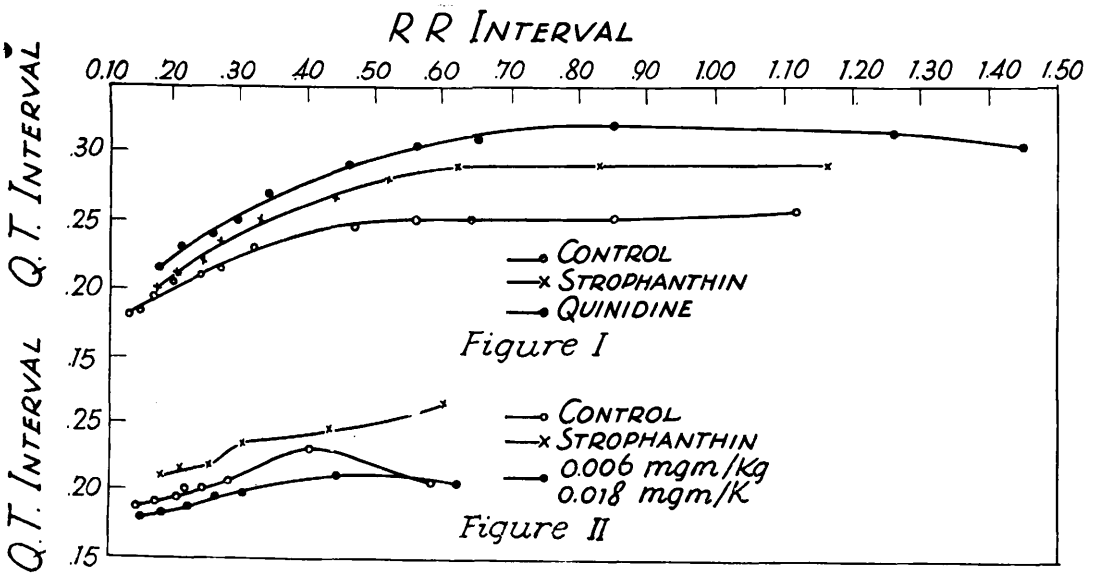

FIG. 1.
Curves relating the QT interval to the cycle length. The effect of digitalis and of quinidine for one experiment is shown.

FIG. 2.
QT-RR curves for a small, and for a large, dose of strophanthin.

determined. Strophanthin has been found,[7] like digitalis, to shorten the QT interval in animal experiments and in human patients. Although the action of quinidine in prolonging refractoriness, *i. e.*, the QT interval, parallels its effect in delaying intraventricular conduction as measured by the width of the QRS complex,[5] this parallelism is lacking for strophanthin, at least in the larger doses.

At fast rates strophanthin and quinidine produce relatively little deviation from the control curve; the effects of increased rates apparently minimize the influence of the drug. Conversely, the most marked changes in the QT interval, produced by these drugs, are usually noted at relatively slower rates of stimulation.

Summary. Curves have been drawn relating the QT interval to the cycle length for the isolated perfused rabbit ventricle. The effect of strophanthin and of quinidine on these curves has been studied.

15518

Effect of Mustard Gas on Mitosis and P^{32} Uptake in Regenerating Liver.*

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Rats (1 month, 40-50 g) were partially hepatectomized and 24 hours later β*is* (β-chloroethyl) sulfide ("HS") was injected into the femoral vein. The HS was dissolved in propylene glycol, at a concentration of 2 mg per cc. (A dose of 2 mg per kilo killed rats in 3-4 days.) Ten minutes later P^{32} as Na_2HPO_4 was administered intra-

* The work described in this paper was done at the University of California under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of California. It was undertaken at the request of the Chairman of Section 9:5 of the National Defense Research Committee.

TABLE I.

Dose in mg HS	Liver P^{32} as % injected dose	% cells in mitosis
0.1	6.34	
	6.02	
	5.91	
	6.09	0.7
0.2	5.84	
	5.72	
	6.26	
	5.94	0.4
0.4	6.21	
	5.30	
	6.56	
	6.02	0.2
0.20 cc (propylene glycol only)	6.55	
	6.84	
	6.05	
	6.48	1.1

venously in doses not exceeding 1 mg Na_2HPO_4 and 1.5 microcuries per gram body weight. Three hours after the P^{32} injection, the livers were perfused with saline and removed. A small portion of the liver was used for P^{32} assay and the remainder for making a suspension of nuclei to obtain counts of the frequency of nuclei in mitosis. The nuclei were isolated as previously described[1] and the counts made in a counting chamber with Neubauer ruling. A minimum of 2,000 cells was counted for each value given in the tables. The results are given in Table I.

The differences in P^{32} uptake in HS-treated and in control animals are not significant. However, mitosis is markedly depressed and the inhibition of mitosis increases with increasing doses of HS. A dose of 0.1 mg of HS will reduce the mitotic rate to about one-half that of the control, while 0.4 mg reduces the rate to one-fifth of the control. Serial sections were made of the livers which on microscopic examination showed no pathological changes. The depression of the mitotic rate cannot therefore be attributed to a direct necrotizing action of the HS.

