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This Week's Citation Classic

Weller T H & Hanshaw J B. Virologic and clinical observations on cytomegalic inclusion disease. *New Eng. J. Med.* **266**:1233-44, 1962.
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The authors delineate virologic and clinical features of congenital cytomegalic inclusion disease in 17 infants, diagnosed by isolation of cytomegalo-virus from urine or liver biopsy material. Cytomegalovirus is incriminated as a cause of intrauterine brain damage, and persistent viruria established as a characteristic manifestation of infection. [The *SCI*® indicates that this paper has been cited over 260 times since 1962.]

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"In 1955, we described a virus isolated from the liver of an infant initially thought to have congenital toxoplasmosis, and then from the urine of two infants exhibiting hepatosplenomegaly and evidence of central nervous system damage.[1] We suggested that the new viruses played an etiologic role. (The historical circumstances and the concurrent isolation of similar viruses by two other groups had been published.[2]) Thus, when James B. Hanshaw (now professor and head, Department of Pediatrics, University of Massachusetts Medical School, Worcester) joined us as a post-doctoral fellow in 1958, we desired to establish the etiologic role of the new agents in congenitally acquired disease and to define the consequences.

"We sought infants who exhibited frank disease in the neonatal period. Generous cooperation was offered by pediatricians at hospitals in Boston, New York, and Philadelphia. By 1962, we had accumulated a group of 17 virologically confirmed cases of congenitally acquired cytomegalic inclusion disease, and had observed them for periods of 11 months to four years. In the interim we had proposed the now accepted name 'cytomegaloviruses' for the agents. We also introduced the obvious term 'viruria' for the phenomenon of urinary excretion of virus, and had presented the first evidence that the viruses constituted a related but antigenically non-homogeneous group.[3]

"Our publication in 1962 embodied these virologic concepts, established isolation of cytomegalovirus from urine as a diagnostic procedure, and delineated the blatant insults of congenital infection with cytomegalovirus, one extreme of a now recognized clinical spectrum. Microcephaly was common. Persistent cytomegaloviruria, often for years, was recorded. At the conclusion of the study, 16 were alive, 13 exhibited mental retardation, 12 had motor disability and three had already been institutionalized. Thus the societal impact of cytomegaloviral infection was documented, a social tax now recognized as exceeding that imposed by rubella virus in the prevaccination era.

"Since 1962, the cytomegaloviruses have been shown to be ubiquitous in distribution and protean in their clinical manifestations. Transmission may be vertical or longitudinal by a variety of methods, including the venereal route. Exhibiting characteristic herpes-like latency, they reactivate in the immunosuppressed host and complicate the handling of the transplant recipient. The field is active and the literature continues to expand rapidly. This provides an opportunity for frequent citation of our clinico-virologic study."

1. **Weller T H, Macaulay J C, Craig J M & Wirth P.** Isolation of intranuclear inclusion producing agents from illnesses resembling cytomegalic inclusion disease. *Proc. Soc. Exper. Biol. Med.* **94:**4-12, 1957.
2. **Weller T H.** Cytomegaloviruses: the difficult years. *J. Infec. Dis.* **122**:532-9, 1970.
3. **Weller T H, Hanshaw J B & Scott D E.** Serologic differentiation of viruses responsible for cytomegalic inclusion disease. *Virology* **12**:130-2, 1960.