# Comments

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I have a brief report on work which Dr. Clyde Dawe and I have been doing. It is in one aspect an extension of the idea Dr. Rubin presented this morning, i.e., the influence of intermediation of other cells in the neoplastic process induced by the virus.

The method consists of transferring submaxillary salivary glands from 1-day-old mice to the sponge matrix system in a plasma clot and studying serially the effects of the parotid tumor (polyoma) virus, in this case. One variant of the polyoma virus that we used is a thymotropic variant which produces 100 per cent thymic epitheliomas in a relatively short time in susceptible mice.

In studying the salivary gland in control and virus-infected materials, it is seen that after 15 days there are very decidedly different patterns in the infected and the uninfected cells. There appears very active proliferation of the epithelial elements with large solid cores of cells infiltrating most of the lumina of the acini. Most of the cytologic changes which are characteristic of salivary tumors *in vivo* are seen *in vitro*. These are nuclear enlargements, very prominent nucleoli, the development of internuclear clear spaces, enlargement of cells, and increased mitotic index.[1]

Interestingly, there is at the same time a cytolytic effect on the stromal elements. This is most prominent where the epithelial changes are most pronounced, that is, in areas of proliferative changes. In areas where the stroma fails to react, there is observed to be no striking effect on the epithelial cells.

Interestingly enough, in submaxillary rudiments from 14-day mouse embryos, the cytopathogenic effects appear a little earlier than in newborn glands, but the epithelial proliferative response occurs later and is less marked than in newborn glands. Going in the opposite direction, if one takes 5-month-old salivary glands, after a month in culture the epithelial proliferative response is more marked than in either newborn glands or 14-day embryo rudiments after the same period in culture. There is, therefore, a cytolytic effect at the same time that there is a proliferative effect on different cell elements. We are interested in the problem of what this transition really means. Periodically we have transferred these transformed cells to the renal capsule of mice: young mice, radiated mice, cortisonized mice, and so forth. To date, several of these have grown progressively.

This brings us to another problem. Not all, and probably very few, of these parotid gland tumors grow progressively when transferred or transplanted into mice of the proper genotype. And this is particularly true of the epitheliomas of the thymus. On the other hand, there was a very rapid induction, in our irradiated repicient mice, of multiple tumors from the transfer of these exceedingly small fragments which had transformed, at least morphologically, toward the typical tumor formation which is seen *in vivo*.

[1] See C. J. Dawe, and L. W. Law, *J. Nat. Cancer Inst.*, **23**:1157–78, 1959.

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*Cancer Res* 1960;20:770.