

showing the beginnings of the same condition and the fourth, which has received filtrate fraction for eighteen months, is still alive and apparently well. This dog has now been placed on pantothenic acid instead of filtrate fraction, since the latter is not entirely free from nicotinic acid.

(V) The two remaining dogs receive pantothenic and nicotinic acids but no "filtrate factor." After six months on the diet one of these dogs, the male, is still well, growing and so far showing no graying of the fur. However, the fur is dull and powdery instead of glistening black and the dog is beginning to show some failure of neuro-muscular control. The other animal, a female, has lost appetite and weight, and is exhibiting much more advanced failure of neuro-muscular control. Her condition is not as good as that of her brother which has at no time received any of the filtrate factors (Group II above).

The following conclusions appear to be justified by these results:

1. Dogs require one or more of the vitamins of the B complex in addition to thiamin, riboflavin, pyridoxin, nicotinic acid and pantothenic acid.

2. Young dogs which receive none of the filtrate fraction, that is, no nicotinic acid, pantothenic acid or so-far unidentified factors, survive, grow moderately well but exhibit gradual depigmentation of hair, lack of activity and elderly behavior.

3. The administration of nicotinic acid or pantothenic acid alone to animals receiving ample amounts of all necessary vitamins except those of the "filtrate fraction" results in their gradual loss of neuro-muscular control and sometimes sudden death.

Attention should be given to the possible danger of the administration of large amounts of certain vitamins such as nicotinic acid to persons subsisting on diets having multiple deficiencies. Fortification of foods with those vitamins such as thiamin or nicotinic acid which are available in large quantities may precipitate conditions worse than the subacute deficiency state produced by the usual diet balanced in its inadequacies. Improvement in all directions equally is essential.

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THE EXAMINATION OF TISSUES FOR CARCINOGENIC FACTORS

IN a recent publication¹ Menke has reported sarcoma production in mice following injection with fatty extracts of human breast cancer tissue. Somewhat similar experiments have been in progress in this institute since 1938 and it seems appropriate to give a résumé of our experiments at this stage as under the present conditions here it is not possible to breed

Dilute Brown mice upon the scale required for a repetition and extension of the work described below.

The mammary glands of female mice of the Dilute Brown (DLB) strain are among the few tissues which can be labelled with some degree of certainty "pre-cancerous." In the experiments described here these mammae have been tested for the presence of a carcinogenic factor. The possibility exists that such a factor might be extractable and capable of initiating or facilitating mammary carcinoma in other mice.

EXPERIMENTAL

1. Mammary tissue was removed from 7 DLB lactating does when their litters were almost weaned. At this stage the mammae are engorged and can be very easily dissected out. The tissue was finely minced with scissors and shaken with distilled ether for about twenty minutes, stored in the refrigerator over night, the ether changed and the whole process repeated twice more. The ether extracts were pooled, evaporated at low pressure and diluted with an equal volume of sterile olive oil. Thirty female mice 6-8 weeks old, of ordinary commercial stock, received intraperitoneally 0.1 cc of the olive oil solution per mouse per injection. Thirty control females of similar stock received 0.05 cc sterile olive oil. Usually a fresh batch of DLB mammae was worked up for each series of injections. After nine injections spread over four months the does were mated; of the thirty injected with the extract fourteen littered, of the twenty-nine controls nineteen littered. The animals lived in all twenty-five months, but neither local reaction nor mammary carcinoma were observed.

2. Experiment 1 was repeated with modifications; this time each series consisted of fifty-two mice; the mammary tissue for each preparation was removed from eight to fifteen DLB lactating does and the injections were made sub cutem. The does (6-8 weeks old) receiving the injections were from the same commercial source as in Experiment 1. Eighteen sets of injections were spread over five months at roughly equal intervals. After the last injection the does were allowed to breed. Of the fifty-one does receiving extract forty-two littered, of forty-seven controls receiving olive oil alone thirty-two littered.

When the experiment had been in progress twenty-two months mammary carcinoma had developed in four olive oil control mice (three at the nineteenth and one at the twenty-second month) while the series injected with tissue extract had developed similar mammary tumors in two animals (seventeenth and twenty-first month) and also a spindle-celled sarcoma in one animal (nineteenth month). The sarcoma has been grafted and is growing in the second generation.

