human heart, pointing out several interesting features in the polygraphic records of the case. These records were of such a nature that interpretation of them was very difficult and led to doubtful conclusions. Since that meeting we have been fortunate in securing excellent electrocardiograms of this heart through the kindness of Dr. H. B. Williams. These records show that the interpolated beats arise constantly in the right ventricle, and probably in the right branch of the A–V bundle; the curves indicate that the abnormal impulse travels to the basal part of the left ventricle and thence to the apex, and that this path is always the same; there is no evidence of retrogression to the auricle, as was suspected from the mechanical tracings, but there is evidence of depression of the conduction system, for the P–R intervals of normal beats following the extrasystoles are often considerably lengthened (we could not be certain of lengthened As–Vs intervals in the polygrams). Phonocardiograms show divided second sounds produced by the abnormal beats and lengthened first sounds. A few compensating pauses have been seen in the electrocardiograms.

Aside from these new facts about the case, our previous report needs no alteration.

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The incidence of cancer in various strains of mice.[1]

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A number of investigators noticed the repeated occurrence of a particular kind of cancer in animals living either in the same cages or

[1] These investigations are the outcome of plans for research which one of us suggested about seven years ago; on that occasion we pointed out the necessity for the study of possible hereditary and infectious factors in cancer directly in breeding establishments. In accordance with these suggestions our investigations were carried out in conjunction with Miss Lathrop in Granby, Mass., one of the most extensive breeders of mice, who supplied at various times different laboratories in this country with ordinary as well as with tumor mice, and from whom we obtained about seven or eight years ago a mouse with a spontaneous tumor which we have since propagated through many generations of mice and which was used in the majority of our experiments.

on the same farm. One of us described such observations in the case of carcinoma of the inner canthus of the eye in cattle found in increased number on a farm in Wyoming and in the case of three sarcomata of the thyroid in a relatively small number of white rats kept in a few cages in the laboratory of the Chicago Polyclinic and compared this phenomenon to the so-called endemic occurrence in man, but emphasized from the beginning that we had to consider not only infectious, but also hereditary conditions as possible causative factors.

While in the case of certain cancers, for instance the squamous cell carcinoma of rats observed by Hanau, the above mentioned carcinoma in cattle and the sarcoma of thyroids of rats and some other similar cases observed by Borrel and others the unusual frequency of the reported cases in certain places could not be doubted, the significance of similar observations concerning the frequent occurrence of mammary cancer in mice were less clear, inasmuch as mammary cancer of mice is found everywhere and sufficient comparative statistics do not exist as yet as to the normal incidence of cancer in various strains of mice.[1] Our investigations were therefore concerned with the incidence of cancer among various strains of mice kept in the same breeding establishment, especially with the view to decide definitely whether or not a hereditary factor was detectible in the occurrence of spontaneous cancers in mice.

The principal results of our investigations which, after a few preliminary observations were begun more than three years ago, and which we hope to be able to continue, may be summarized as follows:

1. Mice raised in the same breeding establishment, under the same conditions of climate and feeding show a very different incidence of cancer of the mammary gland among female mice depending on the strain or family to which the mice belong. To give a few examples: The strain designated "English," 66.9 per cent.; "Carter," 35 per cent.; "No. 8," 30 per cent.; cream, 3⅓

[1] The more or less frequent occurrence of mammary cancer in mice in certain cages or breeding establishments had previously been reported among others by Eberth and Spude, Borrel, Michaelis, Gaylord and Clowes (who also observed the occurrence of sarcoma of rats in cages in which one of us had previously kept rats inoculated with sarcoma), Apolant, Ascher, Henke.

per cent.; hybrids between European and No. 10, 82 per cent.; cancer incidence.

2. The tumor rate in the different strains remains approximately constant in the succeeding generations; a few times we noticed however an apparent increase in the tumor rate after the first two generations. Also different substrains obtained through selection of certain individuals from a large strain which may or may not differ in color or in other peculiarities from other substrains, show usually a similar tumor rate as the main strain.

Thus the substrain "English tan" had a tumor incidence of 73 per cent., "English sable" 76 per cent., "English 101" 65 per cent. It is however, in some cases, possible to detach from the main strain a substrain, that differs markedly from the main strain in the tumor rate. Thus the "English silver," a substrain of the "English," has only a tumor incidence of 8⅓ per cent. In this case the factor or factors determining the origin of tumors seem to be linked with the factor or factors of the silver color.

