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## Relative Efficiency of Commercial Forms of Insulin.

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Protamin zinc insulin preparations are known to exert an effect more prolonged than that of equal unitage of unmodified (regular) insulin. Recently claims have been offered that the effect of insulin in the form of zinc insulin crystals is similarly prolonged, but in lesser degree. The issue has been confused through the use of clinical observations as the basis for reported conclusions. In view of the many factors which can influence the quantitative response to insulin, the need for standardized conditions of study is apparent. If human subjects are to be used, the constancy of insulin requirement should be established through the use of prolonged control periods wherein daily fluctuations of blood sugar are known.

It has been demonstrated recently[1] that with suitable treatment, the insulin requirement of the diabetic child decreases sharply, once aglycosuria is established, the final daily insulin requirement being 30 to 70% lower than that commonly given under customary methods of treatment. Once such stabilization has been accomplished, the child's insulin requirement is relatively constant and he can be maintained for long periods of time in a state of aglycosuria, with relative freedom from shocks and with blood sugar values which approach those of the normal non-diabetic child. Such a subject is eminently suitable for the study of variations in effectiveness of different insulin preparations. The amount of fluctuation of blood sugar values during the 24 hours can be used as an objective method of comparison.

The diurnal blood sugar fluctuation of 12 diabetic children has been studied when the insulin requirement has been given as regular insulin, protamine zinc insulin, and zinc insulin crystals. The studies have involved a total of 1074 days and 1967 determinations of blood sugar.

It was not possible to stabilize the insulin requirement of diabetic children through the use of protamine zinc insulin. Once stabilized, however, when the total insulin requirement did not exceed 1 unit

[1] Jackson, R. L., and Boyd, J. D., Trans. Soc. Clin. Research, Chicago, Nov., 1938, *J. A. M. A.*, 1939, **112**, 1017.

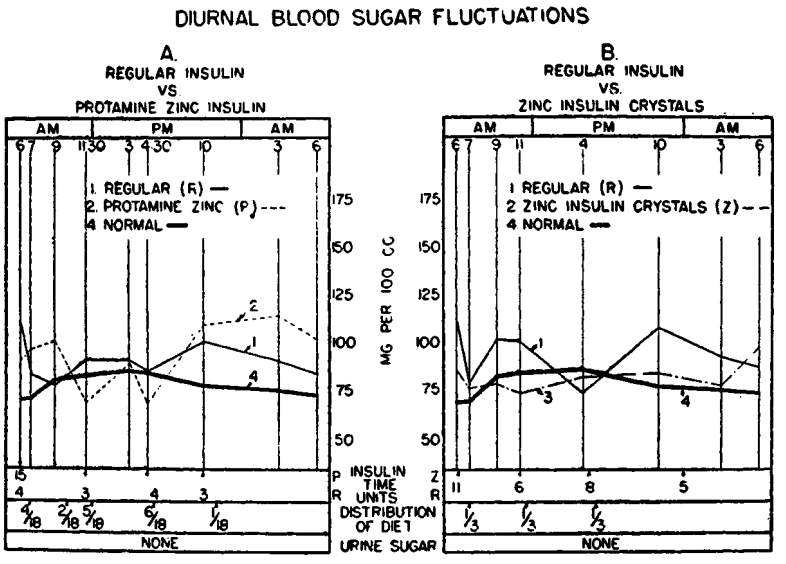


FIG. 1.

Illustrative diurnal blood sugar fluctuation in stabilized diabetic children receiving equivalent unitage of various types of insulin, other factors constant. In each instance the regimen had been constant for several days before the blood sugar values were determined.

A. Blood sugar fluctuations of 10-year-old diabetic girl given
   (1) regular insulin
   (2) protamine zinc insulin
B. Blood sugar fluctuations of 13-year-old diabetic girl given
   (1) regular insulin
   (2) zinc insulin crystals

The heavy line 4 in each chart indicates average blood sugar values observed in non-diabetic children under a comparable dietary regimen. The Folin-Wu blood sugar method was employed, using blood from the finger and Somogyi's method for precipitation of non-sugar reducing substance.

for each kilogram of body weight or a total of 20 units daily, single doses of protamine zinc insulin maintained the blood sugar at approximately normal levels as is shown in Chart A.

When zinc insulin crystals* were substituted for regular insulin, in the same unitage and using the same time of administration (Chart B), no clinically significant prolongation of action was observed. It was possible to interchange regular insulin and zinc insulin crystals at will and repeatedly without altering the customary zone of diurnal blood sugar fluctuation.

* Supplied through the courtesy of Eli Lilly and Company.