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## Studies on Glycogen in the Milk-spots of the Omentum.

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### I. Introduction.

The fact that reticulo-endothelial system stands in an intimate relation to the metabolism of organism has been recognized by many authors, Schilling, A. Shiga et al. from the study on fat and Y. Katô, K. Itô, et al. on sugar.

Since, as is well known, milk-spots of omentum are mainly composed of histiocytic cells (of Kiyono) the relation between them and carbohydrate metabolism is an important one. Nevertheless, only a few papers regarding this subject have appeared. E. Seifert studied this function of the omentum and came to the conclusion that the milk-spots keep their function up to the puberty period like the red bone-marrow and there-

after they gradually altered into fatty nodules, fat-reservoirs, as does the yellow bone-marrow. T. Katase and T. Mitsuda reported on the glycogen-formation of histiocytic cells and stated that these cells of the omentum also exhibit polymerizing function as seen in experimental hyperglycemia. Lately, in the research of the omentum by intraperitoneal injection of grape-sugar, E. Fels came to the conclusion that the omentum may be able to polymerize and store directly grape-sugar introduced intravenously, but not that introduced intraperitoneally.

The above two works are too brief to determine the polymeric capacity of the omentum and systematic studies along this line are needed. Especially those on the milk-spots are very important to clear up the function of the omentum.

## II. Methods.

The rabbits were fed with "Tōfukasu," residual of soya-bean cheese, the main part of which is the seed coat of beans. Tissues from the rabbits were passed through graded alcohols up to absolute and were examined as stretched specimens. Best's potassium-carmin method was mostly used for glycogen-stain and Langhan's iodine method and saliva-reaction were also made use of. Blood-sugar was determined by Kasamatsu and Hattori's methylene-blue method. The blood for sugar-test was obtained from the auricular vein, keeping the animal in natural condition without being fastened. Glycosuria was tested by Nylander's and Trommel's methods.

## III. Healthy adult rabbit.

The presence of glycogen in the peritoneal pavement cells was recognized by Arnold and Klestadt. Kiyoshi Satō entertained a view different from that of these authors. Katase stated that in the omentum of the rabbit (one case) some clasmotocytes contain a little glycogen. Further he made observation on the omentum of man, dog and guinea-pig. From his study on an albino rat Fels stated that many methothelial cells in the neighbouring region of the blood-vessels of the omentum contain glycogen.

There has been so far no detailed study on the glycogen contents of normal omentum or its milk-spots and it is very desirable to investigate the power of polymerizing action of the milk-spots by means of experimental hyperglycemia.

Experiment:—

Experimental results on ten full-grown rabbits are shown in Table I.

Cases 8 and 9. Many histiocytic cells of the milk-spots, especially of the follicular and mixed types exhibit numerous Best's positive granules of various sizes. Fine

Table I. Healthy adult rabbit.

| No. of case and sex. | 1 ♀                  | 2 ♂      | 3 ♂   | 4 ♂   | 5 ♂   | 6 ♂   | 7 ♀   | 8 ♂   | 9 ♀   | 10 ♂  |   |
|----------------------|----------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|---|
| Body-weight (gms).   | 1450                 | 1365     | 1690  | 1625  | 1600  | 1530  | 1555  | 1390  | 1415  | 1315  |   |
| Milk-spots           | Hist. cell           | B. p. g. | ±     | —     | —     | ±     | +     | —     | +     | ‡     | — |
|                      |                      | L. p. g. | —     | —     | —     | —     | ±     | —     | ±     | +     | — |
|                      | Mesothelial cell     | B. p. g. | —     | —     | —     | —     | ±     | —     | ±     | +     | — |
|                      |                      | L. p. g. | —     | —     | —     | —     | —     | —     | —     | —     | — |
|                      | Polymorph. leucocyte | Presence | —     | —     | —     | —     | —     | —     | —     | —     | — |
|                      |                      | B. p. g. | —     | —     | —     | —     | —     | —     | —     | —     | — |
|                      |                      | L. p. g. | —     | —     | —     | —     | —     | —     | —     | —     | — |
| Mesentery            | B. p. g.             | —        | —     | —     | —     | —     | —     | —     | —     | —     |   |
|                      | L. p. g.             | —        | —     | —     | —     | —     | —     | —     | —     | —     |   |
| Blood-sugar. (%)     | 0.102                | 0.119    | 0.112 | 0.098 | 0.107 | 0.115 | 0.097 | 0.103 | 0.099 | 0.094 |   |
| Glycosuria.          | —                    | —        | —     | —     | —     | —     | —     | —     | —     | —     |   |

Note: + indicates positive and —, negative; ‡ strong positive; † relatively strong positive, and ± a trace.