In a second series the 0.2 mg HS in propylene glycol was given at 4, 12, 16, and 22 hours after partial hepatectomy. All animals received P^{32} intravenously 24 hours after the partial hepatectomy and the livers were perfused and removed 3 hours later. There were 3-4 animals in each group. The results are summarized in Table II.

When the HS is injected 4 hours after partial hepatectomy, at a time before the cells have been stimulated to active mitosis (Group 1) the mitotic rate remains at the level observed in non-regenerating livers.[2] If the HS is given 22 hours after hepatectomy and allowed to act for 5 hours (Group 5) the mitotic rate is much reduced but not to a level as low as that of Group 1. The data may therefore be taken to indicate that if the HS gets to the cells before the conditions ultimately leading to mitosis are reached, it prevents the establishment of these conditions. The higher mitotic rates of Groups 3 and 4 as compared with Group 1 suggest either local destruction of HS and/or its reaction products or the removal of these substances from the site of action.

The values for percent P^{32} uptake are given with maximum deviations of individual values from the mean of each group. The mean in Group 4 is depressed by one unusually low value which is probably due to an experi-

TABLE II.

Group No.	Hrs after hepatectomy when solution was injected	Hrs with HS	% cells in mitosis	P^{32} %
1	4	23	0.1	3.9 ± 0.2
2	12 (propylene glycol only)	15	0.5	4.2 ± 0.5
3	12	15	0.3	4.2 ± 0.1
4	16	11	0.3	3.1 ± 1.7
5	22	5	0.2	5.0 ± 0.15

[1] Marshak, A., *J. Gen. Physiol.*, 1941, **25**, 275.

[2] Marshak, A., and Byron, R. L., Jr., PROC. SOC. EXP. BIOL. AND MED., 1945, **59**, 200.

TABLE III.

	10 hrs HS	24 hrs HS	24 hrs cont.	48 hr HS	48 hr cont.
% mitosis	.19	.39	.61	.43	.33

mental error. Group 5 shows a somewhat higher P^{32} content but this is probably not significantly different from Groups 1 and 2.

In a third series, 0.2 mg HS was injected 24 hours after hepatectomy and allowed to act for 10, 24, and 48 hours. Mitotic counts were taken but P^{32} was not followed. Results were as shown in Table III.

Although mitosis is lower in livers examined 24 hours after HS administration than in controls, yet it is higher in those removed 48 hours after HS treatment. The results, as in the previous experiment, suggest that the HS inhibition is temporary, and, upon elimination of HS from the liver, the rate of mitosis increases. Since HS has no effect on the P^{32} uptake of the tissue comparable to that on mitosis, the results suggest that the inhibition observed is not produced by way of the cellular phosphorylating mechanism.

The inhibition of mitosis by HS suggested analogy with similar effects of x-rays which also inhibit mitosis in the nuclear resting stage. A search was therefore made for chromosome aberrations comparable to those found after x-ray treatment. None were observed. In an earlier study, it was shown that treatment with x-rays which also inhibits mitosis in the resting stage produces little if any change in the P^{32} taken up by liver or tumor tissue; however, the distribution of P^{32} between nucleus and cytoplasm was very markedly altered.[4] Obviously, therefore, further work is needed before final conclusions are reached on the effect of HS on the cellular and nuclear metabolism of phosphorus.

Summary. 1. Within 3 hours after intravenous injection, 0.1-0.4 mg of βis (β-chloroethyl) sulfide per 50 g rat produces a marked reduction in the number of cells in metaphase and anaphase in regenerating rat liver. A dose of 0.2 mg inhibits mitosis for at least 24 hours. By 48 hours, this inhibition is released. If the mustard reaches the liver before mitosis is initiated the cells are prevented from entering into mitosis.

2. There is no significant change in P^{32} uptake by liver cells during the interval 3-23 hours after the mustard is injected.

3. Comparison is made with the effects of X-rays on mitosis and P^{32} uptake. No chromosome abnormalities were observed at the dosage levels used.

[4] Marshak, A., *J. Gen. Physiol.*, 1941, **25**, 275.

15519

Application of Gersh's Ferrocyanide Technique to the Study of Experimental Renal Disease.

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Gersh, using histochemical methods, demonstrated in the rabbit, dog, monkey, and other species[1,3] that sodium ferrocyanide was excreted solely by glomerular filtration without apparent tubular reabsorption or secretion;

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[1] Gersh, I., and Stieglitz, E. J., *Anat. Rec.*, 1933-34, **58**, 349.

[2] Van Slyke, D. D., Hiller, A., Miller, B. F., *Am. J. Physiol.*, 1935, **113**, 611.

[3] *Ibid.*, personal communication from Gersh to the above authors, of p. 613.