

Fine Structure of Unassembled Viral Subunits from Human Warts

K. O. SMITH, E. DOUGHERTY, J. L. MELNICK, AND F. RAPP

*Department of Virology and Epidemiology, Baylor University College of Medicine,
Houston, Texas*

Received for publication 31 March 1965

Tubelike structures possessing orderly arrangements of viral protein subunits (capsomeres) have been found occasionally in papovavirus preparations (polyoma virus, Howatson and Almeida, *J. Biophys. Biochem. Cytol.* **8**:828, 1960; Shope papilloma virus, William, Kass, and Knight, *Virology* **12**:48, 1960; and human wart virus, Noyes, *Virology*, **23**:65, 1964). In a quantitative study of virus particles extracted from 40 individual human warts, we found that filamentous forms occurred only rarely (Barrera-Oro, Smith, and Melnick, *J. Natl. Cancer Inst.*

pathological resemblance to warts from other sources. Suspensions were made as described previously by Barrera-Oro et al. The methods employed for electron microscopy were also described previously (Smith and Melnick, *Virology* **17**:480, 1962).

Figure 1 shows typical particles obtained from a suspension of these warts. Particles were stained with uranyl acetate, and then photographed in an electron microscope (lower micrograph, Fig. 1). The preparation was shadowed lightly with chromium metal, and the same area

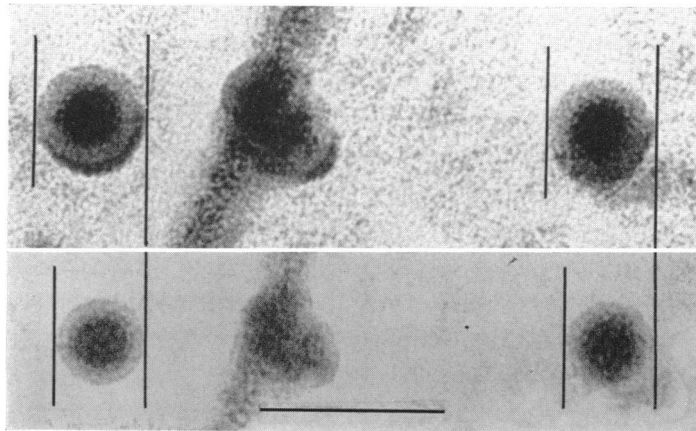


FIG. 1. Human wart virus particles, stained with uranyl acetate (lower figure), and then shadowed with chromium and rephotographed (upper figure; bar equals 100 $m\mu$).

29:583, 1962). The present report describes a patient with unusual warts from which large quantities of filamentous material resembling unassembled viral subunits were obtained.

The warts were obtained from a 23-year-old female with multiple verrucae vulgaris. Onset of warts had been 11 years earlier, and they had spread over legs, thighs, arms, forearms, hands, and soles. For the past 6 years, the number of verrucae had remained essentially the same. Warts were removed either surgically or after application of liquid nitrogen, and were pooled. Histological examination of the warts confirmed

was rephotographed (upper micrograph, Fig. 1). Unshadowed particles averaged about 49 $m\mu$ in diameter. Shadowing added about 23% to this value. These spherical particles are typical of those commonly associated with human warts.

Figure 2 shows another area (similarly treated and photographed), and illustrates the most prominent feature of these preparations: spherical particles were often associated with long cords of filamentous material. There is some suggestion of pattern and periodicity in these filaments (see arrows, Fig. 2). Figure 3 shows phosphotungstate negatively stained areas of this same material in



FIG. 2. Human wart virus preparation, stained with uranyl acetate (lower figure), and then shadowed with chromium (upper figure; bar equals 100 $m\mu$). Arrows indicate periodic pattern of fibers.

