

# HERPES SIMPLEX VIRUS AND GENITAL INFECTIONS IN THAI PREGNANT WOMEN

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## INTRODUCTION

Pregnant women with herpes simplex virus (HVH) infection may transmit the disease to the newborn during delivery. Infection of the newborns with HVH results in devastating disease which may become evident at anytime from birth to 24 days of age (Rawls, 1973, Whitley *et al.*, 1980). It has been reported that the majority of women shed HVH asymptotically (Tantivanich *et al.*, 1981) and these viruses may be reactivated during pregnancy because of depression of cell mediated immunity (CMI) (Lodmell *et al.*, 1973). The objective of this study was to determine the HVH, mycoplasma and *Neisseria gonorrhoea* infection rates in the genital tract of pregnant women during the first visit to the hospital, and to follow-up those with positive HVH culture until delivery in order to assess the extent of maternal transmitted infection in the newborn infants

## MATERIALS AND METHODS

Two groups of women were studied. The first group comprised of 100 asymptomatic pregnant women. The second group comprised of 11 pregnant women with herpetic lesions who attended Phra Mongkutklao Hospital during November 1980 to July 1981.

Vaginal swabs were collected from the first group of women, and processed within 3 hours. HVH was isolated in a confluence monolayer of Vero cells grown in M-199 in the presence of 5% heat inactivated fetal

calf serum, and the CPE observed within 24-48 hours. The mycoplasma was isolated on U3, U9 and A6 media according to the method of Shepard and Lunceford (1970), and *N. gonorrhoea* on Thayer-Martin medium and identified according to the description by Morello and Bohnhoff (1980).

Vaginal swabs were collected from the lesions during the first visit in the second group of women, and repeated every month until the end of the third trimester. Specimens were also taken from the throat, nose, eyes and ears of the newborn infants of women in both groups for HVH isolations.

Sera were taken from the cord blood of these newborn infants for determination of the antibody against HVH1 and HVH2 using ELISA test as previously described (Tantivanich *et al.*, 1980).

Amniotic fluid and breast milk were also collected from the pregnant women of both groups who were positive for HVH from the genital area.

## RESULTS

Positive HVH and mycoplasma were isolated from 25% and 21% of pregnant women respectively in group 1 (Table 1). Mixed HVH and mycoplasma infections were found in 27% of patients while mixed infections with HVH and *N. gonorrhoea* were only 1%.

Monthly culture for isolation of HVH was done in 25 pregnant women who had sole

Table 1

Isolates from 100 asymptomatic Thai pregnant women.

Organism	No. positive (%)
HVH	25 (25)
Mycoplasma	21 (21)
HVH and mycoplasma	27 (27)
HVH and gonorrhoea	1 (1)

infection with HVH. The results presented in Fig. 1 showed gradual decrease in the positive isolation rate and in the last month of pregnancy, only one pregnant mother was positive for HVH. After delivery, HVH was isolated from the breast milk of 8 patients (32%) and from the amniotic fluid of 12 patients (48%). Positive HVH isolations were obtained from 8% of newborn infants, with high percentage from the throat (44%).

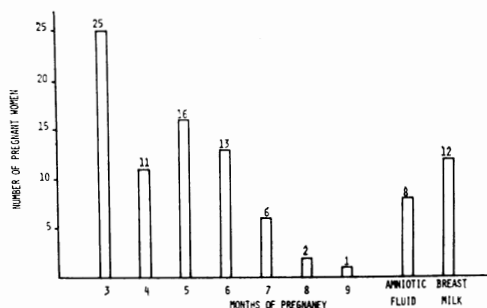


Fig. 1—Positive isolation of HVH from vaginal swab of asymptomatic pregnant women at various times of gestation, and from amniotic fluid and breast milk at the time of delivery.

Positive isolates were also obtained from other sites predominantly from the throat and ears (20%). There was no positive isolate from the eyes except for the multi-site involvement including throat and eye (4%) and eye, ear and nose (4%).

Eleven women with positive herpetic lesions on the first screening also had follow-up cultures done monthly from the vaginal

swabs. Persistent infection was found in 2 patients, one with positive isolates on all 5 occasions, and another on 4 occasions. Four other patients had positive isolates twice, mostly during the first two months of vaginal swabbing. The remaining 5 patients showed positive once only on the first culture. The culture of swabs from their newborn infants showed that 4 were positive for HVH isolated from the throat, 3 had positive isolates from both the throat and the ear, 3 with positive HVH from the throat and the nose, and one with positive isolates from the ear. HVH was also found in the breast milk (72.7%) and amniotic fluid (36.4%). The newborn infant from one of the mothers was still born.

