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Sevoian M, Chamberlain D M & Counter F. Avian lymphomatosis. Part I. Experimental reproduction of the neural and visceral forms. Part II. Experimental reproduction of the ocular form. *Vet. Med.* 57:500-1; 608-9, 1962.
[Massachusetts Agricultural Experiment Station, Univ. Massachusetts, Amherst, MA]

Herpesvirus-induced lymphoid tumors were experimentally produced with a cellular and cell-free inoculum in chickens at a high and repeatable rate for the first time. The rapidity and consistency with which lymphomatosis in chickens was produced at a high rate was unprecedented. We found evidence that neural, visceral, and ocular forms were the manifestations of the same agent. The ability to reproduce a cancerous process (lymphomatosis) within two to three weeks at a high and consistent rate in an experimental animal facilitated studies in neoplasia. [Cited in over 185 publications, this is the most-cited article published in this journal to date.]

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"Avian leukosis is a complex of hematopoetic neoplastic diseases of high incidence in chickens, caused by at least three known serologically distinct viruses. This complex is caused by two types of RNA viruses and a DNA virus. For many years, scientists thought that these neoplastic manifestations in chickens were caused by a single virus, whereas others claimed a multiple etiology. While a young researcher at Cornell University, I was advised by my boss (P.P. Levine, an eminent poultry pathologist and a wonderful human being) to avoid working on avian leukosis because of its immense complexity. I accepted the challenge and immediately went to work on the disease, which resulted in this publication.

"During the 1960s, there was a remarkable succession of research findings that had a profound effect on depicting and defining the causes of the complex.[1,2] The first major breakthrough was a successful transmission of lymphoid tumors with a cell-free agent that resulted in the development of visceral, neural, and/or ocular tumors. The filtrate was labeled JM (acronym for James Martin, infant son, deceased) and was later identified as a herpesvirus, a DNA virus. This recognition led to the identification and differentiation of the multiple causes of the complex.[1,3] Furthermore, this identification led to the attenuation and use of this herpesvirus and related ones as a vaccine.[4] These vaccines are currently used commercially and have been moderately effective in thwarting lymphoid tumor development, but the use of a live virus has resulted in a persistent vaccine viremia.[3,5] Furthermore, the use of the vaccine does not prevent the super-infection of field strains in vaccinated birds. Vaccination results in a viremia, rather than an immunity, hence a cosmetic and economically pragmatic vaccine.

"The importance of immune response in herpesvirus infections cannot be overemphasized. The infection may be immunosuppressive and an immunologic response may surveil tumor development or may contribute to the cellular mass of lymphoid tumors.

"Both humoral and cell-mediated immunity are important in protecting birds against both virus infection and tumor development. Immunity to herpesvirus tumors may be directed toward viral-associated or tumor-associated antigens or both. Currently under development in this laboratory is the use of an attenuated non-producing lymphoid cell line that contains both.[6] Preliminary vaccination trials using these cells or the supernate from same are protective at both the virus level as well as the tumor-cell level without producing a viremia or tumors."

1. **Biggs P M & Payne L N.** Transmission experiments with Marek's disease. *Vet. Rec.* 75:177-9, 1963. (Cited 65 times.)
2. **Churchill A E & Biggs P M.** Agent of Marek's disease in tissue culture. *Nature* 215:528-30, 1967. (Cited 335 times.)
3. **Witter R L, Nazerian K, Purchase H G & Burgoyne G H.** Isolation from turkeys of a cell-associated herpesvirus antigenically related to Marek's disease virus. *Amer. J. Vet. Res.* 31:525-38, 1970. [See also: Witter R L. Citation Classic. *Current Contents/Agriculture, Biology & Environmental Sciences* 11(2):10, 14 January 1980.]
4. **Sevoian M.** Immunity studies in chickens inoculated with a virulent type II avian leukosis strain (JM-V). Unpublished paper presented to the 39th Northeastern Conference on Avian Diseases, 19-21 June 1967. Stony Brook, New York.
5. **Schat K A & Calnek B W.** Characterization of an apparently nononcogenic Marek's disease virus. *J. Nat. Cancer Inst.* 60:1075-82, 1978.
6. **Munch D & Sevoian M.** Growth and characterization of, and immunological response of chickens to, a cell line established from JMV lymphoblastic leukemia. *Avian Dis.* 24:23-36, 1980. (Cited 1 time.)

