the massive lipemia used in this study. This effect persisted even when the anticoagulant activity was destroyed by alkaline degradation. Another potent anticoagulant was found in a highly sulphated galactosan isolated from seaweed. This compound produced extensive pathologic changes in the kidney when administered in large doses.

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Effect of Some Monosaccharides on Serum Inorganic Phosphate in the Normal Dog. (23529)

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Soon after the discovery of insulin, it was found that the hormone has a depressing effect upon serum inorganic phosphate(1). A similar effect was described after glucose administration(2,3). The action of glucose on serum inorganic phosphate appeared to be due to induced insulin secretion since it was not possible to elicit a normal response in the pancreatectomized dog(4), or in the alloxanized dog(5). It seemed of interest to study the effect of various monosaccharides upon serum inorganic phosphate. It has been mentioned that glucose, fructose and galactose show a depressing effect(6,7). It has been also demonstrated that fructose may decrease serum phosphate in the pancreatectomized dog (8). In this paper, the effects of 8 sugars and one polyalcohol (D-Sorbitol), independently injected by vein and in some cases mixed with glucose and/or insulin are reported.

Material and methods. Apparently normal dogs weighing between 12 and 20 kg, fed *ad libitum* on Purina Chow and twice weekly on meat, were used. The animals were previously trained by repeated venipunctures to avoid fear and anger reactions. When the same dog was used for several experiments, a previous test was carried out on a different day with glucose in order to check whether the animal showed a normal phosphate fall. The experiments were carried out after a fasting period of about 15 hours. A venous blood sample was taken, the sugar injected in 3M solution (1 ml/kg) within a period of one minute and new samples obtained at 15, 30, 45 and 60 minutes. D-Galactose was used in 1.5M concentration (2 ml/kg). When 2 sugars were administered, one ml of the 3M solution/kg of each was injected. Glucagon-free insulin (generously furnished by Eli Lilly Co.) was used by vein at the dose of 0.1 U/kg. Serum inorganic phosphate was determined in duplicate using the Fiske and Subbarow procedure(9) adapted to the photoelectric colorimeter. Changes in serum inorganic phosphate were expressed in terms of "Deltas" (differences from the initial values in mg/100 ml). The statistical significance of the results was appraised with the use of the "t" test, by comparison with the spontaneous variation observed by taking blood samples every 15' up to 60', under experimental conditions. The compounds used (C.P.) were:

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TABLE I. Averages and Standard Errors of Changes in Serum Inorganic Phosphate in mg/100 ml (Deltas) after Venous Injection of Different Sugars.

	No. of exp.	Min. after injection 0′	15′	30′	45′	60′
D-Glucose	16	4.11 ± .23	−.26* ± .05	−.42* ± .07	−.42* ± .05	−.23* ± .08
D-Galactose	10	3.97 ± .17	−.10* ± .05	−.22* ± .05	−.23* ± .07	−.20* ± .06
D-Levulose	16	4.08 ± .20	−.09 ± .05	+.09 ± .06	+.30* ± .06	+.38 ± .13
L-Rhamnose	6	3.99 ± .41	+.01 ± .06	−.08* ± .03	−.05* ± .04	−.06* ± .06
D-Sorbitol	6	3.63 ± .20	−.44* ± .15	−.40* ± .08	−.21 ± .19	+.07 ± .88
L-Sorbose	6	4.21 ± .31	−.33* ± .18	−.48* ± .10	−.27* ± .10	−.17* ± .09
L-Arabinose	12	3.87 ± .24	+.07 ± .06	+.04 ± .06	+.04 ± .07	+.14 ± .07
D-Arabinose	10	3.83 ± .23	+.04 ± .06	+.20 ± .08	+.52* ± .12	+.87 ± .10
D-Xylose	10	3.69 ± .16	−.11* ± .03	−.14* ± .04	−.20* ± .07	−.20* ± .05
Spontaneous variations	10	3.96 ± .26	−.10 ± .07	+.13 ± .07	+.10 ± .05	+.37 ± .13

* Statistically significant changes as compared to spontaneous variation; $t > 2$.
(Underlined)—Decreasing effect greater than .30 mg/100 ml.

D-Glucose,† D-Galactose,† D-Levulose (pyranose),‡ L-Rhamnose,‡ D-Sorbitol,§ L-Sorbose (Tech.),‡ L-Arabinose,‡ D-Arabinose‡ and D-Xylose.‡ The 3 pentoses were used alone, mixed with glucose, with insulin and with glucose + insulin.

Results are shown in Tables I and II.

Discussion. Previous work(5) has shown that a decrease in serum inorganic phosphate greater than 0.30 mg/100 ml occurred after glucose injection in normal dogs, as opposed to alloxanized dogs who show little or no response. We have then taken a decrease greater than 0.30 mg/100 ml from the initial level after administration of a sugar as showing a definite effect. Levine *et al.*(8) take as significant a decrease greater than 0.20 mg/100 ml. If the fasting levels of serum inorganic phosphate are taken to vary between 3 and 5 mg/100 ml and a 5% error in the method used is assumed, 0.15 to 0.25 mg/100 ml is the range of uncertainty to be expected in connection with the procedure.

D-Glucose, L-Sorbose and D-Sorbitol have a clear-cut decreasing effect on serum inorganic phosphate. However, statistical comparison with the spontaneous variation makes it appear that D-Galactose, L-Rhamnose and D-Xylose have some effect, apparently masked by the rise in serum phosphate observed after

TABLE II. Averages and Standard Errors of Changes of Serum Inorganic Phosphate in mg/100 (Deltas) Induced by Some Pentoses in Mixture with D-Glucose and/or Insulin.

