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Studies on the Secondary Malabsorption Syndrome with Special Reference to the Therapeutic Effects of Festal

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With 9 figures and 3 tables

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Since ADLERSBERG (1) presented a detailed monograph on the malabsorption syndrome, the authors have been much interested in the problems of digestion and intestinal absorption, from the standpoint of gastroenterology. Various nutrients must be digested to absorbable units prior to intestinal absorption.

In general, the disturbance in intestinal absorption is known clinically as the malabsorption syndrome. The classification of the malabsorption syndrome has been attempted by FIRST (2), GREEN (3), ADLERSBERG (4) and POLLARD (5). Among them, POLLARD's classification (Table 1) is clinically the most valuable. Until 1959, the primary malabsorption syndrome had not been seen in Japan. The first case of primary sprue in Japan was reported by YAMAGATA and ISHIKAWA in Tohoku district in 1960. Primary sprue still seems to be a very rare disease in Japan.

Table 1. Classification of Malabsorption Syndrome after POLLARD, H. M.

- I. Primary Malabsorption (Primary Sprue)
 - A. In children Celiac Disease (GEE-HERTER's disease)
 - B. In adults Idiopathic Steatorrhea
 - 1. Tropical Zone Tropical Sprue
 - 2. Temperate Zone Nontropical Sprue (Idiopathic Steatorrhea)
- II. Secondary Malabsorption (Secondary Sprue)
 - A. Proliferative Infiltrative Diseases
 - 1. Enteritis Idiopathic, Tuberculous, Regional Enteritis, Ulcerative Colitis
 - 2. WHIPPLE's Intestinal Lipodystrophy
 - 3. Amyloidosis, Scleroderma etc.
 - 4. Tumors Malignant Lymphoma, HODGKIN's Lymphosarcoma
 - B. Congenital or Postoperative Disturbances
 - 1. Blind Loop Formation
 - 2. Massive Resection of Intestinal Tract
 - 3. Subtotal Gastrectomy
 - 4. Fistula Formation
 - C. Hormonal Disturbance Dysfunction of Hypophysis and Adrenals

III. Errors of Digestion

A. Pancreatic Disease

- | | |
|----------------|---|
| 1. In children | Cystic Fibrosis of Pancreas |
| 2. In adults | Inflammation, Tumor of Pancreas, Postpancreatectomy |

B. Diseases of Liver and Gall-bladder (Malabsorption usually minimal)

- | | |
|-----------------|------------------------------|
| 1. Intrahepatic | Cirrhosis of Liver |
| 2. Extrahepatic | Common Bile Duct Obstruction |

The second type of malabsorption is called secondary malabsorption and observed rather often even in Japan. The third type of malabsorption is that due to errors of digestion. The pancreatic diseases and the diseases of the gall-bladder are the common digestive diseases in Japan. The malabsorption syndrome usually occurs more or less in the diseases of this type.

In this report, the authors include the second and the third group under the name of "Secondary Malabsorption Group", because they often coexist and the differential diagnosis is not usually very easy.

Methods for the Experiment

1. Digestion state of stool.

An aliquot of the specimen was obtained from the stool of a patient having deficient digestion. The specimen was placed on the slide and stained by Lugol solution and Sudan III solution in order to test the presence of undigested starch granules and fat drops. Then, the specimen was observed microscopically.

2. ^{131}I -triolein test.

Though many absorption tests have been reported, ^{131}I -triolein test for fat absorption and ^{131}I -albumin test for protein absorption can be used in the routine work. Practically, ^{131}I -triolein tests are commonly used and most reliable. Since there are several modifications of this test and a commercial preparation of ^{131}I -triolein is unavailable in Japan, a standardized method is not established yet.

The procedure of the authors' modification of ^{131}I -triolein test is as follows: First, 10 drops of Lugol solution were given daily with about 100 ml of water for 2 days. Blood ^{131}I level after the oral administration of ^{131}I -triolein depends upon the rate of utilization, the rate of urinary excretion and the thyroid uptake as well as upon the rate of absorption. So, it is necessary to block the thyroid with Lugol solution prior to the administration of test meal.