B. p. g. and L. p. g. indicate Best's positive granula and Langhan's positive granula, respectively.

granules are scattered diffusely in cytoplasm and relatively coarse ones are grouped at several phases. These granules can be made out with low magnification. Such a condition is generally indicated with ++ in the tables. The cytoplasmic process filled with Best's positive granules which are sometimes very long and tortuous form fine network anastomosing with the neighboring ones. In these histiocytic cells numerous brownish black granules can be detected by Langhan's iodine method. The mesothelial cells of the milk-spots also possess fine Best's positive granules, but they are generally negative to the iodine reaction.

Cases 5 and 7. Many histiocytic cells of the milk-spots possess Best's positive granules in moderate quantity. Most granules are situated around the nucleus and some in the cytoplasmic process. These granules can hardly be detected under low magnification. Such a condition is generally indicated with + in the tables. These histiocytic cells are slightly positive to the iodine reaction. Some mesothelial cells of the milk-spots possess fine granules around the nuclei, but these granules are too fine to show iodine reaction.

Cases 1 and 4. Some histiocytic cells in the milk-spots have a few Best's positive granules. The granules are usually situated around both the poles of the spindle shaped nucleus and can only be made out under high magnification. Such a condition is generally indicated with ± in the tables. However, these granules usually have no influence on the iodine reaction.

Cases 2, 3, 6 and 10. The glycogen contents in the omentum is quite negative.

Blood-sugar ranges from 0.094 to 0.119 (on an average 0.105).

Glycosuria : always negative.

In 60% of cases glycogen was present in the following proportion:  $(++) : (+) : (\pm) : (-) = 1 : 1 : 1 : 2$ . From the above results, one may observe that there is remarkable individual differences in glycogen contents in the omentum. It is noticeable that glycogen is limited in the milk-spots, especially in the follicular and mixed form (of the author). The histiocytic cells contain most glycogen, while the round wandering histiocytes usually do not. The mesothelial cells on the milk-spots alone are provided with fine Best's positive granules, but they are too fine to be detected by the iodine reaction. The histiocytic cells and the mesothelial cells of mesentery are always negative to Best's and Langhan's methods.

Appendix :

The omentum of healthy adult rats (5 cases) which came under my observation was all glycogen-negative, while Fels obtained positive result, as mentioned above. The granules of mast-cells are distinctly positive to Best's method, but negative to Langhan's, as is well known. The saliva-reaction of the granules is unreliable; for the granules are easily soluble in water. However, it is of interest to note that after the starvation for 82 hours most of the granules became negative to Best's method and only small number of them stained very poorly.

#### IV. Inanition experiments on the rabbits.

Like fat glycogen in the animal-body may be classified in two: one kind of glycogen is very important for the metabolism and is consumed by work or starvation, e. g., that in the liver, muscle. The other kind of glycogen on the contrary is quite indifferent to the metabolism, e. g., that in cartilage, stratified squamous epithelium. The latter corresponds to "sesshaftes Fett" of Treina and neither work nor starvation exerts any effect at all upon it. Pink and Otto reported that no glycogen was found in the liver after the starvation for five and four days, whereas K. Itô obtained the result that small amount of glycogen persists in the liver of rabbit even after six days' starvation.

Experiment :—

In starving four adult rabbits for five days the fate of glycogen in the milk-spots was studied and the results are shown in the following table.

Table II. Inanition experiment.

| No. of case and sex.            |                      | 1 ♂       | 2 ♂   | 3 ♂   | 4 ♂   |   |
|---------------------------------|----------------------|-----------|-------|-------|-------|---|
| Body-weight (gms)               | before starvation    | 1380      | 1515  | 1470  | 1375  |   |
|                                 | after starvation     | 1155      | 1295  | 1090  | 1095  |   |
| Milk-spots                      | Hist. cell           | B. p. g.  | —     | —     | —     | — |
|                                 |                      | L. p. g.  | —     | —     | —     | — |
|                                 | Mesothelial cell     | B. p. g.  | —     | —     | —     | — |
|                                 |                      | L. p. g.  | —     | —     | —     | — |
|                                 | Polymorph. leucocyte | Preceance | —     | —     | —     | — |
|                                 |                      | B. p. g.  | —     | —     | —     | — |
| L. p. g.                        | —                    | —         | —     | —     |       |   |
| Mesentery                       | B. p. g.             | —         | —     | —     | —     |   |
|                                 | L. p. g.             | —         | —     | —     | —     |   |
| Blood-sugar                     | before starvation    | 0.091     | 0.103 | 0.110 | 0.095 |   |
|                                 | after starvation     | 0.053     | 0.068 | 0.058 | 0.049 |   |
| Glycosuria                      | before starvation    | —         | —     | —     | —     |   |
|                                 | after starvation     | —         | —     | —     | —     |   |
| Liver-glycogen after starvation |                      | ±         | ±     | ±     | ±     |   |

In all the cases glycogen on the milk-spots totally disappeared due to starvation. In the liver glycogen remained only in trace.

