THE OCCURRENCE OF SUBCUTANEOUS SARCOMAS IN THE RAT, AFTER REPEATED INJECTIONS OF GLUCOSE SOLUTION

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Last year Mr. Nishiyama caused the actual occurrence of subcutaneous sarcoma in the back of a rat with repeated injections of concentrated glucose solution. Also last year, after repeated concentrated glucose solution injections in the affected part, inflammation occurred, and fibro-blas connective tissue developed and gradually became subcutaneous sarcomas. Therefore this is a very interesting problem and requires continued testing.

(1) The concentrated glucose solution I used was 25 gm/dl (Takeda). Seventy rats were used, and the average weight was 200 gm. The dosage was 2 cc/100 gm weight. Once every day a hypodermic injection was given in the back of the rat. This was gradually increased in three weeks time to 4cc/100gm wt. When the animal became weak the injections were stopped. Sixty-two of the seventy animals died in the first six months, with four more dying in the next six months, and three of the remaining four animals developed subcutaneous sarcomas.

Of the last four animals, the first rat, after 403 days (300 injections), developed small red (Japanese) bean size tumors that you could feel. (Then the process was stopped). After five days the animal died. (408 days.) After the tumor was removed, subcutaneous sarcomas were observed clearly separate from normal tissue, and were hard and pale or light blue in color. One portion of the subcutaneous sarcomas was hemorrhaged. The size of the tumor was 3 x 2.7 x 1.2 cm. Histologically it appears that it is made of cells of spindle or oval shape. There were some regular separations in the tissue. The nucleus was round in shape, and was less chromophillic and showed many obvious mitosis. The protoplasm was soft and fibrous. The many capillaries in the skin showed abnormal fibers developing into subcutaneous sarcomas. A few places were decaying, showing bad color and hemorrhage. This was the picture of Spindelzellensarcom. Surrounding the tumor with connective tissue was a hyalinous fiber.

The second animal, after 466 days (363 injections) developed the same type of tumor that you could feel. The tumors were located at the position of injection. (2cc injections were continued for two days and then stopped), ten days later the tumors were the size of a thumb (human) and were transplanted. Five days after being transplanted another bean size tumor was felt under the shoulder skin. Both tumors gradually increased in size, and some formation was noted between them. After 500 days the animal was dead. After the first tumor was removed the size was noted to be 4.4 x 4 x 2 cm. The tumor remained under the skin, was pale in color, hemorrhaged easily, and had a spot that appeared to be coagulated.

Histologically, they were almost the same as in the first animals but the tumors were elongated, and the protoplasm was more fibrous. Also, the organization of the cells were in the same direction, side by side in a bunch. The bunches were tangled with each other, similar to the picture of Fibrosarcom. The shoulder also remained under the skin with a hard quality, and without noticeable bleeding. The size was 2.5 x 3 x 1.4 cm. Histologically, the picture was found to be a compromise between the preceeding

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studies. At first glance, the picture appeared to be a granulation tissue. However, the tumor cells and the new large cells of the capillaries of the skin were closely related. In some places you could notice two or more large nuclei cells. Between the back growth and the shoulder growth there was a cyst forming which contained bloody liquid. The wall of the cyst was very flat and smooth, while on the bottom there were small firm tumors (like peas). The picture of the histological finding was the same as the preceeding case.

On the third animal, after 510 days (393 injections), there was a fluctuated tumor all over the back of the animal. Gradually the shape of the fluctuation became very distinct, but the tumor remained soft and was transplanted. The tumor had a thick bloody liquid inside. The bottom of the tumor had a necrotic tissue. Immediately after the operation the animal died (530 days). Histologically, it was exactly the same as in the first animal, but the cells were arranged in rings. The cytoplasm was ill-defined and the nuclei stood on a line approximating a circle, located in the position of the big cytoplasm. Two of the transplants from the third animal were successful. One has lived for three generations, and the other for two generations. Both are showing progress. The picture of the transplanted growth showed that it appeared to be in between the picture of the first and second animals. (With reference to back tumors.) In this manner, the facts were confirmed as to the occurrence of oval cell tumors, fiber tumors and mixed tumors due to the glucose solution injections Looking beyond the evidence relating to the histology of the tumors, I think that some of the occurrence of the tumor was due to granulated tissue. The lymphocyte appearance is very rare, and polymorphonuclear leucocyte is very hard to recognize. Therefore the basis for the occurrence is due to the repeated injection of the lesion healing phenomenon.

(2) In order to clarify the above results based on the occurrence procedure, Mr. Nishiyama and I need to contrast our continued once a day hypodermic injections in the back, of 4 cc/100 gm. wt. portions, with Mr. Ringel's solution.

(3) I am trying to use poli-saccharides instead of mono-saccharides, glucose and fructose giving sugar, using a 30 gm/dl solution and a 2 cc/100 gm. wt. portion, this being injected with a hypodermic once a day in the rat's back. It takes time to get the tumor occurrence, and the laboratory tests have still not been completed. The longest test so far has been 285 days. At the present time we are still conducting tests, and when the tests are completed the results will be reported.

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