Lymphocytic Response of Normal Individuals to Transient Hyper- and Hypoglycemia. (17929)

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(Introduced by Co Tui)

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Prompt secretion from the adrenal cortex is elicited by a great variety of stress phenomena(1). The increase in the level of 11-oxycorticosteroids thus produced, causes a reduction in the absolute lymphocyte count, which correlates well with the reduction in adrenal cortex cholesterol level(2). As this latter level is a good index of adrenal cortical activity(3) the lymphocyte response can be used as an indicator for the same purpose. Lymphocytopenia is produced in normal animals(4) and man(5) by the oral administration of glucose, but not in adrenalectomized animals or in Addisonian patients(6). Similarly, hyperglycemia after oral or intravenous glucose in dogs, causes eosinopenia(7), indicating increased adrenal cortical activity. Insulin, administered in sufficient dosage to produce shock, also causes lymphocytopenia both in animals(8) and man(9). However, recent observations showed that, in the rat, adrenal cholesterol increased following oral glucose, and decreased after insulin hypoglycemia(10). Since these results partially contradict those quoted previously, a study in the human of the effect on the absolute lymphocyte response of hyperglycemia and moderate hypoglycemia was attempted.

Materials and methods. Fasting capillary blood samples for glucose were obtained from 6 non-diabetic individuals of average weight and nutritional status. After receiving 25 g of 50% glucose solution intravenously, capillary blood for glucose determinations was collected at 30, 60, 120, and 180 minutes, and simultaneously, samples for the total white blood cell count and for smears for differential counts were taken. Five individuals of this group, and 3 additional persons of similar status, received 0.075 unit of regular insulin per kilo of body weight intravenously. Capillary blood was withdrawn immediately before injection of insulin, and after 20, 30, 45, 60, 90, 120, and 150 minutes, for glucose determination, for total white cell count, and for smears for differential counts. The blood sugar was determined by the Folin micro-method(11). The percentage of lymphocytes was determined by taking the average of three differential counts of 300 cells each.

Results. The blood glucose level at ½ hour was within normal limits for all individuals, and then declined to fasting values at the end of 2 hours. The absolute lymphocyte count decreased in all cases after glucose administration. In 4 patients the lowest count was reached within ½ to 1 hour. In one individual, the lowest level was not reached before 2 hours, and in another person, there was a marked drop at 1 hour, and a second peak drop at 3 hours. The mean rise of blood sugar level compared with the mean decline of absolute lymphocyte count is seen in Fig. 1.

The lowest blood sugar level, after insulin,

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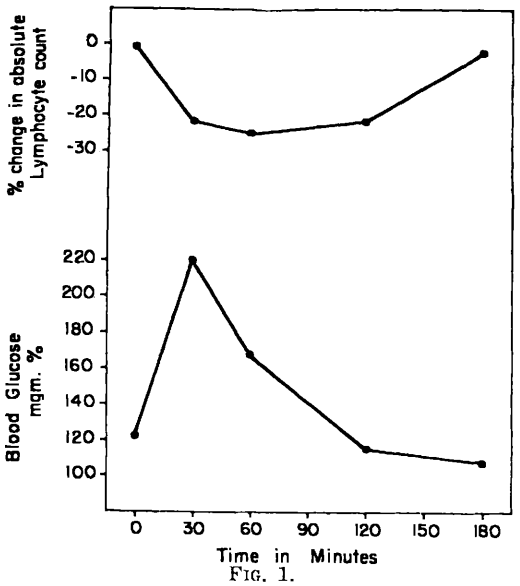

FIG. 1.

Mean percentage change of absolute lymphocyte count in 6 patients following intravenous administration of 25 g of glucose as 50% solution.

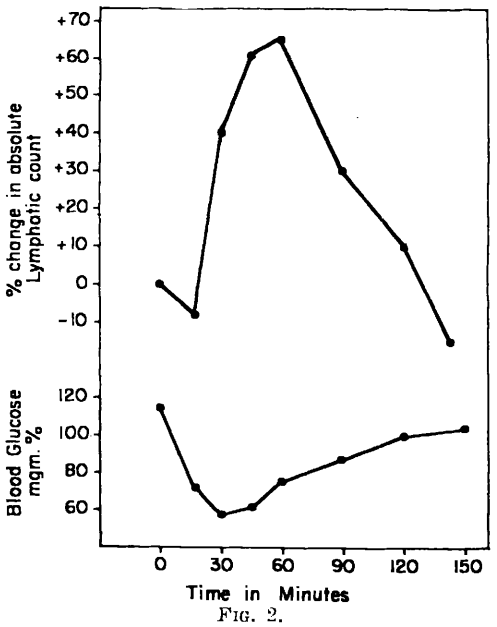

FIG. 2.

