On the History of Experimental Oncology
(Centennial)

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Experimental oncology has developed in an important branch of science. Numerous investigators all over the world work in this field. In many countries there are special institutes and laboratories; a great number of scientific meetings, conferences, symposia and workshops devoted to experimental oncology is held. They take an important place in the work of international and national oncological congresses and all scientific journals and other issues devoted to the problems of etiology, pathogenesis, diagnostics, therapy and prevention of malignant tumors. At last, it should be emphasized that the number of books, monographs, collections and individual papers devoted to experimental oncology grows with years.

Such a state of affairs is quite understandable since experimental reproduction of any disease is a big step in its studying. This, certainly refers to oncology too. The possibility to obtain experimentally a great number of tumors in animals let us investigate step by step their origin and development as well as the result of modern methods for their diagnostics and treatment. What and when are the beginning of experimental studies of malignant tumors?

The first positive result in this way was the successful transplantation of malignant tumors in animals. Several attempts to transplant spontaneous tumors occurring in man and animals into animals of the same or other species had been made for a long time but failed in spite of the fact that such outstanding medical scientists as BILLROTH, LANGENBECK, VIRCHOW et al. participated in them. In a number of cases at the site of transplantation of particles or “juice” taken from human or animal malignant tumors peculiar nodes were observed but, as a rule, they resolved and disappeared as they were not true neoplasms.

Contemporary experimental pathology began to develop only in the middle of 19. century. On the one hand it was closely connected with Virchow’s cellular pathology which had put the basis for morphological investigation and on the other hand — with the rapid development of microbiology due to the works of PASTEUR, MECHNIKOFF et al., requiring numerous experimental investigations in animals. Since the cellular structure of tumors became clear it naturally gave rise to the idea that tumor cells and not some “juice” were necessary for their transplantation.

Though the pathological anatomy is undoubtedly older than many other theoretical medical sciences and its beginning is usually referred to MORGAGNI’s treatise “De sedibus et causas morborum” (On the localisation and causes of diseases)
to 1761, its development as a teaching subject occurred much more later. Thus, in Russia, pathological anatomy as a course of autopsies for students was firstly performed in Petersburg Medico-surgical Academy by the famous surgeon N. I. Pirogov in 1841. The first chair of pathological anatomy in Russia was established in 1849 in Moscow University and headed by A. I. Polunin and in the Medico-surgical academy such chair was organized only in 1859. Its flourish referred to 1867—1878 when it was headed by M. M. Rudnev.

M. M. Rudnev was a character and an outstanding medical scientist of that time. He is the founder of Petersburg Russian school of pathologists. From 1870 to 1877 he edited a special “Journal for normal and pathological histology, pharmacology and clinical medicine”, where a number of papers on pathology and relative sciences including oncology was published. M. M. Rudnev appreciated highly the microscopic as well as the experimental methods of investigation and a special animal house attached to the Chair of Pathological anatomy was established. Rudnev taught both physicians and veterinarians because at that time a veterinary department also entered the structure of the Medico-surgical Academy. Among his pupils and coworkers there were not only medical but veterinary doctors too.

A deep interest to oncological problems was reflected in Rudnev’s “Textbook of general pathology” as well as in a number of papers published both by him and by his pupils. A considerable part of them was devoted to the results of morphological investigations but at the same time questions of comparative and experimental oncology were also considered in some of them.

Rudnev was fully aware that to solve the questions of cancer origin further investigations were needed. He hoped that special experimental studies were able to elucidate these problems. In the paper “General histology of malignant tumors” published in 1870 in the “Journal for normal and pathological histology, pharmacology and clinical medicine” he wrote. “To solve the problem of transplantation it is first of all necessary to transplant cancer juice into a homogeneous animal, then it is necessary to know that all the transplanted elements are alive and have not undergone any regressive metamorphose so characteristic of all cancer and, at last, it should be known that the transplanted elements are young and capable of further development. By observing these main conditions the success is a priori possible.” Thus, Rudnev not only insisted on the experiment of cancer transplantation but even formulated three “main” conditions necessary for its success. And only the investigator capable to solve this problem remained unknown. Mstislav Novinsky turned out to be such one.

M. A. Novinsky (1841—1914) (Fig. 1) was born in Novgorod in the family of a priest. In 1870 he entered the veterinary Faculty of Petersburg Medico-surgical Academy; he graduated in 1874 with honour (summa cum laude). Being a student he carried out a large morphological experimental work on 15 dogs and one horse: “On the question of tissue changes in extremities resulted from the cutting of sciatic nerve and on the influence of the latter on skin wounds healing.”* For this work he was awarded with a gold medal. Beside this paper M. A. Novinsky also published in the same book “Clinical observation on tetanus in a horse cured by long-time administration of chloroform”.