On the third day, at 3 a. m., the same dose of Lugol solution was given after defecation and urination, followed by the oral administration of 1 ml per 1 Kg body weight of test meal. The true dose intake was calculated by the subtraction of the counts remaining in the cup from the counts in cup before drinking. The test meal consisted of 200 ml of peanut oil, 200 ml of water and 15 ml of tween 80, containing about 25 μc of ^{131}I -triolein per 50 ml of the test meal, in accordance with SPENCER. (7) The breakfast should not contain excessive fat and be taken at 9 a. m.

A blood sample was taken by venipuncture using anticoagulant and 1 ml of it was subjected to radioactivity count with the aid of NaI-well type scintillation counter.

Feces sample should be collected in the special vessels for 3 days and at least 3 times when constipated. Be careful to avoid the mixing of urine into the feces sample. The calculation formula was as below:

$$\text{per cent excreted in stool} = \frac{\text{counts in stool-background}}{\text{counts of standard} \times \frac{\text{body weight}}{50} - \text{counts in cup}} \times 100$$

3. ^{131}I -oleic acid test

^{131}I -triolein test is influenced by the disturbance of digestion as well as the disturbance of absorption, as shown in Fig. 2. In order to exclude the influence of digestion, consequently, ^{131}I -oleic acid test should be used.

^{131}I -oleic acid test was performed similarly to ^{131}I -triolein test, but the composition of test meal is a little different. The test meal was made of 200 ml of oleic acid, 200 ml of water and 15 ml of tween 80, containing 25 μC of ^{131}I -oleic acid in 25 ml of test meal. 0.5 ml per Kg body weight of the test meal were administered orally. Other conditions were exactly the same as for the ^{131}I -triolein test.

4. In a series of cases where the above methods were investigated, the results of treatment with Festal were also assessed by the same methods. A Festal¹⁾ dragée contains 192 mg of pancreatic enzymes, such as lipase, amylase, and protease, as well as 25 mg of bile constituents. These active principles break down fats, starches, and proteins so that they can be readily absorbed by the intestine. Festal also contains hemicellulase which promotes the breakdown of vegetable roughage.

Results

1. The effect of Festal on the digestive state

The effect of Festal on the digestive state of the stool was examined microscopically by the method described above. Festal was administered as 3 to 6 tablets a day to the patients with digestive insufficiency. As shown in Table 2, undigested fat drops or starch granules in stool fully disappeared when Festal was administered.

Table 2. The effect of Festal on the digestive state
(total 30 cases)

	without Festal	with Festal
fat	17 / 30	0 / 30
starch	25 / 30	0 / 30

2. The effect of Festal on the symptoms caused by deficient digestion

As shown in Table 3, symptoms caused by deficient digestion, such as heartburn, anorexia and meteorism disappeared or decreased after Festal, 3 to 6 tablets a day.

Table 3. The effect of Festal on the symptoms
(total 30 cases)

	without Festal	with Festal
heartburn	5 / 30	1 / 30
anorexia	15 / 30	3 / 30
meteorismus	21 / 30	2 / 30

3. ^{131}I -triolein test in the secondary malabsorption group

Radioactive ^{131}I -triolein test was performed on 20 cases of secondary malabsorption group and 20 cases of a control group, including stomach ulcer,

¹⁾ Festal is the registered trademark of Farbwerke Hoechst AG.

duodenal ulcer, gastritis, etc. In accordance with Spencer, the excretion ratio in the stool was evaluated as follows; within 2%, normal; within 4%, border-line; over 4%, elevated.