Blood-sugar was 0.091 to 0.110 (in average 0.100) and 0.049 to 0.068, (in average 0.057) before and after starvation, respectively.

Body-weight decreased after starvation to 81% of the normal on an average.

Summarizing the results of the above experiment, it may be concluded that the glycogen-depot of the milk-spots belongs to the same category as that found in such organs as the liver or muscle.

## V. Intravenous injection of glucose-solution.

The question that whether or not glycogen-formation takes place when grape-sugar is parenterally administered has been investigated by many authors. Croftan injected a solution of grape-sugar into the mesenteric vein of the dog and reached the negative result of glycogen-formation in the liver. However, Grube trying a similar experiment did not agree with Croftan's view. Freund and Popper investigated on the dog, and Ishimori, Kôzô Satô and Fujihara on the rabbit and they all came to the conclusion that glycogen-formation takes place after intravenous administration of grape-sugar.

As to the polymeric capacity of the omentum as tested by intravenous administration of grape-sugar, Katase for the first time studied on the rabbits (two cases) and

obtained a positive result. In his research on the omentum by means of intraperitoneal injection of grape-sugar, Fels inferred that the omentum is able to polymerize sugar introduced into the blood-vessel.

### Experiments :—

10 c.c. of the 50% solution of grape-sugar was intravenously injected per kilogram of body-weight and the omentum was examined after one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were examined just before injection and at the sacrifice-time.

Series I. The following table shows the results.

Table III. Intravenous injection of glucose. Series I.

| No. of case and sex.  |                      | 1 ♀        | 2 ♂      | 3 ♂      | 4 ♂      | 5 ♀      | 6 ♂      |
|-----------------------|----------------------|------------|----------|----------|----------|----------|----------|
| Body-weight (gms)     |                      | 1500       | 1315     | 1430     | 1515     | 1790     | 1540     |
| Sacrifice-time (hour) |                      | after 1.   | after 2. | after 3. | after 4. | after 5. | after 7. |
| Milk-spots            | Hist. cell           | { B. p. g. | +        | ±        | —        | ±        | —        |
|                       |                      | { L. p. g. | —        | +        | —        | —        | —        |
|                       | Mesothelial cell     | { B. p. g. | —        | +        | —        | —        | —        |
|                       |                      | { L. p. g. | —        | —        | —        | —        | —        |
|                       | Polymorph. leucocyte | { Presence | —        | +        | ±        | ±        | ±        |
|                       |                      | { B. p. g. | —        | —        | ±        | ±        | ±        |
| { L. p. g.            |                      | —          | —        | —        | —        | —        |          |
| Mesentery             | { B. p. g.           | —          | —        | —        | —        | —        |          |
|                       | { L. p. g.           | —          | —        | —        | —        | —        |          |
| Blood-sugar           | { before injection   | 0.094      | 0.102    | 0.110    | 0.098    | 0.102    | 0.099    |
|                       | { before sacrifice   | 0.415      | 0.315    | 0.170    | 0.158    | 0.126    | 0.114    |
| Glycosuria            | { before injection   | —          | —        | —        | —        | —        | —        |
|                       | { before sacrifice   | +          | +        | +        | +        | +        | —        |

Glycogen: Best's positive granules in the histiocytic cells of the milk-spots exist numerously in Case 2, moderately in Case 1, sparsely in Case 5 and without a trace in Cases 3, 4 and 6. From the above the following proportion will be made out; (++) : (+) : (±) : (—) = 1 : 1 : 1 : 3.

In this series Cases 3, 5 and 6 show numerous polymorphonuclear leucocytes and in Cases 3, 6 the leucocytes are positive to Best's staining. In Case 2, the leucocytes exist in moderate number and are indifferent to Best's staining. In Case 4, a few Best's positive leucocytes can be detected.

