

found in 15 dogs on histamine alone. When the number of cigarettes was doubled the incidence of peptic ulcers or erosions increased from 60% to 100%. Under identical conditions denicotinized cigarettes did not provoke as high an incidence of ulcer-erosion as was obtained with ordinary cigarettes. Exposure to cigarette smoke for 30 days prior to the administration of histamine afforded little protection to the development of gastrointestinal lesions. In 5 dogs the continued simultaneous administration of cigarette smoke and histamine was uniformly fatal in 51 days. Four died of perforation and one of massive hemorrhage. According to Hay *et al.* (8) the

daily injection of histamine to fresh unselected stock dogs produced ulceration in 87.5% in 37 days. About 1/3 of these were perforated. The secretory response of total gastric pouches in dogs was either unaffected or slightly decreased by the inhalation of cigarette smoke.

**Conclusion.** (1) The daily inhalation of cigarette smoke failed to produce peptic ulcers in dogs. (2) Cigarette smoke abets the ulcerogenic effect of histamine in beeswax; this is believed to be a nicotine effect. (3) Cigarette smoke does not stimulate gastric secretion in dogs.

Received June 19, 1951. P.S.E.B.M., 1951, v77.

### Transplantability of Rabbit Ovaries in the Anterior Chamber of the Rabbit Eye.\* (18952)

JULIAN E. WARD, BERNE L. NEWTON, AND HERMAN L. GARDNER.  
(Introduced by C. A. Handley.)

*From the Departments of Pathology and Obstetrics and Gynecology, Baylor University College of Medicine, Houston, Texas.*

Survival and growth of autologous, homologous and heterologous tissue transplants in the anterior chamber of the eye has been observed and confirmed by many investigators (1-7). By the use of this method, Goodman (4) transplanted immature rat ovaries into 60 female and 20 male rats and found the percentage of takes in non-castrated males and non-spayed females, 2 months after transfer, to be 90% and 89%, respectively. Takes

of transplants in females spayed concurrently and in those spayed 2 months after transfer were 100% and 33%, respectively, when examined 6 months after this operation. Continued growth of transplants in normal males castrated 2 months after transfer was evident in 80% of this group. Goodman utilized a Graefe knife for the corneo-scleral incision and curved, smooth, iris forceps to implant the tissue into the anterior chamber. Dunham, Watts, and Adair (6) studied newborn and adult rat ovaries transplanted into the anterior chambers of 137 rats. The percentage of takes was 74% in castrated males and 72% in spayed females, while those in non-castrate males and non-spayed females were 47% and 40%, respectively. A further group of spayed females and castrated males which had received chorionic gonadotrophin 3-14 days prior to tissue transfer yielded the highest percentage of takes (83%). The lowest percentage of takes was found when adult ovarian tissue was used. These workers used an angular keratome to make the ocular incision and donor tissue was inserted with a

\* Aided by grants to the General Research Funds, Baylor University College of Medicine, Houston 5, Texas by the M. D. Anderson Foundation, and by U. S. Public Health Service Cancer Teaching grant 692-C-2.

1. Van Dooremals, J. C., *Arch. Ophth.*, 1873, v19, 359.

2. Schochet, S. S., *Surg., Gynec. and Obst.*, 1920, v31, 148.

3. Markee, J. E., *Am. J. Physiol.*, 1932, v100, 32.

4. May, R. M., *Bull. d'histol. appliq. à la physiol.*, 1940, v17, 51.

5. Goodman, L., *Anat. Rec.*, 1934, v59, 223.

6. Dunham, L. J., Watts, R. M., and Adair, F. L., *Arch. Path.*, 1941, v32, 910.

7. Greene, H. S. N., *J. Exp. Med.*, 1941, v73, 461.

TABLE I. Autologous Ovarian Transplants into Anterior Chamber of Rabbit Eyes.

