in a desiccator or exposed to the atmosphere of the laboratory.

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Manuscript received August 20, 1951.

# Increased Mast Cells in the Thymus of X-Irradiated Hamsters<sup>1, 2</sup>

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Several investigators have observed an increase of tissue mast cells in the thymus of irradiated animals. However, Murray (1) cautions that this increase in mast cells may be more apparent than real, since it may result from condensation of stroma following

depletion of lymphocytes in the thymus. Because of the similarities between the granules in tissue mast cells and heparin and the parallelism between the mast cell content and the amount of extractable heparin in certain organs (2, 3), an actual increase in these cells may be significant in the occurrence of hemorrhage during the postirradiation syndrome.

Thirty-four hamsters were individually subjected to one exposure of x-rays while confined, with ample turning room, in a No. 4 hardware cloth cage  $2.5'' \times 3.5'' \times 5.0''$ . Each animal received a total body dose of 995 r or 1200 r, determined in air with a Victoreen r-meter. The factors used were 200 kv, 152 v, and 20 ma, with 1.00-mm A1 filter, at 36 cm distance, which delivered 181 r/min.

Four groups of hamsters were used to determine the effect that thymic involution produced by means other than irradiation has upon the number of mast cells. Group 1 received 3-21 subpannicular injections of cortisone acetate (Merck, 0.15 mg/100 g body wt) over a period of 10-31 days; group 2, from 1 to 3

TABLE 1

NUMBER OF MAST CELLS PER CROSS SECTION OF A LOBE OF THE THYMUS

Group	No. hamsters (sex)		Extremes of age	No. mast cells per cross section of a lobe					
	F	м	- (days)	18-25	26-50	51-75	76-100	101-200	200 +
Control	6	12	38-387	9	8	1	2		
Pregnant	<b>14</b>		72-260	3	4	5	1		1
Postpartum	7		93-237	1	5	1			
Fetal tissue		7	78-101	4	3				
ACE	4	• 11	80-229	6	7	2			
Alcohol	3	7	79-224	, 3	· 6	1			
Inanition		5	92-207	2	3				
Cortisone		9	31-300	5	4				
Irradiated			i.						
Stage of depletion		,							
Slight	2		62 - 170	2					
Inversion	$1\overline{6}$	5	96-300	-	~		6	12	3
Extreme	ĩ	9	119-382	6	1	3	v		0
Recovery	$\hat{2}$	Ũ	101-172	3	2	Ū		×.	

TABLE 2

SOME POSTIRRADIATION RELATIONS TO THYMIC INVERSION

Stage of thymic depletion	Days after irradiation	No. animals used	Reduction of thymus from normal	Lymphocytes/cu mm jugular blood	Extreme thrombocy- topenia*	Macroscopic hemorrhages*
Early	7–10	2	1/2-1/4	823-1375	1	0
Inversion	3-18	20	1/2-1/10	17-663	18	11
Extreme	6-10	10	1/4 - 1/10	28- 653	10	6
Recovery	31–33	<b>.</b> 2	1/3 - 3/4	2590 - 2716	0	0

\* The figures indicate number of hamsters.

<sup>1</sup>A preliminary report.

<sup>2</sup> This investigation was supported by the Beta Sigma Phi International Endowment Fund.

<sup>8</sup>We are indebted to the Colorado Sanitarium, Boulder, through the courtesy of Mable Page, director of the X-Ray Department, for irradiating the hamsters; to the Uplohn Company for supplying part of the adrenal cortex extract; and to Merck & Co., Inc., for supplying part of the cortisone used in this investigation. injections of adrenal cortex extract in 10% alcohol (ACE, Upjohn, 50 dog units/100 g body wt) over a period of 1–7 days; group 3, 10% alcohol in amounts and time equivalent to that received by group 2; group 4 was kept on a reduced amount of the regular fod until 30–40% of the initial weights was lost.

For comparison the thymi of normal males and

February 1, 1952

females, pregnant, and postpartum hamsters were studied (Table 1). In addition, 7 males were killed 3 days after injection of 1-2 ml of minced dead fetal tissue in saline to determine if the presence of partly resorbed fetuses (estimated to have been dead about 3 days) might have caused the increase in mast cells in 2 of the pregnant hamsters. The thymi were fixed in sublimate-alcohol, embedded in wax, sectioned at 6  $\mu$ , and stained with aqueous toluidine blue. This method clearly demonstrated the mast cells in all sections of the thymus of each group of hamsters.

In order to determine the relation of decrease in size of the thymus to the number of tissue mast cells (4) present, camera lucida tracings were made of cross sections of lobes, and the number of mast cells per section was determined by actual count. Leucocyte counts and smears were made of blood from the jugular vein after cervical fracture and before the heart ceased beating.