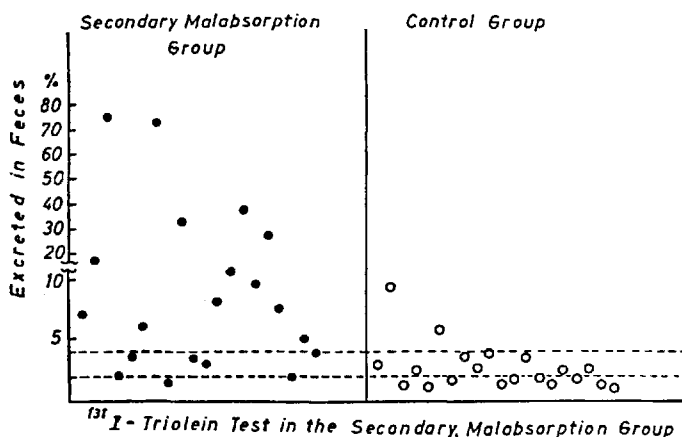


Fig. 1. Vide text

In the malabsorption group, 13 cases were elevated, 6 cases on border-line and only one case was normal, as shown in Fig. 1. On the other hand, 2 cases were elevated, 8 cases on border-line and 10 cases were within normal limits, in the control group.

4. ¹³¹I-oleic acid test in the secondary malabsorption group

Radioactive ¹³¹I-oleic acid test was performed on 10 cases of secondary malabsorption group and 10 cases of the control group. The results obtained are shown in Fig. 2, but no definite conclusion was obtained because the number of cases was so small.

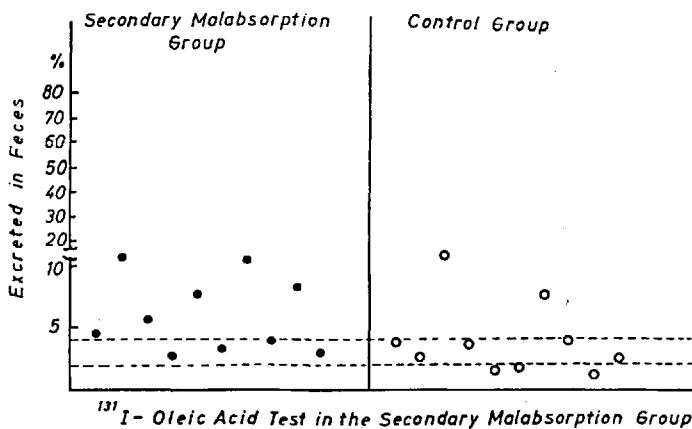


Fig. 2. Vide text

5. Effect of Festal on the excretion ratio in stool with ¹³¹I-triolein test

The effect of the combined drug 'Festal' was observed in the secondary malabsorption group and the control group with the aid of ¹³¹I-triolein test.

First, ^{131}I -triolein test was performed on the malabsorption group without administration of Festal. Then, Festal was administered 6 tablets a day for 2 days. On the following day, ^{131}I -triolein test was repeated with Festal. The test meal and 6 tablets of Festal were administered at the same time, and 6 tablets Festal were given daily during the time feces sample were collected.

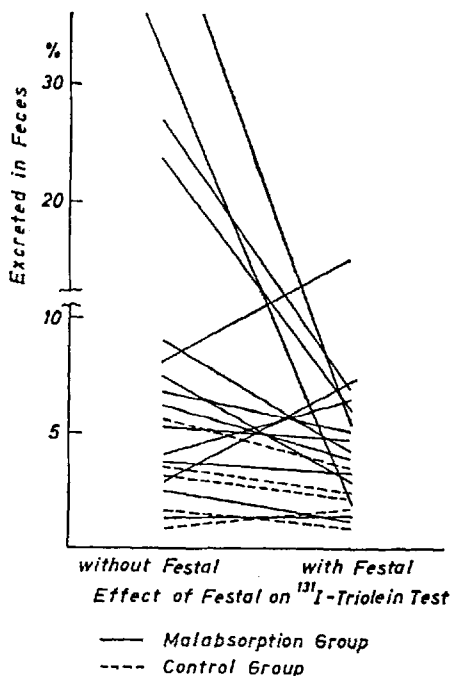


Fig. 3. Vide text

The effect of Festal on the excretion ratio of I^{131} was remarkable, as shown in Fig. 3. Among 15 cases of malabsorption group all except 3 cases were improved. Even in the cases which showed normal values before Festal administration, the excretion ratio in stool was decreased by the administration of Festal.