|            | 4-wk donors |       | 8-wk donors |       | 12-wk donors |       | All age donors |          |
|------------|-------------|-------|-------------|-------|--------------|-------|----------------|----------|
|            | Grafts      | Takes | Grafts      | Takes | Grafts       | Takes | Grafts         | Takes    |
| Spayed     | 4           | 3     | 4           | 3     | 4            | 3     | 12             | 9 (75%)  |
| Non-spayed | 4           | 3     | 4           | 4     | 4            | 3     | 12             | 10 (83%) |

TABLE II. Homologous Ovarian Transplants into Anterior Chamber of Rabbit Eyes.

|                    | Newborn donors |       | 4-wk donors |       | 8-wk donors |       | 12-wk donors |       | All age donors |          |
|--------------------|----------------|-------|-------------|-------|-------------|-------|--------------|-------|----------------|----------|
|                    | Grafts         | Takes | Grafts      | Takes | Grafts      | Takes | Grafts       | Takes | Grafts         | Takes    |
| Castrate males     | 8              | 4     | 8           | 7     | 8           | 8     | 8            | 7     | 32             | 26 (81%) |
| Non-castrate males | 8              | 7     | 8           | 3     | 8           | 5     | 8            | 7     | 32             | 22 (69%) |
| Spayed females     | —              | —     | 4           | 2     | 4           | 3     | 4            | 4     | 12             | 9 (75%)  |
| Non-spayed females |                |       | 4           | 4     | 4           | 4     | 4            | 3     | 12             | 11 (92%) |

modified 19-gauge spinal needle.

It has been suggested by Robertson(8) in accordance with Halsted's(9) law of "endocrine deficiency" that an ovarian endocrine deficiency facilitates successful transfer of homologous ovaries into a new host.

The purpose of the present investigation is to reevaluate the transplantability of autologous and homologous young rabbit ovarian tissue. The donor tissue was removed from rabbits of different age groups.

**Materials and methods.** Sixty-six New Zealand albino and 2 Dutch rabbits of known age were studied in 4 groups: spayed females, non-spayed females, castrate males, and non-castrate males. Castrated male rabbits were allowed several weeks for recovery from this operation before transplants were made. Autologous transfer was made into the right eye and homologous transfer into the left eye of all females; those exposed to a unilateral oophorectomy were considered "non-spayed." Homologous transfers in the females were made at the time of the recipient's uni- or bilateral oophorectomy or on the following day. In the majority of males both eyes were used.

Transplantation of grafts was made under sterile conditions into all animals within 10-15 minutes after the removal of the ovary. The

technic of transplantation used was that described by Greene(7), with the following modification: 15,000 units of penicillin G were given intramuscularly immediately after transfer. All animals were killed by injection of air into the heart. Microscopic sections of all the transplants were fixed in formalin, cut at 7 microns, stained with hematoxylin and eosin, and examined histologically.

**Results.** 114 transplants were made; 2 of these were not included in the results due to death of the recipients the day following transfer. Transplantation data are presented in Tables I and II. Criteria of growth were the presence of vascularity, "rounding off," and increase in size of the fragments, together with histologic evidence of developing follicles and ovarian stroma. In those animals in which growth did not occur, the transplanted fragments slowly decreased in size, and became dense white with no evidence of vascular response and ultimately became tiny scars. The gross assessment of the presence or absence of infection was not reliable. Inflammatory reaction was microscopically demonstrable in 19 cases, of which 16 were successful takes.

Hemorrhagic follicles developed in grafts in 2 non-spayed females within 24 hours after copulation. Glaucoma occurred in 4 grafts (3%); follicle cysts developed in 5 others.