The ratio of experimental to control animals has remained fairly constant throughout the experiment.

¹ SCIENCE, 92: 290.

At the date of writing five mice in the experimental and four in the control series are still alive.

Thus an ether extract of DLB mammary tissue has not promoted mammary cancer in female mice of ordinary mixed stock. However, it is of considerable interest that a sarcoma has developed in one mouse at the site of injection. Sarcoma has thus been obtained in mice by injecting fatty material from DLB mammary tissue, from human breast cancer (Menke) and from the liver of a patient dead of cancer of the stom-

ach (Schabad). In this institute sixteen sarcomas have been obtained in mice injected with fat fractions from the livers of Europeans who have died of cancer or from the livers of Bantu dead from causes other than cancer. This work is now published in the *American Journal of Cancer* (39: 496, 1940).

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A VIBRATING NEEDLE AS A MICROSURGICAL INSTRUMENT

GLASS needles and irredectomy scissors are almost universally employed for performing operations on embryos. These instruments leave much to be desired. Not only does their effective manipulation require considerable skill which is usually attained only after long practice, but certain limitations are inherent in the instruments themselves. Fine-pointed glass needles lack rigidity, are easily broken in use and, since they are necessarily cylindrical rather than knife-shaped, do not have true cutting edges. The tendency of cells to adhere to the blades of irredectomy scissors may result in excessive injury to delicate tissues and, when more than one layer of tissue is to be cut at the same time, the shearing action of the scissors may cause the adhesion of one layer to another. This is undesirable in some types of experiments. Moreover, neither of these instruments is well adapted for the performance of certain operations such as the removal of loose cells from the surfaces of explanted organs, the separation of layers of tissue from one another or the excavation of material overlying the structure to be transplanted or underlying the site of implantation in the host. All these operations may be accomplished more easily and rapidly with the new instrument to be described below.

The vibrating needle was designed primarily to serve as an aid in performing transplantations involving young amphibian larvae and embryos. It is believed, however, that it could also be used to advantage in other microsurgical techniques. The essential feature of the device is a fine steel needle, the tip of which has been converted into a very fine knife. This is set in vibration by means of an electromagnet energized by 60-cycle alternating current. In principle, the cutting action of the vibrating needle resembles that of a single-toothed jig-saw with a very small amplitude of vibration and, as in the case of the jig-saw, its operation is subject to more delicate control than that of knives or scissors. Furthermore, the rapid vibratory motion of the needle and the currents produced in the

water by this motion are useful in performing the other operations mentioned above. The instrument is easily made and may be operated with proficiency after very little practice. The actual details of construction of the device may of course be varied in accordance with the nature of the material on which it is to be employed. The following (see Fig. 1) is a detailed description of a form of the instrument which has proven satisfactory for general purposes:

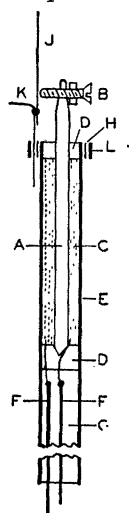


FIG. 1. Sectional diagram of instrument.

The core (A) of the magnet consists of an iron rod, 3" long by $\frac{1}{8}$ " in diameter. It should preferably be made of soft iron, although a tenpenny finishing nail is satisfactory. One end of the rod is slightly flattened laterally by hammering and is drilled and tapped to receive a $\frac{1}{2}$ ", 2-56 iron machine screw which, provided with a lock nut, serves as the adjustable pole (B) of the magnet. The coil (C) is wound between two cylinders of cork (D-D), each $\frac{1}{4}$ " in length and just a trifle larger than the inside diameter (7-8 mm) of the glass tube (E), which serves both as a protective casing and as a handle for the instrument. The coil is 2" long and contains approximately 100 feet of 36-gauge enameled copper wire. (Used wire may be bought at almost any radio repair shop.) The wire should be wound as smoothly as possible and great care should be taken not to injure the insulation. The ends should be scraped free of enamel and fastened to strong but light, well-insulated wires (F). After the finished magnet has been carefully inserted into the lower end of the glass tube, the upper end of the tube is filled with melted pitch or paraffin (G). After solidifying, this material holds the lead wires firmly and also improves the balance of the instrument by raising the center of gravity. The lower end of the tube, to which the needle is to be clamped, should be