Table 2

HVH isolates from 25 newborn infants of asymptomatic mothers.

Source of isolates	No. positive (%)
throat	11 (44)
ear	3 (12)
throat and ear	5 (20)
ear, nose, and eye	1 (4)
throat and eye	1 (4)
throat, ear and nose	1 (4)
neg.	4 (16)

Table 3

HVH isolates from 11 newborn infants of Thai pregnant women with herpetic lesions.

Source of isolates	No. positive (%)
throat	4 (36.4)
throat and ear	3 (27.4)
throat and nose	3 (27.3)
ear	1 (9.1)

The cord blood of all newborn infants had antibody against HVH1 and HVH2, with titers ranging from 1 : 160 to 1 : 640. Detection of IgM antibody against HVH1 and HVH2 showed that one newborn infant from the mother with herpetic lesions had IgM antibodies against HVH1 and HVH2 with the titer 1 : 320 and 1 : 640, respectively. One of the newborn infants from the asymptomatic mother had IgM antibodies against HVH1, and HVH2 with the titer 1 : 160, and two of the infants had IgM antibodies against HVH2 with the titers 1 : 640 and 1 : 160 respectively.

### DISCUSSION

The asymptomatic pregnant women in this study has no history of HVH infection based on the recognition of an ulcerated lesion by the physician or the patients themselves. These women may acquire HVH sometimes earlier in their life and become reactivated during pregnancy because of depression of CMI as reported by Lodmell *et al.*, (1973). In this study, HVH and mycoplasma seem to be the major problem in pregnant women. The reason why the HVH occurs off and on during the gestation period is unknown. Positive cultures from the amniotic fluid indicate that HVH can pass through the placenta and can cause infection in the newborn infants.

The asymptomatic mother was positive for HVH isolated from amniotic fluid but no virus was recovered from the newborn infant. It appears that the virus had passed through the placenta but for unknown reason failed to infect the fetus *in utero*. The disappearance of HVH from the asymptomatic mother after the third isolation could be treated as a case of abortive infection due to an unknown mechanism.

The negative virus isolation from the amniotic fluid of fetus born of HVH positive

mother does not indicate that the virus can not pass through the placenta since HVH has been recovered from the newborn infant. Failure to isolate HVH from the newborn infant born of positive mother could not be explained. One factor may be the late sending of the sample to the laboratory for processing.

Determination of IgM antibody against HVH in the newborn infant showed that only 4 were positive. Since IgM antibody detection in our ELISA was based on the reaction of enzyme conjugated antibody on the immunoglobulin antibody reacting with the antigen fixed to the plastic plate, masking of this reaction by the IgG antibody may occur resulting in a negative IgM reaction despite its presence. The actual presence of IgM antibody is expected to be higher and its presence is a good evidence for intrauterine HVH infection. The absence of IgM antibody in some newborn infants with positive HVH isolation could be interpreted to mean that they acquire the infection during passage through the birth canal and not by intrauterine infections.

The presence of HVH in the breast milk indicated that the virus had disseminated through the blood circulation. Therefore, measures should be taken to prevent the spread of the virus to the infant by stopping breast feeding.

### SUMMARY

Vaginal swabs were collected monthly from 100 asymptomatic Thai pregnant women as well as from 11 pregnant women with herpetic lesions of the vulva for isolations of HVH, mycoplasma and gonorrhoea. In asymptomatic mothers, 25% and 21% of cases were positive for HVH and mycoplasma respectively. Mixed infections of HVH and mycoplasma, and HVH and gonorrhoea were also found in 27% and 1% of cases respectively. Follow-up in asymptomatic

pregnant women and those with herpetic lesions showed positive HVH fluctuations throughout the course of study. Positive HVH was recovered from 48% of amniotic fluid and 32% of breast milk of asymptomatic pregnant women with positive HVH genital isolates, and in 72.7% of amniotic fluid and 36.4% of breast milk in patients with herpetic lesions. HVH was also isolated from 84% of infants of asymptomatic mothers positive for HVH, and 100% of patients with herpetic ulcer. HVH was isolated most frequently from the throat and also from nose, eyes, and ears but with less frequency. IgM antibodies were found in three infants born of asymptomatic mother and in one infant of a mother with herpetic lesion. The low percentage of IgM antibody was interpreted to mean that the HVH isolated from the newborn infants were acquired during passage through the birth canal.

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