1-17-2002

Risk Factors and Outcome of Varicella-Zoster Virus Pneumonia in Pregnant Women

James H. Harger
University of Pittsburgh

Joseph M. Ernest
Wake Forest University

Gary R. Thurnau
University of Oklahoma

Atef Moawad
University of Chicago

Valerija Momirova
George Washington University

See next page for additional authors

Risk Factors and Outcome of Varicella-Zoster Virus Pneumonia in Pregnant Women

James H. Harger,[1] Joseph M. Ernest,[2] Gary R. Thurnau,[3,a] Atef Moawad,[4] Valerija Momirova,[5] Mark B. Landon,[6] Richard Paul,[8] Menachem Miodovnik,[7] Mitchell Dombrowski,[9] Baha Sibai,[7] and Peter Van Dorsten[10] for the National Institute of Child Health and Human Development, Network of Maternal-Fetal Medicine Units[b]

[1]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [2]Department of Maternal-Fetal Medicine, Wake Forest University, Winston-Salem, North Carolina; [3]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Oklahoma School of Medicine, Oklahoma City; [4]Department of Obstetrics/Gynecology, University of Chicago, Chicago, Illinois; [5]Biostatistical Coordinating Center, George Washington University, Washington, DC; [6]Department of Maternal-Fetal Medicine, Ohio State University, Columbus, and [7]Department of Obstetrics and Gynecology, University of Cincinnati, Cincinnati, Ohio; [8]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Southern California School of Medicine, Los Angeles; [9]Department of Obstetrics and Gynecology, Wayne State University, Detroit, Michigan; [10]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston

To determine the factors associated with an increased risk of developing varicella-zoster virus (VZV) pneumonia during pregnancy, a case-control analysis was done in which 18 pregnant women with VZV pneumonia were compared with 72 matched control subjects. VZV infection was identified clinically, and VZV pneumonia was diagnosed by dyspnea and findings on chest radiographs. Of 347 pregnant women with VZV infection, 18 (5.2%) had pneumonia treated with acyclovir, and none died. Mean gestational age at rash onset was 25.8 ± 8.8 weeks for patients with pneumonia and 17.7 ± 10.3 weeks for control subjects, which was not significant in the multivariable model. Women with VZV pneumonia were significantly more likely to be current smokers (odds ratio [OR], 5.1; 95% confidence interval [CI], 1.6–16.7) and to have ⩾100 skin lesions (OR, 15.9; 95% CI, 1.9–130.2). Pregnant women with VZV infection may be more likely to develop varicella pneumonia if they are smokers or manifest ⩾100 skin lesions.

Four million cases of varicella-zoster virus (VZV) infection occurred annually in the United States during 1990–1994. Of these cases, <5% affected adults >20 years old, but 55% of varicella-related deaths occurred in this older population [1]. Before the availability of varicella vaccine, varicella was estimated to cause 4000–11,000 hospitalizations and 100 deaths annually in the United States alone [1]. The most common complication of varicella in adults is pneumonia, usually caused by VZV alone, but occasionally bacterial superinfection is implicated as well.

Before the advent of specific antiviral therapy, the mortality rate of varicella pneumonia was 11.4%–15% for nonpregnant adults [2, 3] and 36%–41% for pregnant women (retrospectively reviewed in [3, 4]). After the advent of parenteral vidarabine and acyclovir (Acy) in 1983 to treat varicella pneumonia, the maternal mortality rate declined to 13%–14% [4, 5]. This decline has been attributed to the antiviral agents, better supportive intensive care, and earlier recognition and treatment.

Varicella pneumonia is so uncommon that large-scale studies are very difficult to conduct. Most published studies represent either collections of small case series or retrospective analyses over many years. Consequently, risk factors for VZV pneumonia in pregnant women have been difficult to identify. The results of 2 small English studies [6, 7] support the belief that smoking is a risk factor for pneumonia in adults with varicella. A noncontrolled retrospective analysis also supports this conclusion [8], and women in the third trimester appear to be at a greater risk for developing VZV pneumonia [5]. Other possible risk factors for VZV pneumonia in pregnant women are more skin lesions at all stages [9] and the presence of pharyngeal varicella lesions.

