

ESHRE position statement concerning prion detection in urinary gonadotropin formulations

A recent laboratory evaluation, partly funded by a company producing recombinant human gonadotropin, questions the safety of urinary-derived human chorionic gonadotropin. Based on the detection of traces of normal prion protein in licensed urinary derived products, the authors surmise that these widely used gonadotropins might also harbor abnormally folded prion proteins that could result in cases of nosocomial transmission of Creutzfeldt-Jakob Disease (CJD).

The ESHRE task-force for transmissible viral diseases has reviewed the study but found no convincing evidence that would support the concern raised by Dorsselaer et al. Biological and epidemiological evidence argues against the possibility of CJD-transmission through urine-derived gonadotropins.

Prion proteins are normally found in human urine and are not associated with CJD. Dorsselaer et al. did not document the detection of the CJD-associated abnormally folded form of prion proteins. The incidence of CJD is extremely rare (1 case / mio/year) and there is no indication that abnormal prion proteins are found in urine prior to the manifestation of the disease. As for urine donors, those contributing samples for hCG extraction, who are pregnant women, are in the age range far before the age of 50 years, when the vast majority of CJD cases are diagnosed. Those contributing samples for FSH extraction are in the menopausal age range, when eventual clinical manifestation of CJD can be diagnosed.

One particular nature of the transmission of prions associated with the development of the diseases is the association between the infectious dose and the latency from infection to disease development (Klöhn et al.). This is a fundamental difference to the transmission of a virus or a bacteria. Thus, low level exposure to the transmissible agent does not result in the development of overt disease during a lifetime. Since urine-derived products are pooled from large numbers of urine samples any specific protein from one individual donor would be diluted. Thus, even in the unlikely event that a young woman donor is shedding abnormal prion protein in her urine, the potentially transmissible agent is so far diluted that it makes transmission of CJD biologically unlikely event.

This theoretical concept is supported by epidemiological evidence. Despite the use of urine derived gonadotropins for more than 50 years by millions of women worldwide, there is not a single case of CJD associated with these products. More importantly, the M/F sex ratio of CJD has remained stable at one (or slightly above at 1.05 in a large french survey 1998-2000; <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=395>).

Further evidence against the suspected possibility of CJD transmission through urine-derived gonadotropins is also summarized in a position statement of the Candadian Fertility and Andrology Society. Based on this careful evaluation of the facts, the ESHRE task force does fully support the use of urine-derived gonadotropins and will continue to follow the published evidence.

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Reference

Klöhn PC, Stoltze L, Flechsig E, Enari M, Weissmann C. A quantitative, highly sensitive cell-based infectivity assay for mouse scrapie prions. Proc Nat Acad Sci 2003, vol 100 (20); 11666-11671.