THE INFLUENCE OF VITAMIN C DEFICIENCY UPON THE RESISTANCE OF GUINEA PIGS TO DIPHTHERIA TOXIN

GLUCOSE TOLERANCE¹

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It has been shown in a number of laboratories that a deficiency of vitamin C is accompanied by a decreased resistance against infections and the injuries resulting from bacterial toxins, as cited in recent reviews (1, 2). It is particularly significant that the lowered resistance can be shown in the zone of depletion before there are signs of scurvy and before there is a marked cessation of growth in young animals. For example, guinea pigs on a severely restricted vitamin C intake (non-scorbutic) and injected with sublethal doses of diphtheria toxin show more extensive tissue damage, greater loss in weight, shorter duration of life (3), larger areas of necrosis, and poorer tooth development (4) than similarly injected animals receiving a more liberal vitamin C intake. The mechanism of detoxification in vivo is probably due to the better nutritional level of the animals, rather than to direct molecular reaction of the vitamin on the toxin. We were unable to confirm earlier reports of detoxification by the vitamin in vitro, except by a non-specific effect of the acid (5).

While studying the effects of sublethal injections of diphtheria toxin on the tissues of guinea pigs on different vitamin levels, King and Menten (3) observed that animals on the low vitamin level developed hydropic degeneration of the islets of Langerhans

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Buckley (6) suggest that the observed phenomena are due to an overstimulation of the adrenal and thyroid glands. Yannet and Darrow (9) stress the significance of hepatic injury and relate the dysfunction to the changes in glycogen forming and glycogen storing ability of the liver. It appears more probable to us that there is a disturbance of essentially the whole organism, and particularly, of the entire endocrine system, as suggested by Elkeles and Heimann (6). When one considers that the glandular tissues are particularly rich in vitamin C, it is not surprising that a partial deficiency of this substance may markedly impair the metabolic processes before scurvy becomes manifest.

Of the groups receiving 2 injections of 0.2 M.L.D. each (table 2) the one on a higher nutritional level showed the greatest disturbance 5 days after the start of toxin injections, and partial recovery 3 days later. The low vitamin group showed an increasing disturbance through the 8th day after the first injection. A comparison of the 120-minute blood sugar values shows most clearly the difference in degree of disturbance and extent of recovery. A similar contrast may be observed for the two groups receiving 0.6 M.L.D. (table 3).

SUMMARY

The glucose tolerance test was used to study the effect of different levels of vitamin C intake on the carbohydrate disturbance in guinea pigs caused by diphtheria toxin. The degree and duration of dysfunction was influenced to a significant degree by the state of nutrition of the animals. Sublethal injections of toxin caused a greater disturbance in animals receiving only enough vitamin to prevent scurvy, compared to those receiving a more generous supply. It is evident from the data presented that the level of vitamin C intake for optimum in vivo detoxification of diphtheria toxin is considerably greater than that necessary to protect from scurvy or to show a favorable growth rate.

REFERENCES

- (1) CLAUSEN: Physiol. Rev., 14, 309, 1934.
- (2) KING: Physiol. Rev., 16, 238, 1936.

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