The subjects in the present study were enrolled in a multisite registry of VZV infection in pregnant women. The primary goal

Received 14 August 2001; revised 9 October 2001; electronically published 17 January 2002.

Presented in part: 46th annual meeting of the Society for Gynecologic Investigation, Atlanta, March 1999 (abstract 94).

Financial support: National Institutes of Health (grants HD-21410, HD-21414, HD-21434, HD-27860, HD-27861, HD-27883, HD-27889, HD-27905, HD-27915, HD-27917, and HD-19897).

[a] Present affiliation: Private practice.

[b] Study team members are listed after the text.

Reprints or correspondence: Dr. James H. Harger, University of Pittsburgh School of Medicine, Dept. of Obstetrics, Gynecology, and Reproductive Sciences, Pittsburgh, PA 15213-3180 (jharger+@pitt.edu).

The Journal of Infectious Diseases 2002;185:422–7

0022-1899/2002/18504-0003

of the registry was to determine the risk of congenital varicella syndrome and embryopathy caused by VZV. Here, we describe the factors associated with varicella pneumonia in pregnant women and the outcomes of the 18 pregnancies.

Materials and Methods

Between March 1993 and March 1996, we enrolled 347 pregnant women who contracted primary VZV infection during any trimester. We excluded from this analysis an additional 15 patients with herpes zoster during pregnancy. The women were enrolled at 10 tertiary perinatal centers participating in the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, by use of a standard protocol.

Physicians in the geographic areas served by these tertiary centers referred patients for assessment and counseling when they developed a typical maculopapular rash with evolving vesicles and/or pustules in a centripetal pattern. This clinical diagnosis of varicella was accepted, since the disease is easy to identify. VZV isolation was not required by the protocol. Patients were questioned about previous episodes of varicella or herpes zoster, the source and dates of exposure, and therapy with varicella-zoster immune globulin (VZIG) or oral antiviral agents. They were asked about initial symptoms of rash, fever, arthralgias, malaise, cough, and dyspnea; later development of cough, fever, and dyspnea was recorded. Each patient also was asked about use of medications, ethanol, illegal drugs (e.g., cocaine, morphine, heroin, marijuana, hashish, amphetamines, and methamphetamine) and cigarette smoking. Chest radiographs were obtained for patients presenting with dyspnea or tachypnea. The diagnosis of varicella pneumonia was confirmed by visualization of interstitial infiltrates or nodular densities in the lung fields.

Recorded physical characteristics included the patient's highest temperature during the illness, the anatomic areas involved with the rash, and the physician's estimate of total papulovesicular lesions at the peak of the rash (classified as <100 or $\geqslant 100$ lesions). The dates of rash and of dyspnea onset and resolution were recorded from clinical study records or patient recall. When recall of details was uncertain, supporting medical records were sought.

All the women diagnosed with varicella pneumonia were enrolled in the study after the diagnosis was made. A disproportionate number were enrolled at one center, so we selected 4 control subjects with delivery information for each case patient, matched by center and serology status.

After enrollment, the pregnant women were treated by their primary obstetrical care providers. Patients who met the diagnosis of varicella pneumonia were treated by physicians in their own hospital or at the tertiary referral center.

Categorical variables were analyzed by χ^2 and Fisher's exact tests. We used the Wilcoxon test for analysis of continuous variables. The baseline factors considered in the univariable analysis—maternal age, third trimester rash onset (yes or no), vesicles (<100 or $\geqslant 100$), multiparous (yes or no), smoking during pregnancy, and drinking ethanol during the pregnancy—were used in a multivariable logistic regression analysis to evaluate further the relationship between the risk factors and VZV pneumonia. A backward selection procedure was used, whereby the least significant term was removed and the model was refitted. The result was checked with a forward selection process. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) then were computed. $P < .05$ was considered to be significant.

Results

Of the 18 women with varicella pneumonia, as defined by dyspnea and a positive chest radiograph, none were lost to follow-up. Two other women with chest radiographic findings of typical changes of interstitial pneumonitis were excluded because of lack of dyspnea or tachypnea.