* Archives of Veterinary Sciences, 1874, book 2, part 3, p. 86.
Postgraduated M. A. NOVINSKY continued to work during 2 years in the Zoosurgical department headed by adjunct-professor V. E. VORONTSOV, a pupil of RUDNEV. VORONTSOV was a highly educated young scientist of that time who later became well-known by his public activity in the field of Russian veterinary. Novinsky was already an experienced investigator who mastered the modern for his time methods of experimentation and histology.

The experiments of NOVINSKY were performed in dogs and horses divided into 2 groups. In the first one transplantation of malignant tumors was carried out in normal animals of the same species. In the second — on “inflamed soil”. For the last purpose skin free from hair was burned or treated by crotone oil. Experiments with inflammation were inspired by the assumption accepted at that time that cancer arose from the elements of granulomatous tissue. All the experiments of this group showed negative data.

But the first group was a success. It consisted of young dogs (puppies) aging nearly a month to which little pieces of spontaneous malignant tissue were introduced subcutaneously in small skin wounds in the area of the breast. One of them was from a carcinoma medullare of the nose, which destroyed bones and induced small multiple metastases in lungs. The second tumor was a recidivacy myxosarcoma medullare of the vagina in a sixyears old dog female.
The first cancer transplantation was made in December, 19, 1875 on a puppy and 2 months and 6 days later, in February, 25, 1876, a tumor node was noted at the site of transplantation which then grew and ulcered. Biopsy and microscopic study of March, 1876 showed identical morphological picture in the transplantate and in the original tumor. Material was taken from the transplanted neoplasma for subcutaneous transplantation into other 3 puppies which was also successful and the morphological structure of the tumors was also identical. Thus, M. A. Novinsky obtained not only the first but also the second generation of the transplanted cancer. These results were published as a preliminary communication in 1876 both in Russian (Medicinsky Vestnik, No 25; Fig. 2), and in German (Zentralblatt für d. Medicin. Wissenschaften, Bd. 14, No 45; Fig. 3).

In the other series of experiments myxosarcoma of the vagina was transplanted. In this case also nearly 2 months later tumor node identical by its structure to the original one appeared and not only the first but the second generation too, i. e. the beginning of what we call now a strain of transplanted tumor had been obtained.

The peculiarities of the technique and all the experimental data were given in detail in Novinsky’s thesis for the degree of Magister of veterinary sciences entitled: “On the question of transplantating malignant tumors (experimental studies)” which was successfully defended and published in 1877 as a single booklet and also in the “Archives of Veterinary Sciences” (1877, book 2, part 3, p. 129—163).

Thus, there is no doubt that Novinsky was the first to prove the possibility of transplantating malignant tumors. The success of that work depended on the transferring of undamaged living tumor cells into young animals of the same species and on the absence of considerable inflammatory reaction, due to the small size of the transplanted tumor pieces. The author wrote: “Homogeneity of the animals is one of the important conditions in the course of transplantation.”

13 years after Novinsky’s preliminary communication Wehr published a paper on a successful transplantation of a genital sarcoma from dog to dog. In the same year of 1889 Hanau informed about a successful transplantation into 2 rats of pieces from a metastatic nodule of a spontaneous epidermoid carcinoma. Both authors cited M. A. Novinsky as the first successful investigator in tumor transplantation. However, M. A. Novinsky’s name was gradually moved away with time. It depended mainly on the fact that after his classical thesis he had to leave scientific work. Despite Rudnev’s and Vorontsov’s desire to keep Novinsky as an assistant in Medico-surgical Academy he was mobilized to the army during the Russian-Turkish War and by the time he returned the veterinarian faculty of the Medico-surgical Academy had been closed, M. M. Rudnev died and V. E. Vorontsov lost his chair. M. A. Novinsky was bound to deal with practical work and had not already returned to science.

The other reason due to which Novinsky’s name was forgotten for a long time is that there was nothing known about his life, beginning of his scientific activity and his great contribution into experimental oncology. Only in 1950 a book (L. M. Shabad: “M. A. Novinsky — the founder of experimental oncology”) was published which contained his biography written on the base of new discovered archives documents as well as the picture of his personality and the analysis of the significance of his work. In 1955 the journal “Cancer” published an article by M. B. Shimkin where Novinsky’s priority in transplanting tumors was acknowledged.