Discussion

1. Blood ^{131}I level after the administration of ^{131}I -triolein or ^{131}I -oleic acid

After the oral administration of ^{131}I -triolein or ^{131}I -oleic acid, ^{131}I in the blood consisted of inorganic ^{131}I and lipid bound ^{131}I . In this experiment, the authors determined the total ^{131}I in the blood. The height of the blood ^{131}I curve is not so significant, and it does not exactly show the rate of intestinal absorption. As for the absorption test, therefore, the excretion ratio in stool is more exact and more significant than ^{131}I level in the blood. The blood ^{131}I level after ^{131}I -triolein administration showed a characteristic curve in each case. Figures 4, 5, 6 show illustrative cases. The curves were obtained by repeated ^{131}I -triolein tests at intervals of a week. Two time curves have very

similar courses. In most cases the peak of blood ^{131}I level was observed 4 to 6 hours after the oral administration, a few cases show their peaks at 8 hours and a few cases at 2 hours.

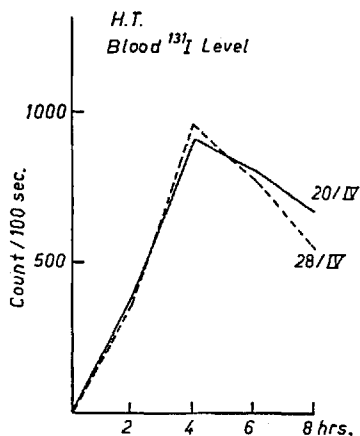


Fig. 4. Vide text

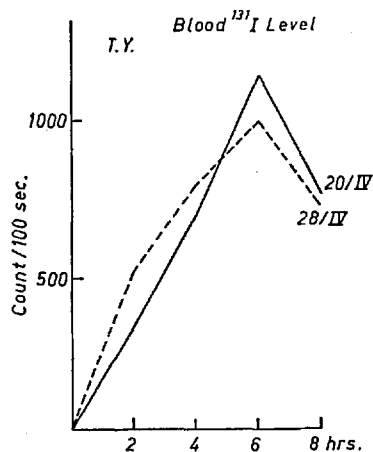


Fig. 5. Vide text

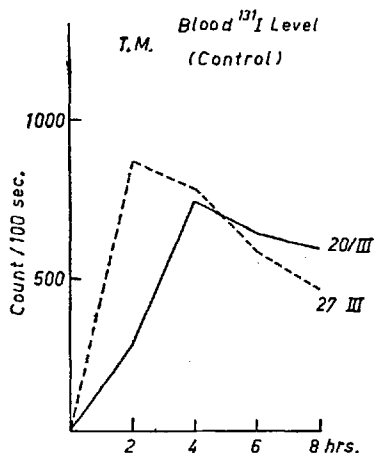


Fig. 6. Vide text

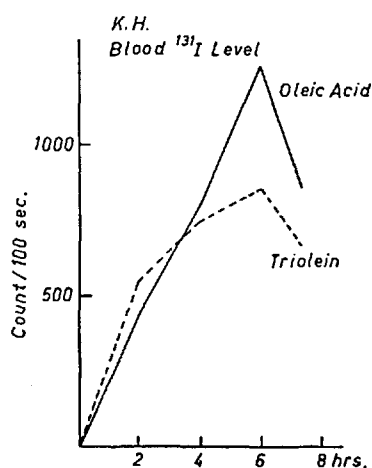


Fig. 7. Vide text

^{131}I curve of blood obtained after the oral administration of ^{131}I -oleic acid revealed a course similar to that obtained after ^{131}I -triolein administration, as shown in Figs. 7, 8, 9.

2. Urinary excretion after the administration of ^{131}I -triolein or ^{131}I -oleic acid

Urinary excretion of ^{131}I after the administration of ^{131}I -triolein or ^{131}I -oleic acid varied independently of the rate of absorption. It seemed to have less value for absorption test.

