Rate of Disappearance From Plasma of Intravenously Administered Methionine in Patients With Liver Damage[1]

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In a previous paper (*2*) it was reported that following the intravenous administration of 1.5 gram of DL-methionine to normal male subjects, a predictable disappearance of the L isomer occurred over a 2½-hour interval.

It was postulated that protein metabolism in patients with liver disease might be sufficiently impaired to decrease significantly the rate of disappearance of the L isomer from the plasma, and that if such proved to be the case, the rate of removal might be construed as the rate of utilization, *i.e.* anabolism or catabolism, exclusive of diffusion or storage.

organism *Leuconostoc mesenteroides* P-60, which detects only the L isomer (*1*). In the majority of cases here reported, assays were simultaneously performed with *Lactobacillus fermenti* 36, which utilizes both D and L isomers (*1*). Urinary methionine was determined on an aliquot of a sample collected over the 12 hours preceding the test, for the 3-hour period during the test, and for the 43 hours after its completion. For the 24-hour period immediately preceding and the 48-hour period following the test, the dietary intake of methionine was maintained at an essentially constant level.

The findings in all controls and in the first 13 patients with liver damage studied are presented in this preliminary report. The rate of disappearance per hour over the 30–180-minute period has been adopted as the index of methionine utilization. All these data, together with other "liver function" values for comparative purposes, are presented in Fig. 1. Study of this graph reveals the following:

(a) With the exception of one high value, the rate of removal in the control subjects varies from 330 to 540 μg./hour with a mean of 410. Additional data obtained since completion of this diagram both in controls and in completely well posthepatitis patients, confirm this range and mean.

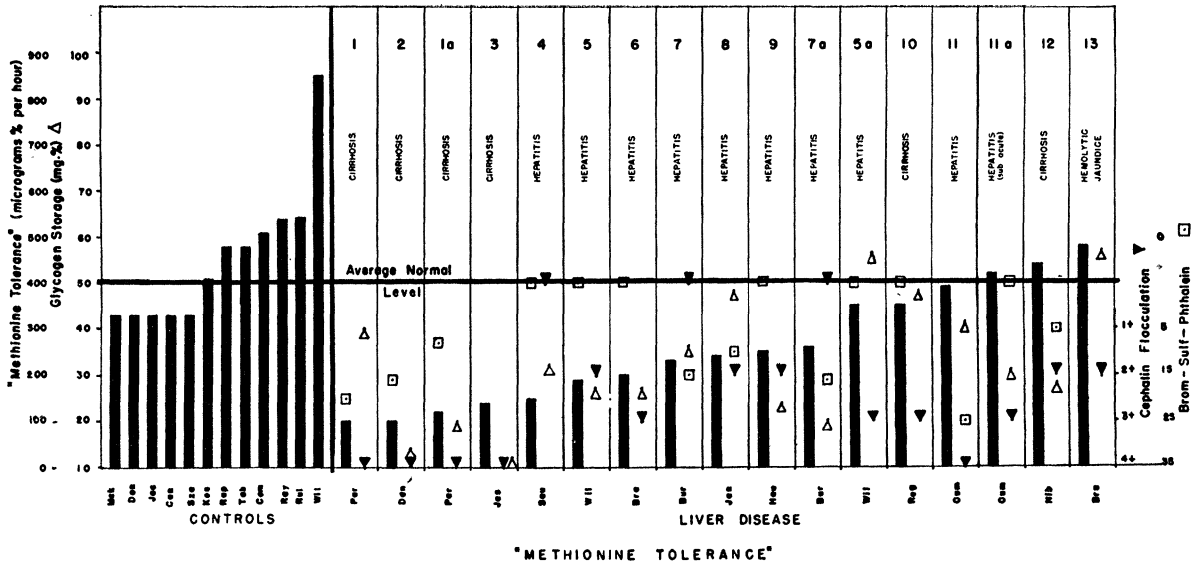

FIG. 1. Columns represent rate of disappearance of plasma methionine in micrograms per cent per hour.
1 and 1a—Values in the same cirrhotic at a 6-week interval—note constancy of all findings. Clinical status unchanged.
7 and 7a—Acute hepatitis patient, 2-week interval; still active hepatitis. A third value obtained 2 weeks later was within normal limits (340 μg./hour)
5 and 5a—Acute hepatitis, 3-week interval—note correlation with glycogen storage index.
11 and 11a—Patient with subacute hepatitis, 12-week interval; considerable fibrosis and round cell infiltration in biopsy specimen.

The same technics were used in the individuals with liver damage as in the normal controls (*2*). These procedures consisted, in brief, of administering 50 cc. of 3 per cent DL-methionine intravenously over a 5-minute period and then determining the plasma L-methionine values at 0 (fasting, premethionine), 15, 30, 60, 120, and 180 minutes postmethionine.

Microbiologic assays for methionine on both blood and urine were carried out as previously described (*2*), using as a test

(b) With rare exceptions, patients with acute or chronic liver damage show a significant decrease in the rate of removal of the administered methionine.

(c) Hepatitis patients progress from abnormal to normal values during convalescence.