	No. of exp.	0′	15′	30′	45′	60′
Insulin	6	3.93 ± .23	−.40 ± .07	−.76 ± .16	− .86 ± .15	− .66 ± .25
L-Arabinose + insulin	9	3.83 ± .25	−.26 ± .07	−.90 ± .12	−1.23 ± .16	−1.23 ± .25
D-Arabinose + "	8	3.75 ± .28	−.30 ± .10	−.55 ± .16	− .40† ± .16	− .10 ± .24
D-Xylose + "	10	4.07 ± .11	−.32 ± .09	−.73 ± .18	−1.02 ± .22	−1.10 ± .20
D-Glucose	16	4.11 ± .23	−.26 ± .05	−.42 ± .07	− .42 ± .05	− .23 ± .08
L-Arabinose + D-Glucose	6	4.09 ± .33	−.14 ± .05	−.32 ± .10	− .17* ± .08	+ .04* ± .07
D-Arabinose + "	6	4.06 ± .40	−.01 ± .18	−.23 ± .17	+ .32* ± .08	+ .62* ± .12
D-Xylose + "	6	3.68 ± .23	−.37 ± .10	−.26 ± .14	− .27 ± .18	− .23 ± .14
D-Glucose + insulin	6	4.19 ± .32	−.74 ± .13	−.99 ± .09	−1.07 ± .16	−1.13 ± .13
L-Arabinose + D-Glucose + insulin	7	3.69 ± .22	−.47‡ ± .08	−.83 ± .09	−1.09 ± .19	−1.11 ± .23
D-Arabinose + " + "	6	3.83 ± .23	−.36‡ ± .09	−.43‡ ± .07	− .35‡ ± .12	− .30‡ ± .12
D-Xylose + " + "	6	3.70 ± .28	−.43 ± .10	−.89 ± .14	−1.06 ± .17	−1.26 ± .20

* Statistically significant modifications in comparison to changes induced by glucose.
† *Idem* insulin.
‡ " glucose + insulin.

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‡ Eastman Organic Chemicals.
§ Pfanstiehl Laboratories.

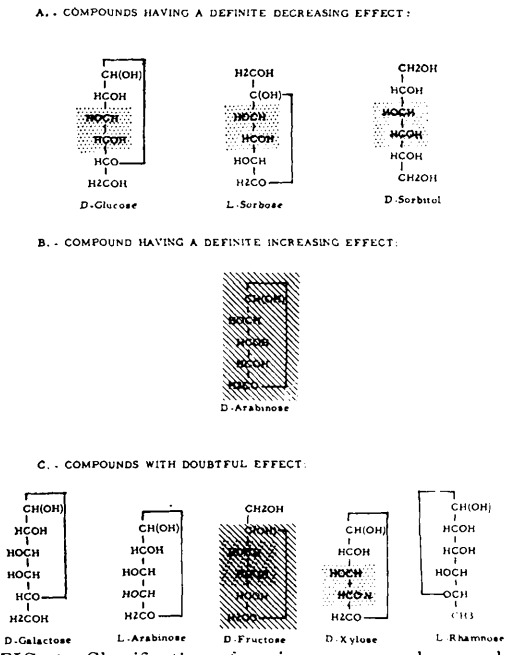

FIG. 1. Classification of various compounds according to their effect on serum inorganic phosphate.

successive blood extractions. Compared with the spontaneous variation, D-Fructose showed a rise at 45′ (Table I). Sixteen experiments with D-Fructose were carried out without being able to confirm previous work(6.7) showing a decreasing effect on serum phosphate. Levine *et al.*(8) reported a clear decrease induced by this sugar in pancreatectomized dogs but they did not carry out experiments in normal animals. The type of fructose used was not mentioned in these papers.

D-Arabinose, which causes serum phosphate to rise distinctly, inhibited almost completely the decrease induced by glucose and partially that produced by insulin or by mixture of glucose + insulin. L-Arabinose showed some inhibitory effect with respect to glucose effect at 15′ after glucose + insulin.

It appears that D-Glucose, D-Sorbitol and L-Sorbose produce a clear-cut decrease in serum inorganic phosphate and that D-Arabinose induces a rise.

By examining the chemical configuration of the substances used(10), (Fig. 1) it seems that the common feature of those exhibiting a definite decreasing effect is the arrangement of the OH groups in carbons 3 and 4 in the hexose molecule. D-Fructose has the same configuration in carbons 3 and 4, however its 5 last carbon atoms have the same structure as D-Arabinose, which has been shown to increase markedly the serum phosphate concentration. D-Xylose also possesses the above-mentioned configuration at the 3 and 4 carbon atoms but in a pentose rather than a hexose skeleton.

Summary. The effect of D-Glucose, D-Galactose, D-Fructose, L-Rhamnose, L-Sorbose, D-Sorbitol, D-Arabinose, L-Arabinose, and D-Xylose on the serum inorganic phosphate in the normal dog has been studied. D-Glucose, L-Sorbose and D-Sorbitol produced a definite decrease, and D-Arabinose a clear cut rise. By statistical comparison with the variation encountered by taking successive blood samples with the same intervals and under the same experimental conditions, it seems that D-Galactose, L-Rhamnose and D-Xylose have some decreasing power. D-Fructose (pyranose) produced an increase at 45′. D-Arabinose showed inhibitory action on the decreasing effect of glucose and insulin. L-Arabinose exhibits some inhibitory action on the effect of glucose and at 15′ after glucose + insulin.

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