Paramaribo, Surinam, and the Sub-Tropical Experiment Station, Homestead, Fla.
4. J. Kahan, *Arch. Biochem and Biophys.* 47, 408 (1953).
5. R. L. Whistler and D. F. Durso, *J. Am. Chem. Soc.* 72, 677 (1950).
6. Kindly supplied by Melvin Cohn, Washington University, St. Louis, Mo.

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Effect of Growth Hormone and Acromegaly on Plasma Phospholipid

We have used the technique of labeling with radiophosphorus to study the effect of administered anterior pituitary growth hormone and of acromegaly on plasma phospholipid. In both cases there is a lowering of the rate of plasma phospholipid formation, if "formation" is defined as the sum of metabolic processes and membrane transfers involved in the entry of newly-formed phospholipid into the blood.

Although it appears that plasma phospholipids are made and destroyed in the liver, these processes are independent of severe liver injury. Experiments in man, by Cornatzer and Cayer (*1*), have demonstrated a constant rate of phospholipid formation in any individual in spite of time and change in liver function. Among individuals, however, they found a wide normal variation. Zilversmit's (*2*) experiments with adrenalectomized dogs have focused attention on endocrine control of the liver-plasma phospholipid system.

In our experiments, 100 to 400 μc of labeled inorganic phosphate were given intravenously, and plasma samples were drawn at 15, 24, 40, and 60 hours. The plasma was extracted with trichloroacetic acid (TCA), and the relative specific activity of phosphorus in both the TCA-soluble fraction and phospholipid fraction was determined. These values were plotted against time; both the curves obtained and the average value of stable phospholipid phosphorus were considered. When the effect of growth hormone was studied, each patient acted as his own control, with pretreatment and treatment curves being determined at an interval of 1 week. Studies were also made on a series of acromegalic patients to show the effect of excess endogenous growth hormone.

Figure 1*A* shows composite curves from six endocrinologically normal patients, each of whom had two series of determinations with no intervening

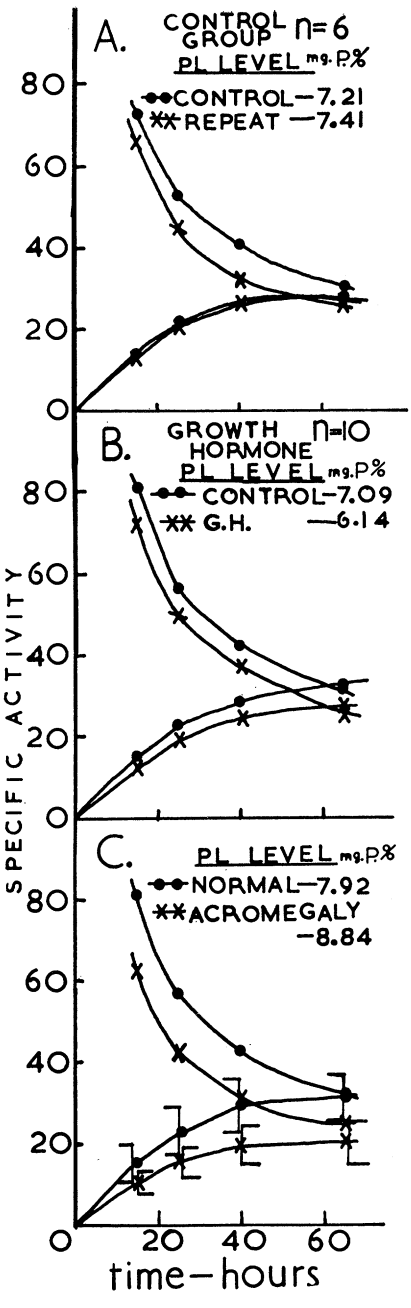

Fig. 1. The specific activity is expressed as a ratio of the percentage of the dose in counts per minute $\times 10^{-4}$ divided by milligrams of phosphorus.

treatment. The rising curves show specific activity of the phospholipid fraction; the falling curves show that of the TCA-soluble fraction. In each case the two phospholipid curves were identical. This confirms the constancy of the curve and the validity of repeating the test after such a short interval. The figure also shows that the TCA-soluble and phospholipid curves intersect at their peaks, giving a Zilversmit product-precursor relationship. There is no significant change in the total phospholipid-phosphorus values.

The effect of the intramuscular administration of growth hormone is shown in Fig. 1*B*. Ten patients received 100 mg daily in four divided doses. The treatment curve is flatter than the control curve, and the plasma-phospholipid phosphorus is significantly decreased. These changes, both of curve and level, were constant in direction in each patient studied and indicate a decrease in the rate of plasma-phospholipid formation. This decrease was the only metabolic effect of growth hormone observed. There was no clinical change, nitrogen retention, or alteration in glucose tolerance.

The study of the effect of increased secretion of growth hormone was made in a series of 16 patients with typical acromegaly. The results are shown in Fig. 1*C*, in which a composite curve for 20 control patients is compared with a composite curve for 16 acromegalics. The crossbars represent the standard deviation for each point in time. The phospholipid curves of the acromegalics are lower, and the specific activity curve of the TCA-soluble fraction does not intersect the peak of the phospholipid curve as it does in normals. This was true in each individual case. The *F* test of variance showed that the difference between the groups is highly significant. The total phospholipid-phosphorus values were not abnormal.

The agreement between the results obtained with administered growth hormone and those found in acromegaly suggests that growth hormone decreases the rate of formation of plasma phospholipid. Since the total value does not fall in acromegaly, the destruction of plasma phospholipid must also be slow, indicating a slow phospholipid turnover in this condition. This is the only constant metabolic effect of growth hormone thus far demonstrated in man.

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References

1. W. E. Cornatzer and D. Cayer, *J. Clin. Invest.* 29, 534 (1950).
2. N. R. Diluzio, M. L. Shore, D. B. Zilversmit, *Metabolism Clin. and Exptl.* 3, 424 (1954).

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The person who won't take advice isn't necessarily any more stubborn than the one who is offering it.—Anon.