

Urine is diluted so that it contains about one mg. % of sulfanilamide. Ten cc. of this diluted urine is measured into a flask, one cc. of 20% toluenesulfonic acid added, and then one cc. of 0.1% sodium nitrite. After 3 minutes, 5 cc. of dimethyl- α -naphthylamine solution (1 cc. in 250 cc. of 95% ethyl alcohol) are added. A standard solution of sulfanilamide is treated in the same way. After 5 to 10 minutes, the solutions can be compared in the colorimeter. To determine the acetyl-derivative in urine, one cc. of urine is mixed with 2 cc. of N hydrochloric acid, heated in a boiling water bath for 30 minutes, neutralized with 2 N sodium hydroxide, and diluted to appropriate volume. The determination of total sulfanilamide is then made as described above.

9256 P

Neoplasms in Albino Rats Resulting from the Feeding of Crude Wheat Germ Oil Made by Ether-Extraction.

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The effectiveness of thymus and pineal extract in controlling the rate of growth and development in the young when administered through successive generations of rats led us to attempt the same procedure with the various vitamins. In administering vitamin E we have employed an ether-extracted crude wheat germ oil[†] prepared by the extraction of fresh wheat germ with ether. All animals fed this preparation of wheat germ oil eventually developed tumors.

The rats used were placed on the stock diet of the Institute, containing the following ingredients: rolled oats 15 parts, cracked corn 60, dried meat scraps 14, powdered milk 10, sodium chloride 1. To each 100 gm. was added 1.25 cc. of cod liver oil. Additional nutrient consisted of green vegetables once a week.

From July 3, 1934, four animals were fed one cc. daily of wheat germ oil, the oil being mixed with the food. On October 29, 1934,

* From the Samuel Bell, Jr., Laboratory.

† This oil was especially prepared for us and kindly donated by E. R. Squibb & Sons. It is not their refined wheat germ oil (Zygon) designed for human use. We wish to express our appreciation to Dr. John F. Anderson for his cooperation in preparing this special oil, and in other ways.

116 days having elapsed, nodules were palpable in the abdomen of 2 of these rats. The rats were killed on November 12, 1934, and pieces of the resultant solid tumors present in the abdomen were transplanted to 2 other rats of the same strain. The grafts grew in both animals. The other 2 animals which were fed with the oil developed tumors 2 months later. These growths have been transplanted through 6 generations.

To check this result 10 albino rats (Wistar strain) were fed about one cc. per rat per day of crude wheat germ oil, beginning November 29, 1934. The only change was the addition to the food of wheat germ oil. Within the next 200 days tumors were palpable in the abdominal cavity of the 10 rats. In one case the tumor weighed 44 gm. In another animal 3 tumors were present, 2 arising apparently from the distal ends of the uterine horns and one from the mesentery. A certain amount of necrosis was not infrequent. These tumors were readily transplantable in the Wistar strain stock animals.

The malignant nature of these tumors is demonstrated by the fatal outcome, the morphology of the tumor cells and the inoculability through 6 generations. The implants grow with great rapidity, attaining a large size and result in the death of the animals. In many instances after the tumor had attained the size of 3x3 cm., it underwent necrosis and ulceration.

Microscopically both the primary and transplanted tumors are composed chiefly of spindle cells. In some areas the cells are small, compact and closely packed, with narrow elongated nuclei; in others the individual cells are larger and separated by fibrous tissue with large hyperchromatic nuclei, frequently showing mitoses. The cellular areas of the tumors and the evidence of rapid proliferation suggest a sarcomatous nature.

Negative results have been obtained to date from the feeding of refined ether-extracted wheat germ oil (Squibb), gasoline-extracted wheat germ oil (Squibb), benzine-extracted wheat germ oil (Squibb), Triticol (an expressed oil, kindly supplied by the Pharmaceutical Specialties Company), certified compressed wheat germ oil and vitamin E concentrate (furnished by General Mills and administered during the last 5 to 7 weeks). Linseed oil, sesame oil, cod liver oil, oleic acid and caritol have also yielded negative results.

Conclusions. Fourteen rats fed with unrefined wheat germ oil which contained the sediment deposited therefrom developed abdominal tumors. The neoplasm following the ingestion of oil is malignant in nature and microscopically a sarcoma. It is readily trans-

plantable and retains its malignancy through 6 successive implantations.‡

9257

Production of Sarcoma in Albino Rats as a Result of Feeding Crude Wheat Germ Oil.

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Subsequent to the work of Rowntree, Lansbury, Steinberg and Anderson,¹ † in which 14 tumors had been observed in 14 rats fed with a crude preparation of ether-extracted wheat germ oil, the Oncologic Hospital group was asked to elaborate this work and to determine and establish the nature of the tumor.

It was found that by increasing the amount of oil fed, the tumor could be produced as early as 60 days. Thus in 34 albino rats of the Wistar and Buffalo strains fed crude wheat germ oil, 100% developed intraabdominal tumors. These tumors have been found in the omentum, in the mesentery, in both small and large intestines, in the area of the uterus and subperitoneally. Many animals have developed multiple tumors in the abdominal cavity. The point of origin thus far has been consistent only in its having been found in the peritoneal cavity. The size of the tumors depends, to some extent, on the duration of the time before the rat is sacrificed. The tumors have been as large as 3x3 cm. There has been no lymphatic extension or metastasis to nodes. The only instance in which another organ has been involved was in one case with direct extension to the liver. If not sacrificed, the tumor becomes large enough to cause death often by intestinal obstruction.

In the Wistar strain, 22 tumors have been successfully transplanted to date. No attempt has been made to transplant the others of this group of tumors, as the animals were found dead in the

‡ We wish to express our appreciation to Drs. J. H. Clark, Joseph McFarland, and Francis Carter Wood, all of whom agree that this tumor is sarcomatous in nature.

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¹ Rowntree, Lansbury, Steinberg and Anderson, *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 424.

† Neoplasms resulting from the feeding of ether-extracted, crude wheat germ oil.