The Best's positive leucocytes mostly possess one or two nuclei which are either round or horse-shoe-shaped. The Best's negative leucocytes possess the strongly lobated nuclei. By hematoxylin-eosin staining, it is confirmed that the former belong to the pseudo-eosinophilic and the latter, neutrophilic. It is noticeable that the polymorphonuclear leucocytes are always negative to Langhan's reaction.

Blood-sugar; it reaches the maximum one hour after injection, and comes back to the normal somewhat rapidly in seven hours.

Glycosuria: from one to five hours after injection, it is positive and after seven hours, negative.

Series II. The similar experiment was repeated here, and its results is as follows.

Table IV. Intravenous injection of glucose. Series II.

| No. of case and sex.  |                      | 7 ♂        | 8 ♂      | 9 ♂      | 10 ♂     | 11 ♂     | 12 ♂     |   |
|-----------------------|----------------------|------------|----------|----------|----------|----------|----------|---|
| Body-weight (gms)     |                      | 1440       | 1400     | 1650     | 1430     | 1325     | 1585     |   |
| Sacrifice-time (hour) |                      | after 1.   | after 2. | after 3. | after 4. | after 5. | after 7. |   |
| Milk-spots            | Hist. cell           | { B. p. g. | ±        | +        | —        | —        | —        |   |
|                       |                      | { L. p. g. | —        | —        | —        | —        | —        |   |
|                       | Mesothelial cell     | { B. p. g. | —        | ±        | —        | —        | —        |   |
|                       |                      | { L. p. g. | —        | —        | —        | —        | —        |   |
|                       | Polymorph. leucocyte | { Presence | +        | —        | +        | ±        | +        | + |
|                       |                      | { B. p. g. | +        | —        | —        | ±        | +        | + |
| { L. p. g.            |                      | —          | —        | —        | —        | —        | —        |   |
| Mesentery             | { B. p. g.           | —          | —        | —        | —        | —        | —        |   |
|                       | { L. p. g.           | —          | —        | —        | —        | —        | —        |   |
| Blood-sugar           | { before injection   | 0.102      | 0.109    | 0.098    | 0.110    | 0.106    | 0.106    |   |
|                       | { before sacrifice   | 0.506      | 0.367    | 0.259    | 0.208    | 0.134    | 0.116    |   |
| Glycosuria            | { before injection   | —          | —        | —        | —        | —        | —        |   |
|                       | { before sacrifice   | +          | +        | +        | +        | ±        | —        |   |

Best's positive granules in the histiocytic cells of the milk-spots exist moderately in Case 8, sparsely in Cases 7, 10 and without a trace in Cases 9, 11 and 12. From this result, the following proportion is obtained. (#) : (+) : (±) : (—) = 0 : 1 : 2 : 3.

The polymorphonuclear leucocytes numerously existed in Cases 7, 9, 11, 12 and Best's positive result is not seen only in Case 9. In Case 10 a few Best's positive leucocytes can be detected. In all cases the polymorphonuclear leucocytes have no influence on the iodine reaction.

Blood-sugar: it reaches the maximum an hour after injection and gradually decrease until it nearly returns to the normal after seven hours.

Glycosuria: from one to four hours after injection it is positive and after five hours, very slightly positive, after seven hours, negative.

Summarizing the results of above two experiments, one may say that the Best's positive proportion of the milk-spots has considerably decreased, comparing with that of the normal material, viz., the normal proportion is (++) : (+) : (±) : (—) = 1 : 1 : 1 : 2, while that after intravenous glucose-injection is (++) : (+) : (±) : (—) = 1 : 1 : 1 : 3, in Series I and (++) : (+) : (±) : (—) = 0 : 1 : 2 : 3, in Series II. From these facts it may be concluded that by hyperglycemia due to intravenous glucose-injection, the milk-spots of omentum do not show any polymerizing function, but the normal glycogen-depot is reduced to some extent.

## VI. Intraperitoneal injection of glucose-solution.

Lately Fels investigated in using two dogs and one rat the behavior of the omentum

by intraperitoneal injection of glucose-solution. In one dog, he found that the omentum was quite free from glycogen, though the mesentery had the glycogen-containing cells in small number. In the other dog, a few mesothelial cells of the omentum had glycogen. In the mesentery, many polymorphonuclear leucocytes and some mesothelial cells were positive to the glycogen test. In the rat the omentum possessed numerous leucocytes and some mesothelial cells which were glycogen positive. These glycogen-containing cells were all situated along the blood-vessels. In the mesentery a few mesothelial cells were glycogen positive. Basing on the above results, Fels concluded that the omentum is not able to polymerize the glucose introduced into the peritoneal cavity.

