from human lungs and for comparison the analysis of a sample of soot from soft coal. In the Kjeldahl digestion for N the pigment can not be dissolved. The figures were obtained by digestion with sulfuric acid until maximum values for N were secured.

It is to be noted that the soot and pigment samples are very similar, the low N figures especially indicating the absence of material derived from tissues, such as was formed in the hydrochloric acid method. In contrast, the residues from clean lungs by the latter procedure contained 8-10% N and only 1-1.2% ash.

If the H of the pigments is calculated as H_2O, then the sum of the C, H_2O and ash obtained by combustion is nearly equal to the quantity taken for analysis. Perhaps if the pigment were dried sufficiently, the H_2O would be decreased.

Although quantitative determinations of pigment in lungs have been reported by several investigators,[1] no previous analysis of the pigment itself has been found in the literature. The present figures leave no doubt that the pigment is exogenous. In both high ash and low N content it resembles soot. If it were melanin, the N content would be in the range of 8-14%.

For the microscopic examination of the tissues, I am indebted to Dr. S. R. Haythorn.

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A Pharmacological Study of Mannitol Hexanitrate.*

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Although mannitol hexanitrate† has been used for many years for the treatment of essential hypertension and as a prophylactic against anginal attacks, few pharmacological studies are available in the literature. This paper is the first of a series designed to test this drug clinically and experimentally.

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† Due to the chemical instability of mannitol hexanitrate, this compound was used, except where specified, in the form of Maxitate, a stabilized preparation furnished by the R. J. Strasenburgh Co., which contains lactose and starch as diluents.

TABLE I.
Toxicity of Mannitol Hexanitrate on Intraperitoneal Injection into Mice.

No. of mice	Dose, mg	Vol. of solution, cc	No. dead	Mortality, %
24*	5.0	.02	0	0
24*	10.0	.04	2	8
24	12.5	.06	4	17
24	14.6	.07	3	12
16	16.6	.08	4	25
20	18.7	.09	8	40
24	20.8	.10	20	84

For probit kill—5.00, log dose—1.26, or L.D.50—18.2 mg per 20 g mouse. L.D.50 is 0.91 g per kg body weight. (For details of statistical procedure see Bliss.[5])

[5] Bliss, C. L., *Ann. Appl. Biol.*, 1935, **22**, 134.

*Solvent for these 2 groups was mixture of 1 part triacetin and 3 parts acetone. For all other groups the solvent was triethylene glycol. One-tenth cc of triethylene glycol appeared not to disturb a group of 24 mice, while 0.15 cc of this solvent killed 9 out of 12. The triacetin-acetone mixture was more toxic but as much as 0.05 cc was tolerated.

Table I shows that the 24-hour toxicity is very low when tested on 20 g mice. In another experiment, a solution of the material in triethylene glycol was given by stomach tube to 6 male rats weighing about 100 g. None of them developed any symptoms although the dosage was 1.25 g per kilogram.

In a study of chronic toxicity, 12 female rats weighing 60 g were given orally 11 mg per day of mannitol hexanitrate mixed in their diet of Purina fox chow. In addition, 6 male rats weighing 110 g received 8.5 mg in a corn oil solution daily from a medicine dropper. Nine stock animals served as controls. After 24 weeks there was no apparent effect of the drug on the rate of growth, general appearance of the rats or food intake. At autopsy they showed no gross pathological changes. Microscopic sections were made of the following tissues from 12 experimental and 5 control rats: liver, heart, spleen, kidney, and brain. These all appeared normal when stained by the H. and E. method except for moderate splenic congestion. Sections of testis and lung from four experimental rats showed no abnormalities.

Clinically it has been observed that the depressant effect of mannitol hexanitrate is more prolonged than that of other nitrate esters, *e. g.*, glyceryl trinitrate and erythrol tetranitrate.[1] Yet the action of these compounds when injected intravenously into anesthetized cats was shown to be evanescent and similar in the blood pressure lowering, confirming the work of Herrman, *et al.*[2] The

[1] Lawrence, G. H., *Arch. Int. Med.*, 1912, **9**, 409.

[2] Herrman, R. F., Leake, C. D., Loevenhart, A. S., and Muehlberger, C. W., *Proc. Am. Soc. Pharm. and Exp. Therap.*, 1926, **27**, 259.

prolonged action of mannitol hexanitrate may depend on slowness of absorption. To test this point the following experiments were carried out with glyceryl trinitrate and mannitol hexanitrate: Young female rats were starved for 48 hours and then given from 15 to 20 mg of the drug in triethylene glycol solution by stomach tube. After varying intervals of time the rats were killed and the entire gut was carefully dissected out, following the Cori technic.[3] Extraction was then carried out with 100 cc ether, after which an aliquot was evaporated to dryness and hydrolyzed with warm 1N sodium hydroxide solution. The Stieglitz and Palmer method[4] was then used with slight modifications to analyze for nitrates.

Glyceryl trinitrate was completely removed from the gastrointestinal tract within 6 hours in the case of 6 rats out of 7. In one instance removal was 60% completed. Four rats showed from 40 to 90% absorption during a 3-hour period. In the case of mannitol hexanitrate, 3 rats showed 20-30% absorption at the end of 3 hours and 6 rats showed 0-20% absorption after 6 hours. Apparently glyceryl trinitrate is taken up much more rapidly than mannitol hexanitrate.

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Influence on Development of Certain Dominant Lethals Induced by X-rays in Drosophila Germ Cells.

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The action of radiant energy in inducing gene mutations and various types of chromosomal alterations has been known for several years.[1, 2] The alterations produced have involved changes in parts of chromosomes, whole chromosomes and apparently in the composition of individual genes. In Muller's classic report[1] on

3 Cori, C. F., *J. Biol. Chem.*, 1935, **66**, 691.

4 Stieglitz, E. J., and Palmer, A. E., *J. Pharm. and Exp. Therap.*, 1934, **51**, 398.

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1 Muller, H. J., *Science*, 1927, **66**, 84.

2 Duggar, B. M., Editor, *Biological Effects of Radiation*, Vol. 2, Chaps. 38 and 39, McGraw-Hill, New York, 1936.