The relationship between pregnancy and tumor development has been investigated by a number of observers, whose results have been, however, in many instances contradictory. For example, Moreau (1) and Herzog (2) found that transplanted tumors grow with unusual rapidity in pregnant animals. Haaland (3), on the other hand, maintained that pregnancy exerts a markedly restraining influence on the growth of transplanted tumors, which continue to develop in their usual fashion after parturition. Bashford and Murray (4) hold that "pregnancy" in the female "and full sexual activity in the male constitute no bar to successful transplantation." Uhlenhuth and Weidanz (5) observed retardation in the growth of tumors during pregnancy and also more frequent spontaneous retrogression. Bridré (6) noticed a low percentage of positive inoculations in pregnant animals, and Ehrlich (7) observed that inoculations into animals bearing young was frequently followed by negative results and that in those successfully inoculated the growth of the tumor was greatly retarded. Then, again, Albrecht and Hecht (8) maintained that pregnancy affects the growth of tumors just as little as the presence of a tumor influences conception or gravidity. Cuenot and Mercier (9) reported a most interesting observation. They noticed that Borrel's tumor "B," which rarely underwent spontaneous absorption, if inoculated before fecundation developed during gestation and receded during lactation. The tumor, however, did not regress if one mouse only was born, thus leaving the activity of the mammary gland at a minimum. Neither did absorption occur even in the presence of several young, if the tumor was so situated that its vasculari-
zation was independent of that of the mammary gland. Fichera (10) explained these various inconsistencies by assuming that when many embryos were present the food stuff was almost wholly consumed by them, while if there were only a few some of this material was available for the tumor cells.

Slye has concluded from her observations of spontaneous tumor growth in the mouse that: First, reproducing females grow much less tumor than do non-reproducing females of the same age, etc. Second, reproducing females grow much less tumor while they are reproductive than they do while they are non-reproductive. In other words, she finds that pregnancy exerts a markedly retarding influence upon growth of tumor.

In re-investigating this problem rats were employed. The animals selected were young adults, sexually mature, vigorous, and in very good condition, which had been separated from male animals for a period of one month to avoid the possibility of unrecognized pregnancies. The rats were mated with strong, vigorous young males that were kept in the same boxes not only during the entire period of gestation but also after the females had littered, in order to impregnate the same animals immediately after parturition. In all cases the date of conception was calculated by counting back twenty-one days before the date of littering. All the animals were inoculated on the same day with 0.003 gram of Flexner's rat carcinoma, the time chosen being two days after the animals had been mated. In all, 105 animals were inoculated. Of these, 43 (41 per cent) became pregnant and littered normally.

In analyzing the cases in which no growth occurred, it is interesting to note that about 7.8 per cent of the males inoculated showed no growth, and that about 8.4 per cent of the females showed no growth. In the group of females without tumor growth, 44 per cent did not become gravid. The other 46 per cent did. These figures tend to show that in the negative cases neither sex nor gravidity played any rôle.

Tracings of the tumors were made every four days, and in this way growth was depicted simply but effectively.

A comparison of the charts (figs. 1 to 4) of the tumors of the pregnant and of the non-pregnant groups shows at a glance
that in these experiments pregnancy had absolutely no effect at all upon the growth of the transplantable Flexner rat carcinoma.

**DISCUSSION**

It seems impossible completely to reconcile all of the conflicting results which have been published in regard to the effect of pregnancy on the growth rate of inoculated tumors, chiefly because we have insufficient data upon which to base any conclusions.
as to the growth capacity of the tumors which the various experimenters have employed. Nor do we know, in many instances, the site of inoculation. Mice are especially unsuitable animals for such a study, as the implanted tumors are apt to be variable in their growth rate, and may become so large as to kill the animal quickly. This obviously complicates the problem and renders careful control and statistical analysis of the results necessary. But it does seem possible to draw a few conclusions,
not entirely inharmonious with the reported experimental work and the facts obtained by clinical observation.

The tumor grafts in the experiments here reported were not placed in the mammary gland but by intent in the axilla; they were, therefore, not affected by the increase in the vascularity of the breast at the beginning of pregnancy as they would be if placed directly in the main mass of the mamma. This increase in vascularity is undoubtedly the explanation of the rapid growth of tumors in the breast observed in human beings. But the conditions in the human female and in female mice are not comparable. A mouse weighing 15 to 20 grams will frequently carry a tumor weighing one-tenth of its weight. Unfortunately, the weights of the tumor-bearing animals are not given in Miss Slye’s paper, though the dimensions of the tumors are furnished.

On the other hand, the weight of the tumor in a human female is rarely more than one one-hundredth or one one-hundred and fiftieth of the body weight. Mammary cancer in a mouse, therefore, may correspond in mass to a rapidly growing breast carcinoma of 10 to 15 pounds in a human female, a tumor which is practically never seen. It is quite possible that the demand for food for such a theoretical tumor if complicated by pregnancy might result in the starvation of the tumor for a time as Moreshi (12) has shown to be possible.

It is, therefore, evident that Miss Slye’s results, while applicable to one species of mammalia under the conditions which she specifies, are by no means obviously transferable even to other types of rodents, much less to human beings.

The fact that in the additional experiments here reported no influence on the growth rate of tumors was shown is probably due to the disproportion between the size of the rat and its embryos, frequently weighing 150 grams with 25 grams of embryos, and the tumors, which are usually not more than one-fiftieth to one-hundredth of the weight of the animal. So, too, in mice the proportionate weight of the embryos demanding food is larger than that ordinarily occurring in the human female, a child rarely being over one-fifteenth of the mother’s weight, while in the multiple mouse pregnancies 5 grams of embryos may be produced at a single birth from a mother weighing only 22 grams.
A grafted tumor, such as we have employed, being a mass of somatic cells growing in a foreign host, affords a possibility for studying the problem of tissue growth independently of organ or other relationships. The tumor is simply implanted in the subcutaneous connective tissue, while a primary tumor of the breast, in its inception at least, has important anatomical correlations with the tissue in which it grows. It is thinkable that some of the results observed by Miss Slye may be due to changes in the connective tissue stroma of the tumor rather than to the epithelium, but in the implanted tumor the connective tissue is furnished by the host, the epithelium being derived from another animal, so that the situation is quite different.

It seems safe to conclude, therefore, from our own experiments, that pregnancy of itself does not necessarily alter tumor growth rates, but that such interference, when it is observed, is due to the forced division of food substance between the tumor and the offspring; similar checking of the tumor can be observed in implanted tumors when the food of the non-pregnant animal is reduced approximately to the starvation point.

A comparable diminution in the tumor growth rate may be seen in human beings in the terminal stages of extreme cachexia with innutrition but, as a rule, in man pregnancy either has no effect on the progress of a cancer or, if the mammary or uterine tissues are involved, hastens the growth.

There is nothing, therefore, in the varying results of published experimental work which cannot be harmonized or which controverts the clinical observations already recorded.

REFERENCES

(1) Moreau: Arch. de méd. expér. et d'anat. path., 1894, vi, 693.