Since adenomas of the breast are probably intermediate between normal and malignant structures, their use has appealed to us as a means of studying several pathologic problems. These tumors occur spontaneously in rats. Bullock and Curtis (1) found 8 of them among 235 rat tumors in 2450 rat autopsies. In our stock of rats bred over a period of several years two mammary adenomas have been found: one in the inguinal, the other in the axillary region.

Various theories have been advanced to explain the origin of adenomas of the breast. Beneke (2) believed the adenoma to be a growth of mature glandular tissue. Stoerck and Erdheim (2) consider it related to mastitis. Ribbert and Wilms (2) suggest the theory that adenomas have their origin from the anlage of the mammary gland, i.e. germinal parts which contain both epithelial and connective-tissue potentialities. Substantiating this theory is the case reported by Leroux and Diamant-Berger (3), in which a pedunculated tumor, present in the axilla of a woman, proved upon removal and sectioning to be a canalicular adenoma. This case would also tend to support the generally accepted theory of the origin of supernumerary breasts in human beings, on the basis of a persistence of a portion of the milk ridge of the fetus. In connection with the theory of a congenitally displaced anlage in the origin of adenomas it might be well to consider the areolar glands (glands of Montgomery) as a possible basis for the tumors. These rudimentary mammary structures possess all of the elements necessary for the development of benign breast tumors.

Sufficient material for future work upon these tumors was necessarily obtained by transplantation. Loeb (4) in 1902 was successful in making an autotransplantation of a mammary adenoma of a rat but homeo transplantation failed. The same results were obtained in 1907 by Loeb and Leopold (5), using a sim-
ilar tumor from a dog. Loeb and Fleisher (6), in 1916, made a study of the transplantability of four different adenomas of rats. Only one of these showed definite growth after transplantation and this was carried through three generations. It is difficult to estimate the percentage of takes obtained by the above authors. The sex of the animals was not recorded in all cases. Furthermore, tumors from rats dead an indefinite period of time were used, and many of the animals died before the success of the transplant could be determined. The method of making the transplants is not clear, except that it was accomplished by the use of a trocar.

Our transplants were made in the following manner. A portion of the tumor was removed under ether anesthesia, and the wound immediately sutured. The tumor tissue was cut into pieces about 0.5 cm. in diameter. The recipients were anesthetized and a small incision made through the skin in the inguinal region. The skin was separated from the abdominal musculature with blunt hemostats for a distance of 0.5 cm. from the incision. The piece of tumor was pushed to the bottom of this pocket, and the incision closed with sutures.

The first transplants were made from a rat bearing a spontaneous adenoma about the size of a walnut ($5 \times 4 \times 2$ cm.) in the right groin. Two female rats received small pieces of this tumor. After one month's time the mass in one of the rats had become distinctly larger. After about two months she bore young and the transplant became several times its original size. In six months it was equal in size to the original tumor. At this time transplants were made from this second tumor generation to three female rats, all of which developed tumors. During a period of six months three other transplants were made from this tumor to 17 rats, making a total of 20 transplants, 11 of which developed into tumors of good size. From two of these tumors of the third generation transplants were made to 14 females and one male. Six of the females developed tumors.

Incidently it should be mentioned that the original tumor was transplanted into a group of two males and one female, in none of which tumors developed. The failure was attributed to a lapse of one and a half hours between the removal of the tumor and its inoculation into the new hosts.

A spontaneous axillary tumor was transplanted into three females two of which developed sizable tumors (Fig. 1).
Microscopic Studies

Original Tumor 117 (Fig. 2): The section was made up of numerous ducts and small groups of acini which were collected in nodular areas. Both were lined by either a single or double layer of low cuboidal epithelium. Some cells showed mitotic figures. Several ducts contained concretions which resembled corpora amylacea. The supportive fibrous tissue was dense and hyalinized, and showed proliferative activity.

Second Generation of Tumor 117 (Fig. 3): The proportion of acini to ducts in the second generation was about the same as in the original tumor. There was less tendency toward proliferation. The lining epithelium consisted of a single layer of cells. Bundles of dense collagen fibrils surrounded the acinar portions and in most areas produced complete obliteration of the lumina.

Third Generation of Tumor 117: The tissue in the third generation tumors showed little alteration from that in the second generation, save that there was a more definite differentiation between acini and ducts. The number of ducts containing concretions was increased, while a few concretions occurred, also, in the alveoli. The surrounding connective-tissue bands showed great variation in width in different areas. The fibroblasts appeared larger and younger than in the original tumor.