The racial composition of the study population (18 case patients and 72 control subjects) was as follows: black, 37 (41.1%) women; Asian descent, 2 (2.2%) women; white, 46 (51.1%) women; and Hispanic, 5 (5.6%) women. At enrollment, 34 women (37.8%) worked outside the home. The source of varicella was a related child in 46 (51.1%) cases, an unrelated child in 15 (16.7%) cases, the pupil of a pregnant teacher in 2 (2.2%) cases, and not certain in 27 (30.0%) cases.

Table 1 shows the demographic and medical factors tested in a univariable analysis for an association with an increased likelihood of developing varicella pneumonia. There was no significant difference with respect to maternal age, race, use of illegal drugs, or drinking ethanol during pregnancy between the 18 women who developed varicella pneumonia and the 72 women who did not. VZIG use was inconsistent in the study population, with only 3 (17%) of 18 case patients and 7 (9.7%) of 72 control

Table 1. Factors associated with varicella pneumonia and multivariable regression analysis.

Characteristic	Pneumonia (n = 18)	No pneumonia (n = 72)	OR (95% CI)
Maternal age, mean years ± SD[a]	25.7 ± 4.9	24.7 ± 5.1	
Black race	7 (39)	30 (42)	0.9 (0.3–2.6)
Multiparous	15 (83)	46 (64)	2.8 (0.7–10.7)
Ever smoked	13 (72)	28 (39)	4.1 (1.3–12.7)
Current smoker	11 (61)	16 (22)	5.5 (1.8–16.5)[b]
Current EtOH drinker	7 (39)	22 (31)	1.4 (0.5–4.2)
Illegal drugs	4 (22)	6 (8.3)	3.1 (0.8–12.6)
GA at rash onset, mean weeks ± SD[c]	25.8 ± 8.8	17.7 ± 10.3	
Rash onset at third trimester[d]	10 (56)	17 (24)	4.0 (1.4–11.9)
$\geqslant 100$ Vesicles[e]	17 (94)	36 (50)	17.0 (2.1–134.6)

NOTE. Data are no. (%) of patients, except where noted. CI, confidence interval; GA, gestational age; EtOH, ethanol; OR, odds ratio.

[a] $P = .46$.

[b] Adjusted OR, 5.1 (95% CI, 1.6–16.7), by multivariable logistic regression analysis.

[c] $P = .0044$. Not significant by multivariable logistic regression analysis.

[d] Not significant by multivariable logistic regression analysis.

[e] Adjusted OR, 15.9 (95% CI, 1.9–130.2), by multivariable logistic regression analysis.

Table 2. Acyclovir (Acy) therapy and outcome in the study population.

Patient	GA at rash onset, weeks	Duration of rash until pneumonia diagnosis, days	Time from pneumonia diagnosis until start of Acy, days	Acy dose/ day, mg	Duration of dyspnea, days[a]
1	38	4	0	940	Missing
2	32	3	1	800	6
3	10	2	2	900	Missing
4 (15)[b]	21	2	0	2182	15
5	5	3	0	1250	4
6	36	4	1	1300	Missing
7 (3)[b]	27	0	0	1350	5
8	21	0	0	800	6
9	28	1	0	500	4
10	16	4	1	1000	0
11	26	3	1	800	Missing
12	23	4	1	1000	3
13	26	0	3	300	24
14 (15)[b]	23	3	0	Missing	7
15	24	6	0	600	85
16	35	4	0	800	1
17	34	6	0	650	8
18	32	3	0	Missing	4

NOTE. GA, gestational age.

[a] The duration of dyspnea was not known in 4 cases because the date of resolution was not recorded.

[b] Received varicella-zoster immune globulin (VZIG). No. in parentheses is the interval (days) between exposure and VZIG injection.

subjects receiving VZIG after exposure (table 2). Of the 10 women given VZIG, only 1 of 3 case patients and 5 of 7 control subjects received it within the recommended 96-h window after exposure to VZV, so no conclusions could be drawn from those data. Women with varicella pneumonia were significantly more likely to have developed varicella at a later gestational age. Pregnant women with varicella pneumonia were more likely to be current smokers. Of the 18 women with symptomatic varicella pneumonia, 17 had ⩾100 skin lesions typical of varicella. There was no significant difference between the 2 groups in the location or distribution of the lesions (data not shown).

