

## 11180 P

**Influence of Estrogen on Insulin Requirement of the Diabetic.**

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This study consists of a series of 9 diabetic women taken from the Metabolic Service of Sea View Hospital. The patients were chosen without regard for an indication for estrogen therapy. They were followed for a period of one year: 4 months before the beginning of estrogen, 5 months during its administration, and 3 months after it had been discontinued. Estrogen was administered intramuscularly in doses of 10,000 International Units twice a week for a period of 4 months.

During the 4 months before estrogen therapy a definite effort was made to maintain the individual insulin dosage at the lowest level compatible with proper control of the diabetes. A patient was considered well controlled when in the absence of acetonuria there was less than 1% of sugar in each of the partition specimens of urine and the total amount of sugar spilled in a period of 24 hours was less than 20 g. To meet these requirements it was necessary to increase our daily insulin dose steadily from 63 units at the beginning of this period of observation to 84 units at the end of this 4-month period.

Two weeks after estrogen was instituted the average daily insulin requirement started to show a significant decline so that during the 5 months in which our patients were receiving estrogen there was a drop in the daily average insulin requirement from 84 to 54 units, representing a saving of 35%.

At the end of this 5-month observation period estrogen was discontinued. The patients were then followed 3 months longer. There was a gradual increase from an average daily requirement of 54 units at the beginning of this time to 63 units at the end. This final figure is still 25% lower than the "pre-estrogen" level of 84 units daily.

The type of insulin used did not influence the results obtained during the administration of estrogen for the percentage of insulin saved in the patients receiving regular insulin and in those on protamine zinc insulin was identical. The patients on regular insulin showed a decrease in the daily average insulin dose of 47%, a drop from 117 to 60 units daily. The requirements for those on protamine zinc insulin showed a decrease from 64 to 34 units daily, again a saving of 47%.

The age of the patient, however, did influence the results obtained with the administration of estrogen. In the premenopausal patients there was a daily insulin saving of 63% represented by a decrease in the daily average insulin requirement from 48 units to 18 units. In the postmenopausal patients, on the other hand, the "pre-estrogen" requirement of 108 units daily fell only 41% to 63 units daily during the administration of estrogen.

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**Diurnal Variations in the Acid-Base Balance.**

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Interpretation of abnormal variation in the acid-base balance of the blood presupposes a definition of what constitutes normal variations. There has been accumulated in the past a large amount of data on the pH, the serum bicarbonate concentration and the CO<sub>2</sub> tension of the blood of normal individuals. It is generally regarded that if, in arterial blood, the pH is between 7.35 and 7.45, the bicarbonate between 24.5 and 27.5 mM per liter, and the CO<sub>2</sub> tension between 40 and 45 mm, a normal acid-base balance of the blood is indicated.

Shock and Hastings,<sup>1</sup> in a series of 131 determinations on 57 normal individuals, found that the variation from individual to individual was no greater than the variation found in a single individual on repeated observations. Whether or not the acid-base balance of the blood of a single individual varies in any consistent manner during the course of a day is still an open question.

Cullen and Earle<sup>2</sup> made 5 or 6 determinations of the acid-base balance of the blood on 10 individuals between 9 in the morning and 9 at night. They came to the conclusion at that time that there tended to be an alkaline shift during the day, although this was not an invariable finding. Shock and Hastings made hourly observations on each of 10 subjects for a total of 22 experiments between the hours of 9 and 6. These individuals were permitted to go about their usual activities. Some shifts in CO<sub>2</sub> tension, in pH and bicarbonate were

<sup>1</sup> Shock, N. W., and Hastings, A. B., *J. Biol. Chem.*, 1934, **104**, 585.

<sup>2</sup> Cullen, G. E., and Earle, I. P., *J. Biol. Chem.*, 1929, **88**, 545.