Résumé

EXPERIMENTAL STUDIES ON CHEMOTHERAPY OF MALIGNANT TUMORS. VII

Nitromin-resistance developed in Chemotherapy of the Hirosaki Sarcoma

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When nitromin was repeatedly injected into the abdominal cavity of the Hirosaki sarcoma bearing rats, the tumor cells in the ascites were remarkably decreased in number showing the enormous giant cells and the abnormal mitotic figures and at last disappeared in the abdominal fluid. But after 2 to 7 weeks the tumor cells appeared again in the ascites and rapidly proliferated even if the application of nitromin was continued. At that time, if the dosis of nitromin was doubled, the tumor cells were unaffectedly proliferated, leading the animals to death owing to the tumor invasion.

In 6 cases the reappeared tumor cells were transplanted into the abdominal cavity of the other normal animals, and then the animals were treated with nitromin starting from a few hours and 4 days after transplantation.

At this time little or no inhibitory effects of nitromin were seen against the reappeared tumor cells, namely the tumor cells in the ascites increased in number showing no giant cells and abnormal mitosis and the survival days of the animals were never prolonged. This fact indicates the developement of nitromin-resistance in the reappeared tumor cells and it might be due to the acquired resistance of the tumor cells against this drug, that the nitromin treated animals could not get rid of tumor relapse.

In the nitromin treatment of the Hirosaki sarcoma, the percentage of the perfectly cured animals was most highly in the intermittently treated group and lower in the daily treated group. This result shows that the developement of the drug resistance was hindered by the intermittent treatment.

EXPERIMENTAL STUDIES ON CHEMOTHERAPY OF MALIGNANT TUMORS. VIII

A Nitromin Resistant Line of the Hirosaki Sarcoma

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The nitromin resistant line of the Hirosaki sarcoma was induced by repeated transplantations during seven generations in nitromin treated rats and then it was successfully transplanted during 240 days with 51 generations. Drug resistance was always constant and even after 225 days it was kept without reduction. The nitromin resistant line showed cytologically, caryologically, patho-anatomically, and histologically the same character as the original line.

Sarkomycin and actinomycin J showed the same antitumor activity as the original line but TEM showed the cross resistance.

SOME OBSERVATIONS ON THE METHOD OF DETERMINATION OF DRUG RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS* OCCURRING IN SPUTA OF PATIENTS

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When the degree of resistance is determined in *Mycobacterium tuberculosis* occurring in sputa of patients by the usual routine method, it should be considered that the results obtained vary depending on the number of viable cells inoculated to each tube. Therefore, the method has been considered not to be suitable to determine the problem of decrease of isoniazid resistance or PAS resistance. For the purpose one should determine the number of resistant mutants per viable cells. In this report, a number of samples of the deter-

mination have been presented. A sputum has been added with an equal volume of 8 per cent sodium hydroxide and mixed. The alkaline solution of sputum has been diluted with saline for obtaining dilutions of 10^0, 10^{-1}, 10^{-2}, 10^{-3} and 10^{-4} The dilutions have been inoculated to tubes containing no drug and to those containing drugs. Approximately 20 to 200 colonies per tube and its dilution have been used for rpractical determination of viable cells, although it has been considered that the use of 30 to 100 colonies per each tube and its dilution are theoretically suitable for such determination.

SOME OBSERVATIONS ON THE METHOD OF DETERMINATION OF DRUG RESISTANCE IN *MYCOBACTERIUM TUBERCULOSIS* OCCURRING IN SPUTA OF PATIENTS.

Following report

The composition of Population of *Mycobacterium tuberculosis* Resistant to Antituberculous Drugs occurring in Sputa of Patients

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Ratios of the number of resistant mutants per viable cells occurring in sputa of patients were determined and thus the composition of population of *Mycobaterium tuberculosis* occurring in sputa was observed. The composition of population of streptomycin-resistant strains occurring in sputa of patients were relatively homogeneous, and those of isoniazid-resistant strains and of PAS-resistant strains were relatively heterogeneous. These results were similar to *in vitro* results obtained by us, which have been concerned with the composition of population of resistant strains isolated in laboraotry. (TSUKAMURA, M., and MIURA, K. A comparison between the composition of population in the streptomycin-resistant strain, in the isoniazid-resistant strain and in the PAS-resistant strain of *Mycobacterium tuberculosis* var. *hominis*. Annual Report of the Japanese Association for Tuberculosis, in press.)