**Discussion.** The incidence of homologous takes was highest in non-spayed females,

8. Robertson, G. G., *PROC. SOC. EXP. BIOL. AND MED.*, 1945, v59, 30.

9. Halsted, W. S., *J. Exp. Med.*, 1909, v11, 175.

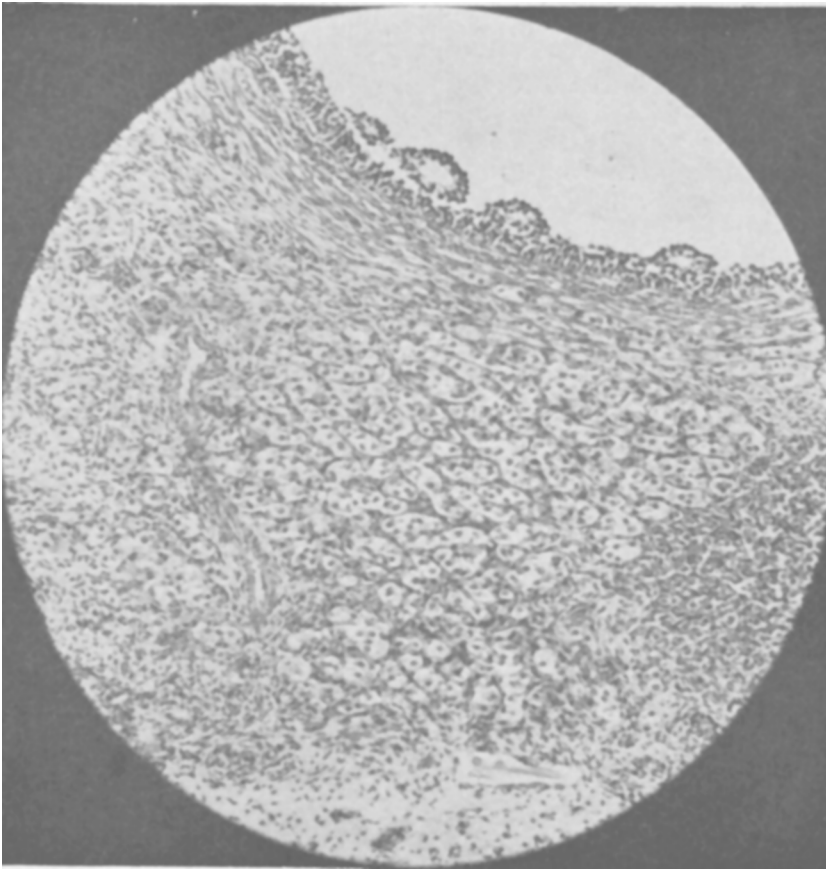


FIG. 1. Viable ovarian graft exhibiting an area of luteinization and a portion of a cystic follicle. Mg.  $\times 115$ .

92%, with takes of 81% and 75% in castrate males and spayed females, respectively. Since none of the grafted ovarian tissues were mature as evidenced by histological examination, our work does not refute Halsted's theory (9). The number of takes in the group of non-castrate males was 69%. It was found that a higher number of autologous takes occurred in non-spayed females, 83%. The best results were achieved in 12-week- and 8-week-old tissue grafts and the poorest in newborn and 4-week. Little difference was found between the overall homologous and autologous female graft takes.

The average weight curve of all animals with viable transplants corresponds closely with a normal weight curve of a control group of non-transplanted animals, thereby giving further support to the supposition of Hill (10)

that functioning ovarian grafts in the ear did not influence weight gain.

The technic of transfer utilized by the investigators cited above when compared with that used in the present experiment, did not appear to appreciably influence transplantability.

*Summary.* In 112 autologous and homologous anterior chamber grafts of ovarian tissue in castrate and non-castrate males, and spayed and non-spayed females, the percentage of homologous takes was highest in non-spayed females, next highest in castrate males and spayed females. The lowest percentage of such takes was in normal males. The incidence in the different categories is not considered to be statistically significant with the

10. Hill, R. T., *PROC. SOC. EXP. BIOL. AND MED.*, 1948, v67, 313.

possible exception of the non-spayed group of females. The ages of the donor grafts were not significant in relation to growth of fragments at the ages investigated. There was no apparent influence of the tissue transplants upon the weight gain of the recipient rabbits.