#### Experiments :—

10 c.c. of 50% glucose-solution was intraperitoneally administered per kilogram of body-weight and examined after one, three, five, seven, twelve and 24 hours. Tests of hyperglycemia and glycosuria were made twice, i. e., immediately before injection and at the time of sacrifice.

The following table shows the results.

Table V. Intraperitoneal injection of glucose.

| No. of case an sex.   |                      | 13 ♂       | 14 ♂     | 15 ♂     | 16 ♂     | 17 ♂      | 18 ♂      |    |
|-----------------------|----------------------|------------|----------|----------|----------|-----------|-----------|----|
| Body-weight (gms)     |                      | 1345       | 1200     | 1635     | 1740     | 1540      | 1360      |    |
| Sacrifice-time (hour) |                      | after 1.   | after 3. | after 5. | after 7. | after 12. | after 24. |    |
| Milk-spots            | Hist. cell           | { B. p. g. | —        | —        | —        | —         | ±         |    |
|                       |                      | { L. p. g. | —        | —        | —        | —         | —         |    |
|                       | Mesothelial cell     | { B. p. g. | —        | —        | —        | —         | —         |    |
|                       |                      | { L. p. g. | —        | —        | —        | —         | —         |    |
|                       | Polymorph. leucocyte | { Presence | ##       | ##       | ##       | ##        | ##        | ## |
|                       |                      | { B. p. g. | +        | ±        | ±        | +         | ±         | ±  |
| { L. p. g.            |                      | —          | —        | —        | —        | —         | —         |    |
| Mesentery             | { B. p. g.           | —          | —        | —        | —        | —         | —         |    |
|                       | { L. p. g.           | —          | —        | —        | —        | —         | —         |    |
| Blood-sugar           | { before injection   | 0.103      | 0.097    | 0.094    | 0.096    | 0.093     | 0.100     |    |
|                       | { before sacrifice   | 0.141      | 0.228    | 0.231    | 0.146    | 0.105     | 0.103     |    |
| Glycosuria            | { before injection   | —          | —        | —        | —        | —         | —         |    |
|                       | { before sacrifice   | ±          | +        | +        | +        | —         | —         |    |

In Case 18 only, Best's positive granules can be detected with difficulty in the histiocytic cells of the milk-spots. From this result the following proportion can be seen: (##):(+):(±):(—) = 0:0:1:5.

In all the cases quite many polymorphonuclear leucocytes infiltrate the milk-spots. The majority of the leucocytes possess the strongly lobated nuclei and are unaffected by staining, while the remaining have one or two nuclei which are rather round or horse-shoe-shaped and are positive to Best's staining. The latter moderately existed in Case 13, 16 and sparsely in the remaining cases.

Blood-sugar; increases to the maximum five hours after the injection and gradually decreases until it nearly



returns to the normal after twelve hours and quite normal after 24 hours.

Glycosuria: an hour after the administration, it is seen in a slight degree and after from three to seven hours, positive and after twelve hours, negative.

Summarizing the above results, one may observe that the proportion of the Best's positive cases obviously decreases;  $(++):(+):(\pm):(-) = 0:0:1:5$ , as compared with the normal one;  $(++):(+):(\pm):(-) = 1:1:1:2$ . Almost all of the cases have totally reduced the normal glycogen-stock in the milk-spots by the intraperitoneal injection of a glucose-solution. The glycogen-containing cells of the mesentery is quite negative in my experiment, though Fels obtained positive results. Still, he emphasized the fact that Best's positive leucocytes are for the glycogen-formation of the omentum. But it is untenable for the reason that the polymorphonuclear leucocytes are nothing but wandering cells for the milk-spots of the rabbit and in addition, they do not show reaction with the iodine-method.

## VII. Administration of diuretin, "piqûre," adrenalin and phloridzin.

These experiments will here be dealt with very briefly and their detailed description will appear as a forthcoming paper.

Glucose-administration does not affect the glycogen-formation of the milk-spots at all, but reduces their glycogen-depots. Then, how do the milk-spots act in the case of central, peripheral and renal glycosuria? As to this subject nothing has been written.

### 1. Diuretin-injection.

10 c.c. of 6% diuretin-solution was subcutaneously injected per kilogram of body-weight and examined at intervals of one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice; once just before injection and the other time when sacrificed. The result may be summarized thus:

Glycogen contents of the milk-spots has remarkably increased;  $(++):(+):(\pm):(-) = 1:3:1:1$ , as compared with the normal case;  $(++):(+):(\pm):(-) = 1:1:1:2$ .

