	1	− 3	0	3	− 3	0	
Pseudothiohydantoin	5–15	4	0	1				
Thiosemicarbazide	10–20				2	−30	2	
Glutathione	10–20	5	0	1	8	− 5	0	Reduced
Methionine	2–20	4	0	0	9	+ 2	1	
Cystine	2–20	3	− 6	1	10	− 5	2	

* Ten minutes after injection.

experiment. In normotensive animals these substances were either inactive or pressor. The blood pressure of animals exhibiting hypertension in the unanesthetized state and normotension under anesthesia was not affected by sulfhydryl compounds.

The substances that appeared to exert this specific action on the hypertension of rats were sodium thioglycolate, β-mercaptopropionic acid, cysteine, 2,3-dimercaptopropanol, mercaptosuccinic acid, and mercaptopyruvic acid. Substances that did not exert this action were 1-methyl 2-mercaptoimidazole, mercaptosalicylic acid, and several benzothiazole compounds. It will be noted that those substances responsible for antihypertensive actions contained sulfhydryl groups on the ends of chains of 2 or 3 carbon atoms, whereas inactive ones were either cyclic structures with the SH group on a ring or in the middle of a carbon chain. Substances with S—S groups, such as cystine, methionine, and oxidized glutathione were inactive; reduced glutathione gave equivocal results in preliminary experiments.

The doses employed were relatively large: 5–10 mg/rat (20–40 mg/kg). Minimal doses did not result in the antihypertensive effect. The duration of the normotension was long (up to 3 hr) in brief experiments.

TABLE 2

INHIBITION OF PRESSOR ACTION IN RAT BY β-MERCAPTOPROPIONIC ACID*

Pressor substance	Control			After injection of 10 mg mercaptopropionic acid			
	No. injections	Av dose (γ/rat)	Av rise diastolic pressure (mm Hg) †	No. injections	Av dose (γ/rat)	Av rise diastolic pressure (mm Hg) †	No. with complete inhibition (< 5 mm Hg)
Nor-epinephrine	12	0.3	27	4	0.3	10	1
"	6	0.7	36	11	1.0	8	4
Epinephrine	7	0.4	23	5	0.8	12	0
Arterenone	5	0.5	19	3	0.7	8	2
Tyramine	3	33.0	13	7	56.0	5	6
Pherentasin	3	0.2	19	3	0.2	5	1
Angiotonin	4	0.2 ml	26	6	0.4 ml	12	3
Isoamylamine	6	50	18	4	50	14	0
Phenethylamine	3	70	6	2	70	4	
Tryptamine	3	100	56	2	100	34	0

* These data represent experiments on 34 rats.
† Average of peak rises.

Unanesthetized hypertensive rats were given 2,3-dimercaptopropanol intramuscularly at daily intervals. Reduction of blood pressure to normotensive levels occurred for 2 and 3 hr but not for 4; no permanent hypotensive effect was attained unless pyruvic acid was also given, in which case the rats died after several days with hypotensive levels of pressure.

A further property of sulfhydryl compounds of interest to the problem of hypertension lay in their ability to render rats insensitive to many naturally occurring pressor substances. The material employed to explore this action was, in most experiments, β-mercaptopropionic acid; other similar compounds, with the exception of cysteine, also exhibited this activity. A pressor dose of one of several naturally occurring or closely allied amines was inactive in an animal previously prepared by the intravenous injection of some sulfhydryl substances. The antipressor effect could be overcome only by giving excessively large doses of the pressor agent. The action of the following pressor amines was abolished or markedly depressed by prior injection of β-mercaptopropionic acid: norepinephrine, epinephrine, arterenone, tyramine, angiotonin (hypertensin), and pherentasin, the pressor substance obtained from human hypertensive blood (*4*). The action of the following was not inhibited: isoamylamine, phenethylamine, and tryptamine. It will be remembered that all the compounds inhibited by the sulfhydryl substance (except angiotonin, the formula of which has not yet been discovered), contain either hydroxyl or carbonyl groups; those not affected do not contain these groups. The order of magnitude of inhibition is shown in Table 2. Inhibition of pressor action occurred in both hypertensive and normotensive rats, the blood pressure of the latter being unaffected by the sulfhydryl compound (Fig. 1).

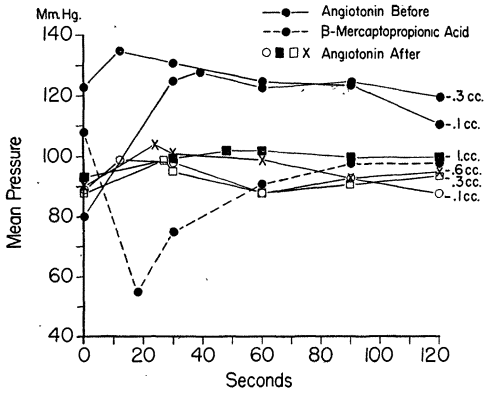

FIG. 1. Suppression of response in the rat of a pressor agent (in this case angiotonin or hypertensin) by a sulfhydryl compound. The lines indicate mean blood pressure calculated from Hamilton manometric photokymographs. Injections were made at zero time. Note the almost complete inhibition of the response to the pressor substance, even in larger doses, after the injection of the sulfhydryl compound (in this case β-mercaptopropionic acid neutralized to pH 7.4 with sodium bicarbonate). The solution of angiotonin (hypertensin) was adjusted to such a strength that 0.1 cc gave a minimal pressor reaction. These curves are typical of those obtained with other pressor agents. Pulse pressure was relatively unchanged by the sulfhydryl compounds and by the pressor agents subsequently injected.

Lowering of blood pressure in chronic renal hypertensive dogs was obtained by both 2,3-dimercaptopropanol given intramuscularly and β-mercaptopropionic acid given intravenously. In one experiment reduced glutathione appeared to cause a slight effect. The durations of the changes were short (2–4 hr), and were sometimes followed by hypertensive reactions. In hypertensive patients, 2,3-dimercaptopropanol given in doses of 100–150 mg intramuscularly also lowered blood pressure temporarily (1½–4 hr), although the usual response of normal subjects is elevation of blood pressure (*5*). Repeated doses apparently caused depression of blood pressure for several days in a few subjects. As in dogs, occasionally hypotensive responses were followed by hypertensive ones. Cysteine in doses as high as 2.0 g intravenously exhibited little or no effect.

From these experiments it appears that the administration of certain sulfhydryl compounds of simple molecular structure can cause temporary lowering of blood pressure in experimental and human hypertension without affecting normal blood pressure similarly. Furthermore, the pressor action of a number of naturally occurring amines is markedly depressed. The application of these findings to the control of human hypertension deserves further study.

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The Distillation of Lithium Metal

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If a piece of lithium is heated in air in a glass test tube, the metal first darkens because of the temperature-accelerated reaction with the nitrogen, oxygen, and other constituents of the air. At, or a little above, the melting point (*1*) 186° C, a spectacular reaction with the glass occurs. The test tube grows red, then white hot. In a short time, the bottom falls out of it and the metal burns with a brilliant white flame, like that of magnesium. It has been reported (*2*) that the lithium in this reaction reduces the SiO_2 and silicates of the glass to form lithium silicide. Attempts to purify Li on a laboratory scale by distillation in glass have usually ended in failure, accompanied by a fireworks display similar to that described above. It is the purpose of this paper to show how a glass system can be used to carry out this process.

[1] The Knolls Atomic Power Laboratory is operated by the General Electric Company for the Atomic Energy Commission. The work reported here was carried out under contract No. W-31-109 Eng-52.