We consider M. A. Novinsky to be the father of experimental oncology which, consequently, has reached its centennial in this year of 1976. Novinsky’s work
О прививании раковых новообразований.

Предварительное сообщение ветеринарного врача Новинского.
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Привить во внимание существующее мнѣніе, что близкородственными животными гораздо легче воспринимаются заразу другъ отъ друга, мы для большаго успѣха, ограничивъ свои опыты только на собакъ. Дѣло въ общемъ чрезвычайно велось такъ: новообразованіе раковой натуры поступавшихъ въ клинику собакъ подвергались клиническому и микроскопическому изслѣдованию, послѣ этого биоструи съ раковыхъ поверхностей открывали всегда по периферіи раковой язвы, откуда и брались большие кусочки опухоли, что удачны для пересадки на другое животное подъ кожу. Послѣднему предварительно выбрита шерсть, дѣлились разрѣзы кожи въ одинъ центиметръ, а иногда въ пять миллиметровъ.

Въ одномъ случаѣ накладывался шовъ, въ другихъ, гдѣ разрѣзы были не значительны, ранку оставляли безъ шва. Всѣхъ прививаний съложено 42, изъ нихъ на воспаленной почвѣ 27,—у 8-ми собакъ совершенно здоровыхъ и взрослыхъ и 15-ть прививаний у 6-ти щенковъ на нормальной почвѣ. Первая категорія прививаний на воспаленной почвѣ не дала положительныхъ результатовъ, тогда какъ изъ числа 6-ти щенковъ второй категории два случая были вполнѣ удачны.

Изъ этихъ опытовъ видно, что при благопріятныхъ условіяхъ кусочки раковой опухоли, перенесенные подъ кожу собакъ, прививаются и что заразительность раковыхъ новообразований не подлежитъ сомнѣнію. Опыты продолжаются. Подробное описание нашихъ изслѣдований появится въ непрідолжительномъ времени.
Zur Frage über die Impfung der krebsigen Geschwülste.

Vorläufige Mitteilung von Matthias Nowinsky. (Aus dem Zentrallaboratorium des Prof. Wozniacki in Petersburg.)


In dem zweiten Fall entnahm ich für die Impfung Stückchen der krebsigen Geschwulst aus dem ersten Knoten der vorjährigen Versuche. Geimpft wurde an einem, drei Monate alten, jungen Hunde, welcher dann 4½ Monate nach der Impfung an der Pestkrankheit starb. Bei der Section des Cadavers fand sich in der Narbe, wo die Impfung geschehen war, ein kleiner Knoten von der Grösse einer Erbse, ohne metastatische Knotchen in anderen Organen. Bei der

Aus diesen Experimenten ersieht man, dass wenn bei günstigen Bedingungen die kleinen Stückchen der krebsigen Geschwülste unter die Haut der Hunde versetzt werden, sie sich einimpfen. So ist die Infection der krebsigen Neubildung unzweifelhaft. Die Versuche sollen fortgesetzt und die ausführlichere Beschreibung später gegeben werden.

Fig. 3. Preliminary communication in German.
is the source of all the experimental cancer research not only because this man had the luck and honor to realize the conditions of the experiment formulated by M. M. RUDNEV and to obtain the first success in the transplantation of tumors. This work denotes even something more. It has given a method which has been in use during hundred years up to now. No matter which laboratory all over the world you visited you would see everywhere the results of tumor transplantation, i.e. the using of NOVINSKY’s method.

Such state of affairs is awfully clear if take into consideration how much we have achieved in understanding the nature and the new ways of diagnostics and treatment of neoplasms thanks to tumor transplantation. It was the most striking demonstration of their autonomy and progression and at the same time a good object for studying their variability and the influence of modifying factors. Tumor cell transplantation witnesses in favor of their cellular nature but at the same time it was the transplantation of some tumors in fowls that had showed (ROUS, 1911) the possibility to carry them by non-cellular filtrates and had put the beginning to all the virological oncology. At last, tumor transplantation presents a model for metastasizing and a fine object for testing new ways of diagnostics and treatment of tumors. Modern biochemical, immunological and genetic investigations would be impossible without tumor transplantation. All the modern chemotherapy has grown and develops thanks to the possibility of tumor transplantation.

That is why neoplasma transplantation should be considered as the actual beginning of all the experimental cancer research.