Among 18 patients with varicella pneumonia, the onset of the rash occurred during the first 13 weeks of pregnancy (first trimester) in 2 cases (11%), during the second 13 weeks (second trimester) in 6 cases (33%), and at ⩾26 weeks of gestation (third trimester) in 10 cases (56%) (table 2). In contrast, of 72 women without varicella pneumonia who developed a varicella rash, 35 (48.6%) did so in the first trimester, 18 (25%) did so in the second trimester, and 19 (26.4%) did so in the third trimester. The multivariable logistic regression analysis (table 1) showed only 2 factors significantly correlated with an increased chance of varicella pneumonia: ⩾100 skin lesions (OR, 15.9; 95% CI, 1.9–130.2) and smoking during the affected pregnancy (OR, 5.1; 95% CI, 1.6–16.7).

Among the 18 women with varicella pneumonia, the median incubation interval between exposure and onset of the rash was 13 days (range, 7–23 days) in the 16 case patients with known exposure; for 2 case patients, the source was unknown. The median interval between the onset of rash and diagnosis of varicella pneumonia was 3 days (range, 0–6 days); 4 women presented with dyspnea on the day the rash appeared. The median duration of dyspnea was 5.5 days (range, 1–85 days) in the 14 women for whom the date of resolution was recorded. In the single case of known duration in the first trimester, dyspnea lasted 4 days. The median duration of dyspnea was 6.5 days (range, 1–85 days) in the 6 second-trimester cases and 5 days (range, 1–24 days) in 7 of 10 third-trimester cases.

Intravenous Acy therapy was initiated at a dose of 5–15 mg/kg of body weight every 8 h on the day that varicella pneumonia was diagnosed in 11 cases, 1 day after diagnosis in 5 cases, 2 days after diagnosis in 1 case, and 3 days after diagnosis in 1 case. The dose of intravenous Acy administered was not subject to the protocol and was determined by the responsible physician(s) at each tertiary center. Table 2 shows the daily dose of intravenous Acy used for 16 of 18 women treated; the median dose was 800 mg per day in 3 divided doses. The exact dose was not available for 2 women. Because of the unknown safety of oral Acy during pregnancy and its uncertain benefits during the study period in 1993–1996, neither case patients nor control subjects were treated with oral Acy before the diagnosis of varicella pneumonia.

Table 3 shows the outcomes of the 18 pregnancies. One woman developed a rash at 24 weeks, vaginally delivered a 710-g stillborn baby at 25 weeks of gestation, and developed varicella

Table 3. Outcome of pregnancy in women who had varicella-zoster virus infection.

Patient	GA at rash onset, weeks	Time from pneumonia to delivery, days	Birth weight, g	Mode of delivery	GA at delivery, weeks
1	38	10	3013	Low forceps	40
2	32	45	3232	Cesarean	39
3	10	207	3410	Spontaneous vaginal	39
4	21	127	3033	Cesarean	40
5	5	238	3730	Cesarean	40
6	36	2	3266	Cesarean	37
7	27	101	3714	Spontaneous vaginal	41
8	21	113	2989	Spontaneous vaginal	37
9	28	78	3490	Spontaneous vaginal	39
10	16	153	3080	Cesarean	38
11	26	75	2810	Spontaneous vaginal	37
12	23	110	3005	Spontaneous vaginal	39
13	26	94	2962	Cesarean	39
14	23	115	2270	Spontaneous vaginal	40
15	24	1	710	Spontaneous vaginal	25
16	35	112	2225	Low forceps	36
17	34	33	3770	Low forceps	40
18	32	43	2807	Spontaneous vaginal	38

NOTE. The only fetal death was the child of subject 15; all others were born alive. GA, gestational age.

pneumonia on the first postpartum day. The other 17 infants were delivered at gestational ages at or beyond 36 4/7 weeks with no evidence of neonatal varicella. Another patient developed varicella rash at 36 2/7 weeks of gestation and presented with severe respiratory failure 4 days later. After intravenous Acy was started at 15 mg/kg of body weight every 8 h, an endotracheal tube was placed for mechanical ventilation, and her condition worsened. For that reason, the 3266-g infant was delivered by low-transverse cesarean section. The mother recovered without sequelae after 7 days of intravenous Acy therapy. The infant was treated with VZIG and Acy and recovered without evidence of morbidity from VZV.