Another section was taken to show the intimate relationship established between the adjacent normal breast tissue and the transplanted adenoma (seven months after transplantation). The breast and adenoma were lactating (this was nine days post partum). The glandular structures of the adenoma close to the breast tissue were increased in number and were actively secreting. The lining epithelium was cuboidal in type, and some cells contained mitotic figures. The ducts were dilated and filled with milk. Some assumed cystic proportions and were lined by a single layer of flattened epithelium. Others showed heaping up of the hyperplastic epithelium. The fibrous supportive stroma was proportionately decreased in amount.

The acini of the breast tissue were lined by the same type of epithelium as in the adenoma. The lumina were more widely dilated. They were surrounded by a fine fibrous reticulum and embedded in adipose tissue.

The adenoma showed areas of necrosis in portions at some distance from the breast tissue.
Original Tumor 13 (Fig. 4): The lumina of the ducts and alveoli contained milk. Many of the ducts were widely dilated, and the epithelium was flattened. In other ducts and in the acini the epithelial cells were swollen and the cytoplasm contained fat-like globules. Concretions, such as those previously described, abounded.

The whorled fibrous stroma was relatively small in amount and was of the adult connective tissue type.

Discussion

Owing to our purpose of obtaining numerous tumors for other studies we have confined ourselves solely to homeo transplantation. The conditions under which growth of transplanted tissues takes place are not known. Obviously a piece of tissue cut off from its blood supply temporarily would have less resistance to bacterial decomposition than tissue well supplied with circulation. Therefore, a strict asepsis is essential. It was noted, on microscopic examination, that the circulation in the transplant was maintained by an ingrowth of capillary blood vessels from the surrounding tissue of the host. This was particularly marked in the sections taken from the periphery of the tumor at the points of contact with the surrounding tumor capsule. It would also seem reasonable that tissue cells should not be injured by maceration or pressure and that a minimal interval of time should elapse during the transfer from one host to another. For this reason we have considered the method of inserting the tissue through an incision superior to that of injecting a cylinder of tissue through a trocar. In all cases we completed the transfer within one hour.

Judging by the size of the mass, growth of the transplanted tissue does not immediately take place. It may retain its original size for several weeks or slightly diminish before an increase is noticeable. This was observed by Loeb. He further noted that pregnancy seemed to stimulate growth, a fact which we, too, have observed. This phenomenon is possibly peculiar to mammary tissue alone. It is certain that it is much more difficult to obtain a successful transplant of mammary adenoma in a male rat than in a female. Loeb mentions one "take" in a male rat but notes that after nine months the tumor "had grown very slowly." We have not had the least semblance of "take" in any of 16 male rats inoculated.
In our experience successive transplants have neither increased nor decreased the rapidity of growth of the tissue. The interval required before active growth can be demonstrated varies in different animals but we believe the recipients should be observed for at least three months. The microscopic sections from the third generation of transplanted tumors showed more active and apparently younger fibroblasts in the supporting stroma and greater differentiation between acini and ducts than the original tumor. This might be accounted for simply by the relative age of the tumors themselves, as we had no way of knowing the age of the original tumor.

The majority of our transplants have been made upon the abdominal wall in the mammary region. It has been suggested that the apparent stimulating effect of pregnancy is due to the increased vascularity of the pregnant breast. Slye (7) does not believe that pregnancy influences the growth of tumors in mice. We have recently had a successful transplant in the mid-dorsal region and several in the abdominal cavities in virgin rats.

The microscopic sections from the original axillary tumor showed active lactation. Further studies of lactation occurring in breast adenomas are reported in the following paper (see page 191).

While we have used only two spontaneous adenomas both of these have been successfully transplanted. Approximately 50 per cent of the animals inoculated have produced tumors. It is quite possible that improvements in the technic will yield an even greater percentage of positive results.

**Conclusions**

1. Transplantation of two different strains of pericanalicular adenoma of the breast of the rat has been successful.
2. The transplantations of one of these have been carried to the fourth generation.
3. The microscopic pictures up to the third generation remained unaltered. At this point an increase in viability was noted.
4. A failure to secure successful takes in males was observed.
5. Pregnancy may stimulate growth, but is not the only factor influencing successful transplantation.
6. Transplants have succeeded in the subcutaneous tissue of the back and in the abdominal cavity.
Bibliography

5. Loeb, L., and Leopold, S.: On the difference in the results obtained after inoculation of tumors into the individual in which the tumor had developed spontaneously and into other individuals of the same species, J. Med. Research 17 (n.s. 12), 299, 1907.