Blood-sugar: 0.108, 0.176, 0.201, 0.156, 0.133 and 0.121 as measured one, two, three, four, five and seven hours after injection, respectively. Glycosuria: an hour after the injection is negative, from two to five hours, positive, seven hours, in trace.

### 2. "Piqûre."

Puncture of the sugar-centre was performed according to Eckhard and examination was made after two, four, six, eight, twelve and 24 hours. Hyperglycemia and glycosuria were tested twice, i. e., just before puncture and at the time of sacrifice.

## Series I.

Glycogen contents has remarkably increased;  $(++):(+):(\pm):(-) = 3:0:1:2$ , as compared with the normal case.

Blood-sugar: 0.147, 0.160, 0.185, 0.200, 0.105 and 0.108 as measured two, four, six, eight, twelve and 24 hours after the operation, respectively. Glycosuria: from two to eight hours after operation, positive, after twelve hours, in trace and after 24 hours, negative.

## Series II.

Glycogen contents has remarkably increased;  $(++):(+):(\pm):(-) = 2:1:1:2$ , as compared with the normal case.

Blood-sugar: 0.158, 0.165, 0.191, 0.135, 0.142 and 0.115, as measured two, four, six, eight, twelve and 24 hours after respectively. Glycosuria: in the all cases positive.

## 3. Adrenalin-injection.

0.4 c.c. of adrenalin chloride 1:1000 was subcutaneously injected with the ratio of per kilogram of body-weight and examined after one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice, i. e., just before injection and at the time of sacrifice.

## Series I.

Glycogen contents has remarkably decreased;  $(++):(+):(\pm):(-) = 0:0:2:4$ , as compared with the normal case.

Blood-sugar: 0.275, 0.306, 0.304, 0.326, 0.314 and 0.222 as measured one, two, three, four, five and seven hours after the injection, respectively. Glycosuria: positive in all cases.

Series II. The quantity of the adrenalin injected was increased to 0.8 c.c. per kilogram of body-weight.

In all the cases no glycogen was found, while hyperglycemia appeared very remarkably.

Blood-sugar: 0.253, 0.368, 0.406, 0.313, 0.362 and 0.223 as measured after one, two, three, four, five and seven hours, respectively. Glycosuria: positive in all cases.

## 4. Phloridzin-injection.

0.2 gr. of phloridzin was subcutaneously injected per kilogram of body-weight and examined after one, two, three, four, five and seven hours. Hyperglycemia and glycosuria were tested twice, i. e., just before injection and at the time of sacrifice.

Glycogen contents is nearly normal;  $(++):(+):(\pm):(-) = 1:1:2:2$ , compared with the normal case.

Blood-sugar: 0.095, 0.095, 0.102, 0.093, 0.094 and 0.095 as measured one, two, three, four, five and seven hours after the administration. Glycosuria: positive in all cases.

### VIII. Summary and discussion.

The polymerizing capacity of the omentum is limited to the milk-spots, especially to the follicular and mixed types. When the histiocytic cells sparsely contains glycogen, the Best's positive granules are found both the poles of the spindle-shaped nucleus and when it abundantly exists, the relatively coarse granules are grouped in places in the cytoplasmic process and the finer ones are diffusely arranged. However, this phenomenon may not be a normal arrangement *in vivo*, but due to alcohol fixation, according to Neukirsch, Prof. Andô et al. The round wandering histiocyte possesses no Best's positive granules. The mesothelial cell of the milk-spots, particularly those of follicular and mixed types, may be presumed to have a little capacity of polymerization. Glycogen-formation in the mesentery can never be seen.

The changes in the milk-spots during hyperglycemia caused by various ways may be summarized as follows. In case of hyperglycemia is produced by the intravenous injection of glucose, glycogen decreases in the milk-spots to some extent. Intraperitoneal injection of glucose reduces the normal glycogen-depot in the milk-spots markedly. Central glycosuria induced by diuretin or piqûre, glycogen increases very much. At peripheral glycosuria by adrenalin-injection glycogen remarkably diminishes or totally disappears. Renal glycosuria caused by phloridzin-injection does not change the amount of glycogen at all.

Why is the quantity of glycogen of the milk-spots diminished by sugar-administration?

