HPV subtypes in cervical cancer biopsies between 1930and 2004: detection using general primer pair PCR and sequencing

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Abstract Our objective was to investigate the practicability of sequencing DNA from formalin fixed, paraffin embedded tissue stored for up to 75 years and to study human papillomavirus subtype distribution in cervical neoplasias between 1931 and 2004. Three protocols for DNA retrieval were tested, and magnetic bead DNA extraction proved advantageous, as it gave superior specimen purity and effortless sequencing. Successful sequencing was achieved in more than 70% of the specimens from 1931 to 1960. This technique was utilized in the study of papillomavirus subtypes using general primer pair PCR with sequencing of the products in a series of 97 cases of neoplastic and non-neoplastic cervical specimens from 1931 to 1960 and 73 similar cases from 1992 to 2004. HPV was detected in 61% of neoplastic specimens from 1931 to 1960, and in 89% of those from 1992 to 2004. In specimens from 1931 to 1934, only HPV type 16 was detected, whereas in the specimens from 1940 and up, other HPV subtypes were identified in one-third of the cases. The difference was significant and suggests an increase in papillomavirus subtype heterogeneity in Western Norway during 1930–2000. The results strongly support the feasibility of using DNA from paraffin-embedded specimens for studying cancer etiology and genotypes over extended time periods.

Keywords Uterine cervical neoplasms - Human papillomavirus - Base sequence - History