The data on urinary excretion of L- and DL-methionine, and on blood levels of D (DL- minus L-)-methionine will be considered in detail in a later paper. On the basis of data so far obtained one may, however, make the following statements:

(a) Urinary excretion of L-methionine in normal individuals and in patients with liver damage is minimal, in no instance exceeding 6 mg. during the 3-hour postinjection period.

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The methionine used in this study has been supplied through the courtesy of the Wyeth Company.

(b) D-methionine, on the other hand, is excreted rapidly, during and following the intravenous administration of the DL-preparation, up to 35 per cent of the administered dose being excreted during the 3-hour test period. This is of obvious importance in a consideration of the net retention of an administered dose of the DL compound. The blood levels show a higher initial peak than in the case of the natural isomer with a more rapid rate of disappearance, which is at least in part referable to rapid excretion.

It is thus concluded that the rate of removal of intravenously administered L-methionine serves as an index of liver function.

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A Chemical Control of Seedstalk Development in Celery[1]

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Premature seeding, commonly called "bolting," poses as one of the most serious problems in the production of early celery. Cold spring weather, conducive to bolting, frequently follows field transplanting of the early crop. The plants, normally biennial, react as annuals, frequently developing seedstalks the first year if they are repeatedly exposed to temperatures below 50° F. (*2*). Attempts which have only partially overcome the adverse effects of low temperatures include the use of various field protective coverings, the introduction of strains having nonbolting tendencies, and late planting after danger of cold weather has passed—all of which result in either considerable loss or expense to the grower. On the assumption that some chemicals of the plant growth hormone type might have the faculty to affect flowering and subsequent seedstalk development in celery, the following experiment was designed.

Celery (Cornell 19, Stock No. C 6313, Ferry Morse) was sown in the greenhouse January 28, transplanted March 5 into 3-inch clay pots, and held at a minimum night temperature of 60 ± 1° F. On April 4 the potted seedlings, arranged in groups of 20, were sprayed with various concentrations of several growth-regulating substances. Ten treatments and a control were compared. Water sprays of the various chemicals were applied by means of small household sprayers, care being taken to insure complete coverage of all aerial plant parts. Thirty-six hours following spraying, one-half of each group was removed to a cold frame, where the plants were exposed to minimum night temperatures of 41 ± 2° F. The other half remained in the greenhouse at the night temperature of 60° F. On May 26, both lots were transplanted into the open in muck soil as two randomized replications for each of the two temperature treatments. The four blocks were adjacent, and each plot contained 5 plants.

Seedstalk development was evident after one month on control plants which received the cold frame exposure. By July 13, two and one-half weeks later, 80 per cent of the plants had bolted. Seeding was 100 per cent by August 21, and mature seed was present on the same plants September 1. In sharp contrast, celery plants sprayed with 100 ppm of α-o-chlorophenoxypropionic acid (*4*) showed no evidence of seedstalk development throughout the experiment. All plants so treated remained strictly vegetative and attained a marketable size (Fig. 1).

Similarly, seeding on the control celery plants from the warm greenhouse occurred by August 20, and on September 30, 80 per cent had bolted. Again, without exception, those plants which had received the spray of α-o-chlorophenoxypropionic acid, yet otherwise identically treated, remained vegetative.

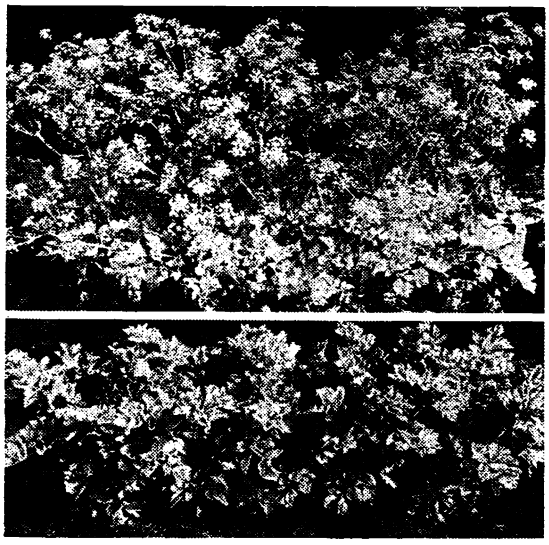

FIG. 1. Prevention of premature seeding of celery by treatment of plants with α-o-chlorophenoxypropionic acid. *Above*: Controls (no treatment). *Below*: Treated plants four months after treatment.

The supposition that organic chemicals having the properties of phytohormones might be introduced into a plant at different stages of growth and affect its development was formulated by Cholodny (*1*). Van Overbeek's recent work (*3*) on the control of flowering in the pineapple supports this concept. It is now a well-known fact that physiological manifestations resulting from the action of growth regulators on plants are dependent on concentration as well as on qualitative differences in the various chemicals. We have assembled evidence demonstrating that, for a given plant, the same substance may accelerate or retard flowering, as the case might be, depending on the concentration used. Our data strongly suggest possibilities in controlling seedstalk development (flowering ?) in certain vegetable crops by applying hormone-like chemicals before the temperature-induction of flowering occurs. A continuance of these studies with the many practical ramifications as objectives should be fruitful in providing a key to some of the causal factors in the flowering process in higher plants.

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