decrease in cholesterol observed one hour after 10 cc. injection of tissue extract (9 injections) was 12.7%; the average deviation from the mean was 9.7%.

Summary. The results indicate that pancreatic tissue extract produces a lowering of the plasma cholesterol within one hour in cardiovascular arteriosclerosis. The cholesterol remains lowered, but with a tendency to return almost to former level in 24 hours. The effect is transitory, lasting about 24 hours, more or less. For sustained effect and progressive drop in plasma cholesterol, patients require doses at frequent intervals. When treatment is interrupted or dosage inadequate, the plasma cholesterol rises and there is an exacerbation of symptoms, precordial pain and intermittent claudication.

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Active Form of 2-4 Dinitrophenol in the Stimulation or Inhibition of Oxygen Consumption of Excised Rabbit Muscle.*

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Field, Martin and Field[1, 2, 3] have shown that the stimulation or inhibition of yeast respiration by 2-4 dinitrophenol (DNP) and several related compounds depends upon the concentration of the undissociated form. Since this finding appears to have important physiological and pharmacological implications, we have undertaken an investigation of the action of DNP on excised rabbit striated muscle (diaphragm) to see whether the undissociated form is the active agent in stimulation of oxygen consumption of a mammalian tissue as well as of yeast.

Rabbits were killed by a blow on the back of the neck. The diaphragm was rapidly excised, and strips of proper thickness (*c. f.* Warburg[4]) were placed in Ringer's solution containing 0.2% glucose and buffered at the desired pH with M/150 phosphate. Res-

* Supported in part by a grant from the Rockefeller Fluid Research Fund of the Stanford University School of Medicine.

1 Field, J., II, Martin, A. W., and Field, S. M., PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 56.

2 Field, J., II, Martin, A. W., and Field, S. M., *J. Cell. and Comp. Physiol.*, 1934, **4**, 405.

3 Field, J., II, Martin, A. W., and Field, S. M., *J. Pharm. and Exp. Ther.*, 1935, **53**, 314.

4 Warburg, O., *Über den Stoffwechsel der Tumoren*, Berlin, 1926.

piration was measured by the Warburg manometric method[4] at 37° ± 0.02°C. in an atmosphere of oxygen. The respiration of each piece of tissue was followed for 30 minutes before addition of DNP from the vessel sidearms, to obtain a preliminary control period in each case. In addition to these individual controls in at least one case in every run (6 to 13 vessels), Ringer's-glucose was added from the sidearms instead of DNP to determine the rate of decrease of oxygen consumption with time under the conditions of these experiments over a longer period.

TABLE I.

Showing effects of graded concentrations of DNP, total and undissociated, on oxygen consumption of rabbit striated muscle (diaphragm) in Ringer's-glucose at pH 6.2, 7.2 and 8.0. DNP concentrations given in millimols. Plus indicates stimulation, minus inhibition. Optimum effects in italics.

Total DNP Concentration	% effect at pH			Undissociated DNP Concentration	% effect at pH		
	6.2	7.2	8.0		6.2	7.2	8.0
2.23 x 10-4	+38						
				2.34 x 10-7			+21
4.46 x 10-4	+34	+4					
				2.88 x 10-7		+4	
1.11 x 10-3	+120						
				4.68 x 10-7			+46
2.23 x 10-3	+162	+22	+21				
				1.44 x 10-6	+38	+22	
3.33 x 10-3	*+192*						
				2.33 x 10-6			+35
4.46 x 10-3	+97	+29	+46				
				2.88 x 10-6	+34	+29	
1.11 x 10-2	+123	+58					
				3.49 x 10-6			+60
2.23 x 10-2	+56	*+207*	+35				
				4.68 x 10-6			+94
3.33 x 10-2		+177	+60				
				7.18 x 10-6	+120	+58	
4.46 x 10-2	—19	+184	+94				
				1.17 x 10-5			*+252*
1.11 x 10-1		+200	*+252*				
				1.44 x 10-5	+162	*+207*	
2.23 x 10-1		+77	+63				
				2.15 x 10-5	*+192*	+177	
1.11		—26	—8				
				2.33 x 10-5			+63
2.23			—35				
				2.88 x 10-5	+97	+184	
				7.18 x 10-5	+123	+200	
				1.17 x 10-4			—8
				1.44 x 10-4	+56	+77	
				2.33 x 10-4			—35
				2.88 x 10-4	—19		
				7.18 x 10-4		—26	

Calculations of percentage stimulation (Table I) were based on the assumption that had no DNP been added the rate of decrease of oxygen consumption after the initial control period would have been the same as that observed in the longer control experiments. Controls showed this assumption valid within ± 5%. Accordingly, no change in oxygen consumption was considered significant unless it exceeded 10%.

If undissociated DNP is the active agent in the stimulation or inhibition of tissue respiration by this substance, one would expect to find the optimum total concentration to be a function of pH, while the optimum concentration in terms of the undissociated form should be quite constant. Furthermore, it should be possible to find a total DNP concentration which would stimulate respiration at one pH level and inhibit at another. It is shown in Table I that these expectations were realized. Such results are most directly explicable on the assumption that, over the pH range investigated, undissociated DNP is the active agent in the stimulation or inhibition of oxygen consumption of rabbit striated muscle (diaphragm).

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Metabolism of Anesthetized Rats.

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The experiments reported in this paper were undertaken chiefly in order to find out whether or not anesthesia could be used with advantage in metabolism studies as a means of reducing the variability of metabolic rates between different rats.

Female rats weighing from 65 to 163 gm. were anesthetized with a suspension of one per cent sodium amytal in 0.9% NaCl solution. The effect of intraperitoneal injection of the drug was tested in 15 rats. When 2 out of 3 rats injected intraperitoneally with 1.5 to 2 cc. of the suspension per 100 gm. of body weight died, the dosage was reduced, yet the mortality among the intraperitoneally injected rats remained high, so that only 6 results of this group could be used for comparison. The dosage of amytal for these intraperitoneally injected rats varied from 7.6 to 10.4 with an average of 9.2

* The authors are indebted to C. F. Winchester for the measurement of the respiratory exchange of the rats.