In Tables III, IV and V, it will be noticed that the polymorphonuclear leucocytes infiltrate the milk-spots. The intravenous injection of sugar-solution may causes leucocytosis and the infiltration takes place in the milk-spots. The intraperitoneal injection of the solution, on the contrary, may give a stimulus there and the milk-spots are infiltrated by the leucocytes. In the omentum, such stimuli as mentioned in the above two cases may act especially on the milk-spots, since the leucocytes are mainly restricted to the milk-spots. It is noticeable that the more the leucocytes increases, the more the glycogen of the milk-spots decreases. As previously mentioned, the glycogen of the milk-spots are mostly deposited in the histiocytic cells, very susceptible to those stimuli which cause the leucocytosis. It may, therefore, be considered that the stimulus caused by sugar-injection prevents the polymerizing capacity of the milk-spots, and not only that, it reduces the glycogen previously existed. Kôzô Satô claimed that adrenalin- or diuretin-injection gave an hindrance to the glycogen-formation in the liver. My opinion

is supported by his and will become clearer by the following experiment.

**Experiment:—**

6% solution of diuretin was subcutaneously injected in the dose of 10 c.c. per kilogram of body-weight. One hour after the injection, 1—2 c.c. of indian-ink was intraperitoneally injected and two hours after the last injection the animals were sacrificed. The blood-sugar and glycosuria were tested twice; once just before diuretin-injection and the other time at the time of sacrifice.

The result is shown in the following table.

Table VI. Diuretin-injection followed by indian-ink.

| No. of case and sex. |                      | 55 ♂       | 56 ♂  | 57 ♂  | 58 ♂  |   |
|----------------------|----------------------|------------|-------|-------|-------|---|
| Body-weight (gms)    |                      | 1350       | 1570  | 1510  | 1540  |   |
| Indian-ink (c.c.)    |                      | 2.0        | 1.5   | 1.0   |       |   |
| Milk-spots           | Hist. cell           | { B. p. g. | —     | —     | —     | + |
|                      |                      | { L. p. g. | —     | —     | —     | ± |
|                      | Mesothelial cell     | { B. p. g. | —     | —     | —     | — |
|                      |                      | { L. p. g. | —     | —     | —     | — |
|                      | Polymorph. leucocyte | { Presence | ##    | ##    | ##    | — |
|                      |                      | { B. p. g. | —     | ±     | —     |   |
| { L. p. g.           |                      | —          | —     | —     |       |   |
| Mesentery            | { B. p. g.           | —          | —     | —     | —     |   |
|                      | { L. p. g.           | —          | —     | —     | —     |   |
| Blood-sugar          | { before injection   | 0.105      | 0.098 | 0.099 | 0.102 |   |
|                      | { before sacrifice   | 0.396      | 0.289 | 0.278 | 0.206 |   |
| Glycosuria           | { before injection   | —          | —     | —     | —     |   |
|                      | { before sacrifice   | +          | +     | +     | +     |   |

The glycogen in the histiocytic cells of the milk-spots, totally disappeared in Cases 55, 56 and 57, while in control (Case 58) it increased very much. In Cases 55, 56 and 57 there existed many polymorphonuclear leucocytes, while in control non was found.

Blood-sugar: in the cases injected with indian-ink, it measured on an average 0.321, against the control, 0.206. Glycosuria: in all cases positive.

The reduction of the glycogen takes place in all the histiocytic cells of the milk-spots, while the indian-ink-particles invade only a few of them. Therefore, the stimulus which causes the reduction of the glycogen may not only directly be influenced by the particles of indian-ink, but also indirectly. Taking the above result into the consideration, whenever a certain stimulus acts upon the histiocytic cell of the milk-spots, it loses its polymerizing capacity and furthermore, it reduces the glycogen previously existed.

### IX. Conclusions.

1. In 60% of cases the omentum of the healthy adult rabbits contain glycogen, though its quantity is greatly subjected to individual difference.

2. In the normal condition and in the case of experimental hyperglycemia, polymerizing capacity of the omentum is restricted to the milk-spots, especially to those of follicular and mixed types. As to the glycogen-depot, the histiocytic cells of the milk-spots play an important rôle. The mesothelial cells of the milk-spots may have a slight capacity of polymerization.

3. After five days' starvation glycogen in the milk-spots disappears.

4. Glycogen of the milk-spots is considerably decreased after intravenous injection of glucose-solution and it almost entirely disappears after intraperitoneal administration of glucose.

5. A certain stimulus which acts directly or indirectly upon the histiocytic cells in the milk-spots not only hinders their polymerizing function, but also reduces the amount of glycogen previously existed.