The authors wish to acknowledge the valuable assistance of Dr. Hebbel E. Hoff, Department of Physiology, B.U.C.M., and Dr. G. Gordon Robertson, Department of Anatomy, B.U.C.M.

Received June 29, 1951. P.S.E.B.M., 1951, v77.

### Parenteral Nutrition. XI. Studies with Stable and Unstable Fat Emulsions Administered Intravenously.\* (18953)

ROBERT P. GEYER, DONALD M. WATKIN, LEROY W. MATTHEWS, AND FREDRICK J. STARE.

*From the Department of Nutrition, Harvard School of Public Health and the Department of Biological Chemistry, Harvard Medical School.*

It has been clearly demonstrated that suitably prepared emulsions of fat can be given safely in large quantities to various species of experimental animals(1,2), and to man(3). Furthermore, studies concerning nitrogen and potassium balances(3,4), rates of growth(1,4), and analyses of body fat(1,4), have demonstrated the utilization of the fat in such emulsions. Experiments with emulsified C<sup>14</sup>-labeled trilaurin(5) and tripalmitin(6) have shown the metabolism of these lipids to be rapid and extensive. *In vitro* studies with emulsified C<sup>14</sup>-labeled trilaurin have indicated that various rat tissues have a high capacity to metabolize this and other lipid substrates(7). Rat blood, moreover, has

little effect on these substrates directly or in affecting the metabolism of these substances by tissue slices. Thus, the evidence supports the assumption that the blood plays a minor direct role, if any, in the utilization of intravenously administered emulsified fats.

The question arises, however, as to the ability of the body to remove extracellular fat which, for example, has become lodged in capillaries. This problem is of *no* concern when finely dispersed, stable emulsions of fat are employed. It is of great concern when an emulsion is administered intravenously which (a) is not finely dispersed, but contains large particles of fat (3 to 15  $\mu$ ), (b) is finely dispersed, but breaks down when in contact with plasma, or (c) is finely dispersed, but breaks down because of concurrent infusions of materials not compatible with the emulsified fat. Studies with iodinated fat emulsions of both a high and low degree of dispersion have been reported(8). The data presented in this paper deal with both stable and unstable emulsions which were studied from two standpoints: (1) the increase in the fat content of various tissues following the administration of such emulsions and (2) the rate of removal from the tissues of the excess fat which resulted when these emulsions were given.

*Experimental.* A number of emulsions of

\* Supported in part by grants-in-aid from The Upjohn Company, Kalamazoo, Mich., The Nutrition Foundation, Inc., New York City and The Cancer Research Grants Branch, National Cancer Institute, Bethesda, Md.

1. Mann, G. V., Geyer, R. P., Watkins, D. M., Smythe, R. L., Dju, D., Zamcheck, N., Stare, F. J., *J. Lab. and Clin. Med.*, 1948, v33, 1503.

2. Woerner, C. A., *Anat. Rec.*, 1949, v104, 61.

3. Gorens, W. G., Geyer, R. P., Matthews, L. W., and Stare, F. J., *J. Lab. and Clin. Med.*, 1949, v34, 1627.

4. McKibbin, J. M., Ferry, R. M., Jr., and Stare, F. J., *J. Clin. Invest.*, 1946, v25, 679.

5. Geyer, R. P., Chipman, J., and Stare, F. J., *J. Biol. Chem.*, 1948, v176, 1469.

6. Lerner, S. R., Chaikoff, I. L., and Entenman, C., *Proc. Soc. Exp. Biol. and Med.*, 1949, v70, 384.

7. Geyer, R. P., Matthews, L. W., and Stare, F. J., *J. Biol. Chem.*, 1949, v180, 1037.

8. Sato, G., *Tohoku J. Exp. Med.*, 1931, v13, 120.