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Influence of 2-4 Dinitrophenol on Liver Lipids of the White Mouse.

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The prominent rôle attributed to the liver in fat metabolism has led to the study of many substances which produce changes in the fat distribution and concentration in this organ. Although many drugs and poisons increase the liver total lipid, the liver phospholipid is usually a constant percentage of liver moist weight. An exception has been noted by Cahn¹ who found increases of 4 to 40% in the phospholipid of dog liver after lethal doses of 1-2-4 dinitrophenol. However, of all the substances studied, only thyroxine² has been found to produce an appreciable decrease in the liver phospholipid. Since dinitrophenol also has the property of increasing the metabolic rate,³ it seemed reasonable that the chronic administration of this drug might also reduce the phospholipid content of the liver.

Methods. Mice in groups were given subcutaneously various doses of dinitrophenol for periods up to 7½ weeks (Table I). Standard lipid methods were used for the liver analyses.^{5, 6, 7}

Results. Both the phospholipid and cholesterol percentages decreased; the phospholipid from 3.67%, the normal value, to 3.06%, the cholesterol from .35% to .25%. These decreases have been shown to have a high degree of statistical significance.⁸ In 7 mice the neutral fat was decreased also; however, the average neutral fat values were not significantly different from normal.

Since the livers were of normal weight the phospholipid decrease indicated a real loss of phospholipid. Both thyroxine and dinitrophenol increase the metabolic rate and both decrease the phospholipid of the liver. This correlation points to the metabolic function of

¹ Cahn, T., *Ann. Physiol. Physicochim. Biol.*, 1933, **9**, 393.

² Schmidt, L. H., *Am. J. Physiol.*, 1935, **111**, 138.

³ Ronzoni, E., and Ehrenfest, E. J., *J. Biol. Chem.*, 1936, **115**, 749.

⁴ Hodge, H. C., MacLachlan, P. L., Bloor, W. R., Stoneburg, C. A., Oleson, M. C., and Whitehead, R., *J. Biol. Chem.*, 1941, **139**, 897.

⁵ Bloor, W. R., *J. Biol. Chem.*, 1929, **82**, 273.

⁶ Bloor, W. R., *J. Biol. Chem.*, 1928, **77**, 53.

⁷ Kelsey, F. E., *J. Biol. Chem.*, 1939, **127**, 15.

⁸ Fisher, R. A., *Statistical Methods for Research Workers*, 1938, 7th Ed., London.

TABLE I.
Average Data on Liver Lipids of Dinitrophenol Injected Mice.

Adminis- tration time	Liver moist wt, g	Liver per g mouse	Neutral fat % moist wt	Liver		
				Phospho- lipid % moist wt	Cholesterol % moist wt	Total lipid % moist wt
24 hr*	1.385	69.5	2.22	2.75	0.23	5.38
	1.359	64.6	2.21	2.75	0.23	5.21
	1.150	54.6		3.21		
Avg	1.298	62.9	2.21	2.86	0.23	5.30
96 hr	1.123	56.1	1.18	4.68	0.30	6.16
	1.041	52.1	1.00	3.24	0.27	4.52
	1.220	61.0	0.62	3.54	0.24	4.40
	.930	46.5	2.50	3.10	0.28	5.88
	1.077	53.8	1.28	3.38	0.21	4.87
Avg	1.078	53.9	1.12	3.59	0.26	5.16
6 wk†	1.647	68.7	0.86	2.81	0.26	3.93
	1.780	73.9	2.51	2.00	0.25	4.77
	1.623	67.7		2.89	0.25	
	1.612	67.4		2.81		
Avg	1.665	69.4	1.68	2.63	0.25	4.35
7 wk‡	1.045	41.9	5.31	2.93	0.30	8.54
	1.360	54.4	2.16	2.50	0.31	4.97
	1.490	59.6		2.89		
Avg	1.298	52.0	3.73	2.77	0.30	6.75
7½ wk§	1.857	74.3	1.13	2.95	0.09	4.28
	1.323	52.9	1.15	3.40	0.21	4.76
	1.429	57.2		3.19		
Avg	1.536	61.8	1.14	3.13	0.20	4.52
Avg treated	1.359	60.0	1.97	3.06	0.25	5.21
Std. Dev.				±.54	±.037	±.18
S. E. Mean				±.13	±.01	±.33
Avg normal	1.332	60.0	1.52	3.67	0.35	5.54
Std. Dev.				±.26	±.13	±.047
S. E. Mean				±.058	±.029	±.01

*High dosage, 37 ½ mg/kg body wt.

† " " 25 " " "

‡Medium " 10 " " "

§Low " 5 " " "

phospholipid in the liver, previously established by Sinclair⁹ and others.¹⁰

In mice given dinitrophenol, the heightened metabolic demands tend to remove rather than increase body lipids. The fact that with increasing metabolism the liver loses cholesterol emphasizes the view

⁹ Sinclair, R. G., *J. Biol. Chem.*, 1932, **96**, 103.

¹⁰ See bibliography of Sinclair, R. G., *Physiol. Rev.*, 1934, **14**, 351.

that cholesterol plays a rôle in the fat metabolism of the liver.

Summary. Under the stress of increased metabolic rate, due to dinitrophenol injection, liver phospholipid and cholesterol are decreased. These changes are consistent with the belief that at least part of the phospholipid and cholesterol of the liver are important in fat metabolism.

The authors wish to express their thanks to Dr. W. R. Bloor for his advice on this problem.

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Localization of Colloidal Dyes in Animal Tumors.

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Introduction. It has long been known that certain colloidal dyes when injected intravenously exhibit properties of selective accumulation in tumor tissue.* The possible use of such dyes or other similarly behaving colloids as "carriers" for localizing radioactive and slow neutron capturing materials in neoplastic tissue for internal radiation therapy was suggested recently by Zahl and Cooper.^{3, 4} With the radiation properties of these materials in mind (that is, type of emitted particle, penetration path, ionization density, etc.), it seemed of value, in an effort to probe the usefulness of such a concept, to reexamine the localization features of such "carriers" in tumor tissue. This seemed of particular importance in relation to (a) the gross distribution within the body and (b) the distribution pattern in the tumor mass.

The localization of certain dyes in tumors has been described in some detail by Ludford⁵ and Duran-Reynals¹ on animal material, and grossly by Brunschwig, Schmitz and Clarke² on human material. Some of the points presented here are in general confirmatory of

* For recent appraisal of this subject, *vid.*:1,2

¹ Duran-Reynals, F., *Am. J. Cancer*, 1939, **85**, 98.

² Brunschwig, A., Schmitz, R. L., and Clarke, T. Howard, *Arch. Path.*, 1940, **30**, 902.

³ Zahl, Paul A., and Cooper, F. S., *Science*, 1941, **93**, 64.

⁴ Zahl, Paul A., and Cooper, F. S., *Radiology*, 1941, in press.

⁵ Ludford, R. J., *Proc. Roy. Soc. London*, Ser. B, 1929, **104**, 493.