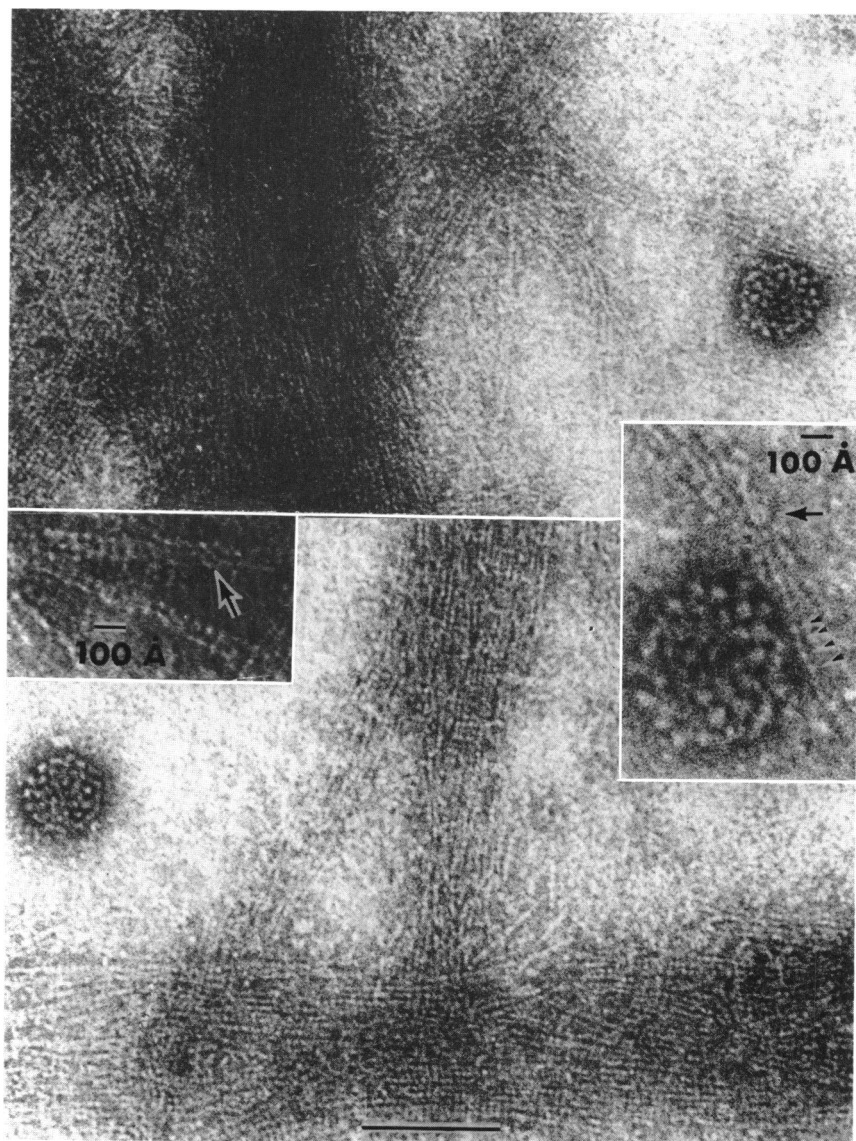


FIG. 3. Human wart virus preparation, stained with potassium phosphotungstate. Subunits in fibers are more clearly seen (large bar equals 100 μ ; small bars equal 100 Å).

which the filamentous structures can be seen more clearly to consist of regular subunits. These subunits measured about 30 Å in diameter and occurred in single (Fig. 3, right-hand inset) and double rows (Fig. 3, left-hand inset). Double rows of subunits occurred frequently. Subunits in the double rows were often arranged so as to form combinations which closely approximate the diameter (80 Å) and general appearance of capsomeres (see Fig. 3; *also* Noyes, *Virology* **23:65**, 1964). The 30 Å subunits may represent the individual protein molecules which form the capsomeres.

Production of wart virus in this patient was unusual in that far larger quantities of viral subunits were produced than were assembled into spherical particles. Such quantities of viral material were not seen in any of the other human

warts which we have examined. The structures observed probably are accumulations of viral subunits which, for reasons yet unknown, are not assembled into complete, spherical particles. Warts from this seriously affected patient were removed at different intervals and always showed the excess amounts of viral subunits. Suspensions of these warts have been inoculated into newborn baboons and monkeys. After several months of observation, no physical reaction has been noted in the animals.

This investigation was supported in part by Public Health Service grant CA-04600 from the National Cancer Institute, and by Public Health Service Research Career Development Award 1-K3-CA-13,120 from the National Institutes of Health.