For the 18 study women, delivery was vaginal in 12 cases, including 2 low forceps deliveries, and cesarean in 6 cases. Five cesarean deliveries were performed for obstetrical indications and 1 (mentioned above) for acute maternal respiratory failure. Postpartum morbidity in the 18 women included cortical venous thrombosis in 1 after cesarean delivery 45 days after varicella pneumonia. Another woman, who was intubated and received mechanical ventilation for 6 weeks because of bacterial superinfection, had only 40% of the expected values on pulmonary function tests at the onset of her next pregnancy 1 year later. None of these 18 cases resulted in maternal death (95% CI, 0%–17.6%).

Discussion

The frequency of varicella pneumonia has been difficult to determine in most populations. The incidence has been reported as 1 in 2000 to 1 in 10,000 pregnancies [10, 11]. Only 8 cases of varicella pneumonia (~1.3/10,000 pregnancies) were reported in the 60,000 pregnancies studied during 1959–1965 in the Collaborative Perinatal Project [12], but these data from 35 years ago are not applicable to the present. The frequency of varicella in all adults was estimated to be 1.2–4.5/100,000 hospital admissions in Stockholm during 1980–1989 [13] and 6/100,000 in Scotland during 1989–1990 [14]. Miller et al. [14] reported an increasing frequency of varicella in adults in England and Wales over the past 2 decades, and a recent upward shift in the age distribution of varicella has been reported in the United States [15]. Although the reasons for such changes in age distribution are complex, they could herald more frequent encounters between pregnant women and varicella pneumonia. On the other hand, the advent of extensive varicella vaccination may decrease this hazard appreciably.

The diagnosis of varicella in the pregnant women in this study was made by clinical identification of the typical rash. With respect to radiographic diagnostic criteria for varicella pneumonia, a report of 110 chest radiographs in 114 US Army recruits who developed varicella during basic training showed that 18 (16.3%) had interstitial and/or nodular infiltrates indicative of pneumonia. Only 4 of those 18, however, complained of a "dry, nonproductive cough" and only 2 (11.1%) complained of dyspnea [16]. In our study group, 68 (20.7%) of 329 pregnant women with varicella but no radiologic evidence of pneumonia also reported dyspnea. These findings could be explained by the pregnancy itself, since pregnant women occasionally feel dyspneic even when they do not have varicella or any other respiratory infection. In a retrospective emergency room study of 130 adults affected by varicella, dyspnea occurred in 7.7% of 117

patients with normal chest radiographs and in 61.5% of the 13 patients with radiographic evidence of pneumonia [17]. These results support the belief that radiologic changes alone do not predict clinically significant pneumonia requiring treatment. For that reason and because a chest radiograph immediately after rash onset might not detect later development of varicella pneumonia, routine chest radiographs are not warranted for all pregnant women who develop varicella.

This study was not designed to evaluate varicella pneumonia therapy and, therefore, contained no guidelines to standardize the therapy, as shown by the variation in daily doses of intravenous Acy. Previous case series of maternal varicella pneumonia reported a case-fatality rate of 36%–41% before the introduction of specific antiviral agents such as Acy [3, 4]. Reports since the advent of Acy therapy still indicate a maternal mortality rate of 13%–14% [4, 5]. The lack of maternal mortality in our 18 cases probably represents the result of early diagnosis and vigorous antiviral drug treatment but could be merely fortuitous. Only 10 (11%) of 90 exposed pregnant women were given VZIG after exposure to a varicella source contact, and only 6 of these 10 women received VZIG within 96 h after exposure. This finding strongly suggests the need for education of physicians and antepartum patients to improve the appropriate use of this protective preparation.

We identified a history of smoking as a significant feature of pregnant women with pneumonia when they contracted varicella (OR, 5.1; 95% CI, 1.6–16.7). This finding is consistent with earlier reports in the literature [6–8], although the previous studies also involved adult men and nonpregnant women. Of 29 adults admitted to the hospital in Manchester, United Kingdom [6], 7 (37%) of 19 smokers (only 1 pregnant woman) developed varicella pneumonia, compared with none of 10 nonsmokers ($P = .032$). Among 67 immunocompetent adults described elsewhere [7], 16 (47%) of 34 smokers developed varicella pneumonia, compared with 1 of 33 nonsmokers. In a series of emergency room patients between 1979–1987, 7 (64%) of 11 adults treated early for varicella pneumonia and 20 (74%) of 27 adults not treated with Acy reported smoking, but the comparison group was merely the overall smoking rate of 30% in the region during that time [8]. Similarly, 11 of 13 women treated in the United Kingdom with Acy for varicella pneumonia were smokers, but no comparison figure was provided [18].