Mast cells ranged from 18 to 65/cross section of a thymic lobe of control, pregnant, or postpartum hamsters, with the exception of 2 females that had partly resorbed fetuses (Table 1). Resorption of fetal tissue did not appear to be the causative factor, for the number of mast cells was not increased in the 7 adults injected with minced dead fetal tissue (Table 1). No variation due to age differences of 38–387 days was found in the number of mast cells, although the thymi of older hamsters were considerably smaller. Slight depletion of the thymus by 1–3 injections of ACE, and extreme depletion by cortisone or starvation, did not increase the mast cells per cross section, although the thymi of these groups were reduced to  $\frac{1}{4}-\frac{1}{8}$  normal size and had marked condensation of the stroma.

A significant increase of mast cells occurred in all 20 of the 34 irradiated hamsters which had thymi in the inversion (shift of lymphocytes from cortex to medulla) stage of involution. Fifteen of the 20 had over 100 mast cells/cross section, more than twice the number that occurred in sections of the thymus of all other groups except 2 of the pregnant hamsters (Table 1).

In the irradiated group, thymi of the 10 animals in the extreme depletion stage were as small as those in the inversion stage—or smaller  $(\frac{1}{4}-1/10 \text{ normal size})$ ; they had fewer lymphocytes and more condensed stroma, but no increase in the number of mast cells like those thymi in the inversion stage.

Macroscopic gastroenteric hemorrhage occurred in 11 of 20 hamsters in the inversion stage of thymic depletion and in 6 of 10 with extreme depletion of the thymus. Since mast cells are considered to be a source of heparin, their increase during involution may augment the effects of the thrombocytopenia that occurred in all the irradiated hamsters (Table 2).

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Manuscript received August 16, 1951.

## Tetrahydropyrimidine Derivatives as Potential Foliage Fungicides

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In the course of a study of the fungitoxicity of some organic chemicals, a group of derivatives of tetrahydropyrimidine was found to constitute a new class of compounds possessing high fungistatic value. Various materials in this class have been prepared and evaluated in the laboratory and greenhouse; results are summarized in this paper.

The 2-alkyl or 2-aryl tetrahydropyrimidines listed in Table 1 were prepared (usually in good yield) by reaction of 2,4-diamino-2-methyl-pentane or 1,3diaminopropane with the appropriate acid or its methyl or ethyl ester. A side product in the reaction of acid with diamine was the salt of the tetrahydropyrimidine with the starting acid; production of this side product was minimized by heating the reaction mixture above  $250^{\circ}$  C. 2-Mercapto-4,4,6-trimethyltetrahydropyrimidine was obtained through the reaction of 2,4-diamino-2-methylpentane with carbon bisulfide.

The slide-germination method (1) was used for the determination of the fungistatic  $LD_{50}$  values. This method consists essentially of placing a given concentration of spores in contact with a known concen-

TABLE	1
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# Fungistatic ${\rm ld}_{50}$ Values of Tetrahydropyrimidines

	$LD_{50}$ values (ppm)		
Æ	1. circinans	M. fructicola	
2-Heptyl-4,4,6-trimethyl-		•	
tetrahydropyrimidine	180.0	36.0	
2-Undecyl-4,4,6-trimethyl-			
tetrahydropyrimidine	2.5	5.0	
2-Pentadecyl-4,4,6-trimethyl-			
tetrahydropyrimidine	0.54	0.13	
2-Heptadecyl-4,4,6-trimethyl-			
tetrahydropyrimidine	0.29	0.13	
2-(8'-Heptadecenyl)-4,4,6-tri-			
methyltetrahydropyrimidin	e 1.90	0.78	
2-Heneicosyl-4,4,6-trimethyl-	<b></b>	• •	
tetrahydropyrimidine	25.0	9.0	
2-β-Pyridyl-4,4,6-trimethyl-			
tetrahydropyrimidine	800.0	36.0	
2-p-Tolyl-4,4,6-trimethyl-	0.00.0	100.0	
tetrahydropyrimidine	360.0	180.0	
2-p-Octylphenyl-4,4,6-tri-	10.0		
methyltetrahydropyrimidin	e 16.0	18.0	
2-Phenoxymethyl-4,4,6-tri-	100.0	100.0	
methyltetrahydropyrimidin	e 180.0	180.0	
2-Mercapto-4,4,6-trimethyl-	2000.0	2000.0	
tetrahydropyrimidine	2000.0	2000.0	
2-Heptadecyltetrahydro-	5.0	2.5	
pyrimidine	5.0	2.0	