Mean percentage change of absolute lymphocyte count in 8 patients following intravenous administration of 0.075 unit of regular insulin per kilo of body weight.

was reached within 20 to 30 minutes, whence it rose gradually. Seven out of 8 individuals showed a marked absolute lymphocytosis, which reached its peak at 45 or 60 minutes. In one subject, the rise was delayed until 120 minutes. In 4 persons the absolute lymphocyte count started to rise immediately, whereas in the other 4 cases, there was an initial small drop followed by a rise. None of the patients showed symptoms of insulin shock. The mean values of blood sugar levels and per cent changes in absolute lymphocyte counts are shown in Fig. 2.

Discussion. From the data it appears that, in the normal individual, administration of glucose causes lymphocytopenia, whereas moderate insulin hypoglycemia causes lymphocytosis. It may then be assumed that hyperglycemia stimulates, whereas moderate insulin hypoglycemia inhibits, adrenal cortical secretion. Our findings do not coincide with those of other investigators(8,9) who reported lymphocytopenia after administration of insulin. This apparent discrepancy may be attributed to the fact that the dosage used by them was sufficient to produce shock, whereas with the dosage employed by us, none of the individuals showed symptoms of hypoglycemia, thus avoiding the stress factor. The role of the adrenal cortex in the mechanism for the regulation of the blood sugar level has not as yet been clarified. It is usually considered to oppose the action of insulin, and to raise the blood sugar level. Our observations, however, suggest a response of the adrenal cortex both to hyper- and hypoglycemia, within physiologic limits, which helps to maintain homeostasis. A similar view has been expressed by others(12,13) on the basis of animal experiments. In support of this hypothesis, are the observations that cortical extracts retard the fall of glycogen in perfused livers(14), and that there is, in experimental animals, an inhibition of adrenalin hyperglycemia by cortin(15), thus indicating an anti-glycogenolytic activity for the cortical hormone. In addition, when glucose and 11-oxysteroids are administered to

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the adrenalectomized animal, more liver glycogen is deposited than when either is administered alone(16).

These findings suggest that the stimulation of secretion of adrenal cortical hormone by exogenous glucose, in the normal individual, allows more of the administered glucose to be taken up by the liver and stored as glycogen, thus enabling the blood sugar level to return rapidly to normal. On the other hand, the inhibition of the adrenal cortex caused by hypoglycemia should tend to restore the blood sugar level to normal, probably by allowing glycogenolysis to take place.

There is an alternative explanation of the lymphocytosis after insulin, based on the finding that initially epinephrine administration causes lymphocytosis(17). This explanation is, however, partially negated by the fact that adrenodemedullated animals exhibit a normal insulin tolerance curve(18), and it is therefore unnecessary to assume that moderate hypoglycemia elicits epinephrine production.

Summary. The intravenous administration of 25 g of glucose in 50% solution was accompanied by a significant lymphocytopenia which reached its lowest level at ½ to 1 hour in 5 normal subjects and at 2 hours in the sixth. The intravenous administration of 0.075 unit of regular insulin per kilo of body weight evoked a significant absolute lymphocytosis which reached its peak at 45 to 60 minutes in 7 normal persons, and at 120 minutes in the eighth. The lymphocytopenia after glucose administration is inferred to be a result of adrenocortical stimulation caused by the change in the blood sugar level. The absolute lymphocytosis after insulin is similarly assumed to result from adrenocortical inhibition due to the moderate hypoglycemia. The discrepancy between our findings and those of others, who noted a decrease of lymphocytes following insulin, is explained by the small amounts of insulin used by us, thus avoiding shock and concomitant adrenocortical stimulation. This study suggests that the response of the adrenal cortex to hyper- and hypoglycemia serves to maintain homeostasis.

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A Small Bore Polythene Shunt to Prevent Mechanical Shock after Prolonged Cross-Clamping Thoracic Aorta.* (17930)

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Prolonged cross-clamping of the patent thoracic aorta distal to the left subclavian artery is uniformly followed by severe neurological and visceral damage(1,2,3,4,5). Initially, the injury is not dependent upon cardiac failure, but upon the effect of diminished circulation to those susceptible structures distal to the cross-clamped area. Later effects are consistent with a progressive reduction in an effective circulating blood volume as this fluid pools in the anoxic, hypotensive region(1). It is therefore necessary

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