3. Various strains of mice do not only differ in regard to the incidence of cancer, but also in regard to the age at which the cancers appear. Thus in the English strain as a whole (excluding the silver substrain) tumors appeared in 68 per cent. of the cases in mice at the age of 12 months or below, and in only 4.6 per cent. of the mice the tumors appeared above the age of 17 months, while in the strain No. 8 approximately 72 per cent. of the animals have tumors above the age of 12 months and 36 per cent. above 17 months. In the "Carter" strain the tumors appear in 63 per cent. at or below the age of 12 months and in the hybrids between European and No. 10, which have the high tumor rate of 82 per cent. the tumors appear in 69 per cent. above 12 months and in 22 per cent. above 17 months of age, therefore considerably later than in the English, who also have a very high tumor rate. In various English substrains the tumors appear therefore much earlier than in all the other strains, although the tumor incidence as a whole is not as high in the English strain as in the hybrids between European and No. 10. In valuating this fact we have however to take into consideration the usually shorter duration of life of the English in contradistinction to some other strains.

The youngest mice in which we observed tumors were 5½ months old at the time their tumors were first noticed.

4. Although in several strains the incidence of cancer increased with advancing age, in another strain (No. 8) a maximum was reached between the age of 14 and 20 months, after which again a decrease took place in the percentage of mice affected by cancer.

5. In mating a strain rich in tumors (English) with a strain very poor in tumors (cream) we received hybrids which have so far been rich in tumors. In this case the male which is itself not liable to have tumors transmits the liability to have tumors to the daughters; the latter have tumors, although they are nursed by mothers which are not liable to have tumors. We wish however to collect still further data concerning this point before we regard this conclusion as definite.

6. It is not always probable to predict from the known cancer rate of the parents the cancer rate of the hybrids. Thus No. 10 mated to a strain called "European" gave hybrids with a tumor rate of 82 per cent., while No. 10 mated to No. 8 seems to give a very low tumor rate, although pure Europeans had a lower rate (13 per cent.) than No. 8 (30 per cent.). In this respect the inheritance of the tumor rate may be compared to the inheritance of color, in which also in many cases until a complete analysis of the various factors has been made the color of the hybrids cannot be predicted.

7. There are certain other peculiarities observed in the case of strains with different tumor rates. Thus the cream which have the lowest tumor rate are mice which grow and mature more slowly than any other strain of mice, although they reach ultimately a large size, and they are very poor breeders. The hybrids between No. 10 and European which have the highest tumor rate grow rapidly and are very good breeders. The English strain also grows well and breeds well. But the parallelism between these characteristics and the incidence of tumors in the various strains is not apparent in every case. Thus certain strains grow very well and are good breeders without having a high tumor rate.

8. Mice belonging to strains with a low tumor rate did not develop tumors either by living in boxes in which mice with spontaneous tumors had lived a long time, although the boxes had been kept unaltered (not cleaned) during the course of the experiment or by living in the same box with mice spontaneously affected with cancer.

This agrees with the previous observations of Loeb, who under similar conditions, in which however rats with inoculated instead of spontaneous tumors were used, never observed a transmission of a sarcoma to another rat. It is however noteworthy that in strain No. 8 the large majority of cancers appeared in groups, inasmuch as several, in one case even as much as five mice, which were kept in the same box were simultaneously affected by cancer. Whether we have in this case which was not duplicated in the case of other strains to deal with an accidental occurrence we are unable to state at present.

9. From our investigations we may conclude that hereditary factors play a great part in the incidence of cancer among mice and that hereditary transmission is to a great extent responsible for the so-called endemic occurrence of cancer among animals. Certain observations especially of Borrel and Fiebiger concerning the occurrence of parasitic worms in certain kinds of cancer of animals indicate that also other factors of an infectious character may be responsible for this endemic occurrence.[1]

Miss Maud Slye, of Chicago, in experiments carried on simultaneously with our own, also came to the conclusion that the incidence of cancer varies in the different strains of mice which she had under observation according to a preliminary communication she made at the last meeting of the American Association for Cancer Research in May, 1913. In the discussion to Miss Slye's paper we mentioned some of the results of our work.

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The influence of pregnancies on the incidence of cancer in mice.

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In order to analyze still further the various factors causing the spontaneous development of cancer of the breast in mice we

[1] On a previous occasion (*Centralblatt f. allg. Pathologie*, Bd. XII, N. 22, 1911, p. 994) we published already a tree of one of the families of mice under our observation in which the hereditary transmission of tumor had been apparent. Cf. also *Interstate Medical Journal*, Vol. XX, No. 5, 1913.