Third National Health and Nutrition Examination Survey 1988–1994

Documentation, Codebook, and Frequencies

Surplus Sera Laboratory Component:
Antibody to human herpes virus 8 (Surplus Sera)

Survey Years:
1988 to 1994

SAS Export File:
SSHV8AC.XPT

First Published: May 2006
Last revised: April 2007

NHANES III Data Documentation

Laboratory Assessment: Antibody to human herpes virus 8 (NHANES III Surplus Sera)

Years of Coverage: 1988-1994 **First Published:** May 2006 **Last Revised:** April 2007

Component Description

Human herpes virus 8 (HHV8) antibody testing of stored sera specimens from NHANES III (1988–1994) was conducted to estimate the seroprevalence of HHV8. HHV8 is also known as Kaposi sarcoma associated herpes virus.

Eligible Sample

Participants aged 6+ years from of NHANES III with stored sera (N = 18,168).

Description of Laboratory Methodology

HHV8 antibody testing was performed using enzyme immunoassays (EIAs) to detect antibodies to the HHV8 K8.1 structural glycoprotein (expressed during lytic viral replication) and orf73 (also known as LANA, a viral regulatory protein expressed during latent infection). Sera were diluted 1:20 for the K8.1 EIA and 1:100 for the orf73 EIA. HHV8 testing was conducted over a period of six months. Quality control criteria determined an acceptable range for variation in the controls, and plates that had control optical density (OD) values outside the acceptable range were repeated. To account for remaining plate-to-plate variability, OD results were adjusted by regressing them against the mean OD of the positive controls on the respective plate. The regression equations were:

$$OD_{ij}^{sample} = -0.109 + 0.169\, OD_{i}^{positive\ control} + R_{ij}$$ for the K8.1 assay,

and

$$OD_{ij}^{sample} = -0.128 + 0.169\, OD_{i}^{positive\ control} + R_{ij}$$ for the orf73 assay,

where i denotes the plate, j denotes the sample, and the Rij are the residuals from the regressions. A sample's residual value Rij can be interpreted as the amount that the sample's OD was above or below the expected value for that plate. For most samples, these residuals clustered in a single peak with low antibody levels, while there were a minority of individuals who had higher reactivity. Cutoffs were chosen for the residuals after visual inspection of histograms (1.20 for the K8.1 assay, 0.70 for the orf73 assay), with subjects whose residuals were

above the cutoff classified as seropositive. The cutoffs chosen from the regression were highly conservative, to increase the specificity of the EIAs and enhance the positive predictive value of the test results. As a consequence, seroprevalence results may underestimate the true prevalence of HHV8 infection, but comparisons of results across groups should be valid.

Results using alternative cutoffs used previously for these EIAs are also provided: for the K8.1 EIA, the cutoff was $0.75 + \mathrm{OD}_i^{negative\ control}$, and for the orf73 EIA, the cutoff was $0.20 \times \mathrm{OD}_i^{positive\ control}$. These cutoffs yielded higher seroprevalence estimates, but did not fully account for the plate-to-plate variability captured by the regression method.

Both K8.1 and orf73 antibodies were measured because some infected individuals, including those with Kaposi sarcoma, make antibodies only to lytic or latent antigens (2). The K8.1 ELISA is estimated to have 91-100% sensitivity and 92-100% specificity (1;3). Sensitivity and specificity of the orf73 ELISA have not been established, although the widely used indirect immunofluorescence assay for LANA antibodies has reasonable but perhaps more variable sensitivity (80-100%) and specificity (57-100%) (1;3).

Laboratory Quality Control and Monitoring

Sera were run concomitantly with known positive and negative controls. Plates with anomalous values for these controls were re-run.

Data Processing and Editing

Data Access: All data are publicly available.

Analytic Notes

There are four variables for human herpes virus 8 antibody measurements:
SSH8PK: result on K8.1 ELISA (1=positive, 2=negative)
SSH8POR: result on orf73 ELISA (1=positive, 2=negative)
SSH8PK2: result on K8.1 ELISA using alternative cutoff (1=positive, 2=negative)
SSH8POR2: result on orf73 ELISA using alternative cutoff (1=positive, 2=negative)

Please refer to the Analytic Guidelines for further details on the use of sample weights and other analytic issues.

References

(1) Engels EA, Whitby D, Goebel PB, Stossel A, Waters D, Pintus A, Contu L, Biggar RJ, Goedert JJ. Identifying human herpesvirus 8 infection: performance characteristics of serological assays. J Acquir Immune Defic Syndr 2000;23:346-54.

(2) Biggar RJ, Engels EA, Whitby D, Kedes DH, Goedert JJ. Antibody reactivity to latent and lytic antigens to human herpesvirus-8 in longitudinally followed homosexual men. J Infect Dis 2003; 187:12-8.

(3) Engels EA, Sinclair MD, Biggar RJ, Whitby D, Ebbesen P, Goedert JJ, Gastwirth JL. Latent class analysis of human herpesvirus 8 assay performance and infection prevalence in sub-Saharan Africa and Malta. Int J Cancer 2000;88:1003-8.

(4) E.A. Engels, J.O. Atkinson, B.I. Graubard, G.M. McQuillan, C. Gamache, G. Mbisa, S. Cohn, D. Whitby, J.J. Goedert. Seroprevalence of human herpesvirus 8 among adults in the United States and evidence for sexual transmission. J Infect Dis, in press.

Locator Fields

Title: Antibody to human herpes virus 8 (NHANES III Surplus Sera)

Contact Number: 1-866-441-NCHS

Years of Content: 1988-1994

First Published: May 2006

Revised: April 2007

Access Constraints: None

Use Constraints: None

Geographic Coverage: National

Subject: Antibody to human herpes virus 8 (SSHV8AC)

Record Source: NHANES 1988-1994

Survey Methodology: NHANES 1988-1994 is a stratified multistage probability sample of the civilian non-institutionalized population of the U.S.

Medium: NHANES Web site; SAS transport files

National Health and Nutrition Examination Survey
Codebook for Data Production (1988-1994)
(NHANES III)

Antibody to Human Herpes Virus 8 (SSHV8AC)
Person Level Data

First Published: May 2006
Last Revised: April 2007

SEQN	Target
	B(6 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Respondent sequence number
English Text: Respondent sequence number.	
English Instructions:	

SSH8PK	Target
	B(6 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	K8.1 assay result
English Text: K8.1 assay result	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
1	Positive	355	355	
2	Negative	17813	18168	
.	Missing	0	18168	

SSH8POR	Target
	B(6 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Orf73 assay result
English Text: Orf73 assay result	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
1	Positive	261	261	
2	Negative	17907	18168	
.	Missing	0	18168	

SSH8PK2	Target
	B(6 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	K8.1 assay result alternative cutoff
English Text: K8.1 assay result alternative cutoff	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
1	Positive	1341	1341	
2	Negative	16827	18168	
.	Missing	0	18168	

SSH8POR2	Target
	B(6 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Orf73 assay result alternative cutoff
English Text: Orf73 assay result alternative cutoff	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
1	Positive	1401	1401	
2	Negative	16767	18168	
.	Missing	0	18168	