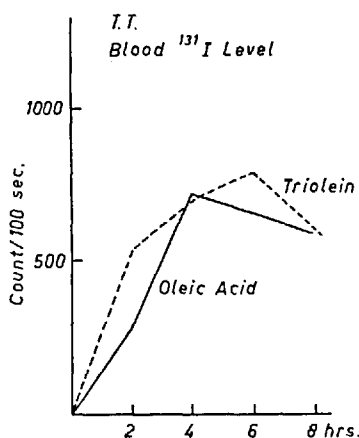


Fig. 8. Vide text

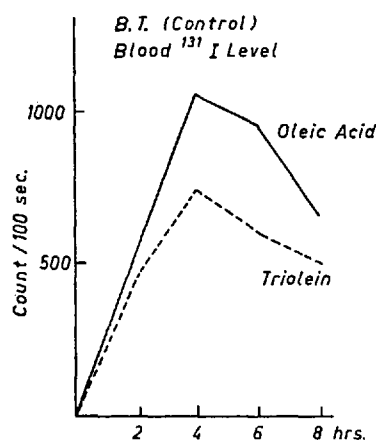


Fig. 9. Vide text

3. Thyroid blockade

Thyroid blockade by Lugol solution was sufficient in the authors' modification. ^{131}I uptake ratio of the blocked thyroid measured by scintiscanner showed less than one-thirteenth of the normal thyroid.

4. Effect of Festal on the deficient digestion

Symptoms caused by deficient digestion and digestive conditions of the stool were much improved by the administration of Festal.

In the absorption tests, the effect of Festal was also remarkable. Three cases of malabsorption group in which Festal had no effect were chronic enterocolitis.

Consequently, Festal is recommended in deficient digestion, especially in pancreatic insufficiency or diseases of gall bladder as well as malabsorption of enteric origin.

Summary

1. Modified ^{131}I -triolein and ^{131}I -oleic acid tests were performed on patients of the malabsorption group.
2. Elevated excretion ratio of ^{131}I in stool was observed in the malabsorption group. So, this test has a diagnostic value in the malabsorption group.
3. Festal showed a remarkable effect on the absorption test in malabsorption group as well as in a control group having a sufficient digestion.
4. Symptoms due to deficient digestion, especially meteorism, were much improved by Festal.
5. Digestive condition of the stool was also improved by the administration of Festal.
6. Festal had no side effects.

Zusammenfassung

1. Bei Patienten mit schlechter Absorption wurden modifizierte I^{131} -Triolein- und I^{131} -Oleinsäure-Tests durchgeführt.

2. Eine erhöhte Ausscheidung von ^{131}T im Stuhl wurde bei diesen Patienten beobachtet. Insofern hat der Test für diese Gruppe diagnostische Bedeutung.

3. Festal bewirkte einen bemerkenswerten Effekt auf den Absorptions-Test bei dieser Gruppe von Patienten, ebenso bei der Kontrollgruppe von Personen mit ausreichender Verdauung.

4. Symptome, welche zu unzureichender Verdauung führen (insbesondere Meteorismus) konnten durch Festal gebessert werden.

5. Die Stuhlzusammensetzung wurde durch die Anwendung von Festal ebenfalls verbessert.

6. Festal zeigte keine Nebeneffekte.

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Alimentary Production of Gallstones in Hamsters

10. The effect of orally ingested bile acids on development of cholesterol gallstones in hamsters fed a fat-free diet with glucose as carbohydrate component *)

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With 3 tables

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Formation of cholesterol gallstones in young hamsters takes place with great regularity when the animals are reared on a fat-free diet in which the carbohydrate source is an easily absorbable sugar such as glucose (DAM and CHRISTENSEN, 1961 a, b, and the present communication).

With a basal diet of this composition the efficacy of dietary additions in preventing formation of cholesterol gallstones can be tested, so that only the most active substances will show a marked effect.

In the present study five different bile acids: cholic, deoxycholic, dehydrocholic, lithocholic and hyodeoxycholic acids have been tested in this way at a dietary level of 0.1 per cent.

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