6. In case of central glycosuria caused by the diuretin-injection or piqûre, glycogen in the milk-spots is remarkably increased. During peripheral glycosuria due to adrenalin-injection, glycogen in the milk-spots almost entirely disappears. Renal glycosuria due to phloridzin-injection shows no effect whatever upon the amount of glycogen.

In concluding, I wish to acknowledge my indebtedness to Profs. O. Tamura and H. Tanabe and also to express my gratitude to Dr. Fujihara who has kindly put valuable materials at my disposal.

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## 内 容 大 意

# 大 網 乳 斑 ノ 糖 原 質 ニ 就 テ

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網狀内皮細胞系統ガ物質代謝ト密接ナル關係ヲ有スルコトハ多數ノ學者ニヨリテ認メラレタル所ニシテ，就中 Schilling, 志賀亮氏等ハ脂肪ニ就テ，又加藤芳治, 伊藤幸憲氏等ハ糖ニ就テ研究ヲナセリ。

大網乳斑ハ主トシテ組織球性細胞ヨリ構成サル，而シテ余ハ此等細胞ノ網狀組織ヲ形成スルヲ認メタリ。從ツテ乳斑ト含水炭素物質代謝トノ關係如何ハ興味アル問題ナリトス。然ルニ本問題ニ關シテハ文獻甚ダ少數ニシテ，E. Seifert ハ大網ノ生物學ニ關スル研究ヲ發表シ，乳斑ハ懷春期ニ至ル迄本來ノ機能ヲ有スルコト赤色骨髓ニ於ケルガ如ク，其後ハ漸次脂肪球ト化シ生體ニ對シテ脂肪ノ貯所トシテ役立ツコト黄色骨髓ニ於ケルガ如シト論ジタリ。片瀬及ビ密田氏ハ組織球性細胞ノ糖原質形成機能ニ關シテ研究シ，大網ニ於ケル此ノ種ノ細胞モ亦實驗的過血糖ニ際シ糖原質形成機能ヲ示スモノナリト論ゼリ。最近 Fels 氏ハ葡萄糖溶液ノ腹腔内注射ニ於テ

ル大網ノ態度ニ就テ研究シ、大網ハ腹腔内ニ注入セラレタル葡萄糖ヲ直接糖原質トナスコト能ハザルモ、恐ラク血管内ニ注入セラレタル糖ハ之ヲ糖原質トシテ貯藏スル機能ヲ有スペシト推論セリ。

上記二者ノ報告ハ甚ダ簡單ニシテ大網ノ糖原質形成機能ヲ決定センガタメニハ尙ホ系統的研究ヲ要シ、就中生物學的ニ重要ナル役目ヲ有スル大網乳斑ニ就テ特ニ研究スルノ必要アリ。

余ハ健康家兔、飢餓動物、種々ナル實驗的過血糖症及ビ一定ノ刺戟ヲ與ヘラレタル場合ニ於ケル乳斑ノ糖原質ヲ研究シ大略下ノ如キ結論ニ達セリ。

1. 健康成熟家兔ノ大網ニ於テハ 60% ニ於テ糖原質陽性ナリ、而シテソノ糖原質含量ハ稍々著明ナル個體的差異ヲ示ス。
2. 健康時並ニ實驗的過血糖時ニ於ケル大網ノ糖原形成機能ハ乳斑、殊ニソノ濾胞型及ビ混合型ニ限定サル。糖原ノ貯藏ニ關シテハ乳斑ノ組織球性細胞ガ重要ナル役目ヲ有シ、乳斑ノ漿液膜細胞モ亦僅カニ之ニ參與ス。
3. 健康時ニ含有スル乳斑ノ糖原質ハ 5 日間ノ飢餓ニテ全く消失ス。
4. 健常乳斑ニ含有スル糖原量ハ葡萄糖溶液ノ靜脈内注射ニ際シテハ中等度ノ減少ヲ示シ、腹腔内注射ニ於テハ殆ンド全く消失ス。
5. 乳斑ノ組織球性細胞ニ作用スル直接或ハ間接ノ一定ノ刺戟ハ乳斑ノ糖原質形成機能ヲ阻止スルノミナラズ、豫メ含有セル糖原質ノ消失ヲ來ス。
6. 「チウレチン」注射或ハ糖刺ニヨル中樞性糖尿ノ際ニハ乳斑ノ糖原含量ハ著明ナル増加ヲ示ス。「アドレナリン」注射ニヨル末梢性糖尿ニ際シテハ乳斑ノ糖原質ハ殆ンド全部消失ス。又「フロリヂン」注射ニヨル腎性糖尿ニ於テハソノ糖原含量ハ略ボ尋常ナリ。