Other reported risk factors for varicella pneumonia include the trimester of rash onset. The case series of Acy therapy reported by Smego and Asperilla [5] revealed no maternal deaths among 12 women with varicella in the second trimester, but 3 of 9 women who developed varicella during the third trimester died of pneumonia and complications. In a different collection of case series including 28 pregnant women affected by varicella pneumonia, 3 women were in the second trimester and 21 were in the third trimester [19]. Four of the women in the latter report had an unknown gestational age, and there were 3 maternal deaths (10.7%), but the gestational age of only 1 of the 3 was specified (30 weeks). Compared with these heterogeneous mixtures of case series, gestational age and trimester of onset appeared to be significant factors in our study as well, but these gestational age factors dropped from the multivariable model.

A higher number of skin lesions has been reported to be associated with greater frequency of varicella pneumonia [9], but the findings of an Australian study did not support that conclusion [20]. In the present study, we found a significantly greater proportion (94.4%) of patients with varicella pneumonia afflicted with $\geq$100 skin lesions than control subjects (50.0%), and this factor remained significant in the multivariable model (OR, 15.9; 95% CI, 1.9–130.2). Our data support the concept that identifying more lesions increases the risk of developing varicella pneumonia, perhaps because of a greater virus load during viremia. In view of the high maternal mortality rate of varicella pneumonia, however, there is a significant hazard in using this arbitrary estimate to delay vigorous diagnostic approaches to women with $<$100 skin lesions at first examination. For a pregnant woman with dyspnea or tachypnea, waiting for 100 skin lesions to appear before obtaining a chest radiograph or an arterial blood gas reading or starting intravenous antiviral therapy would be unwise.

Our demographic and medical information for 18 pregnant women with varicella pneumonia provide meaningful contemporary data on a rare complication of a common childhood disease. Because of the standardized data collection method, information about maternal age, gravidity, parity, gestational age at the onset of rash, smoking history, number of maternal skin lesions, and peak temperature, we could determine statistically significant features associated with an increased likelihood of developing varicella pneumonia. Physicians caring for pregnant women who contract varicella may use these findings to formulate management plans that will permit earlier recognition of varicella pneumonia and earlier therapy with intravenous Acy.

National Institute of Child Health and Human Development, Network of Maternal-Fetal Medicine Units Study Team Members

The following investigators participated in the study: Phyllis Jones and Marshall Lindheimer (University of Chicago, Chicago, Illinois); Nancy Elder and Tariq A. Siddiqi (University of Cincinnati, Cincinnati, Ohio); Elizabeth Thom and Mark Klebanoff (George Washington University, Biostatistical Coordinating Center, Washington, DC); Steve N. Caritis and Margaret A. Cotroneo (Magee-Womens Hospital, Pittsburgh, Pennsylvania); Charlotte Catz and Sumner Yaffe (National Institute of Child Health and Human Development, Bethesda, Maryland); Jay D. Iams and Francee Johnson (Ohio State University, Columbus); Arlene Meier (University of Oklahoma, Oklahoma City); Beth A. Collins and Roger B. Newman (Medical University of South Carolina, Charleston); Brian M. Mercer and Risa Ramsey (University of Tennessee, Knoxville); Paul J. Meis,

Eberhard Mueller-Heubach, and Melissa Swain (Wake Forest University, Winston-Salem, North Carolina); and Sidney F. Bottoms (deceased) and Gwendolyn S. Norman (Wayne State University, Detroit, Michigan).

References

1. Anonymous. Varicella-related deaths among adults—United States, 1997. MMWR Morb Mortal Wkly Rep **1997**;46:409–12.
2. Triebwasser JH, Harris RE, Bryant RE, et al. Varicella pneumonia in adults: report of seven cases and review of literature. Medicine (Baltimore) **1967**;46:409–23.
3. Harris RE, Rhoades ER. Varicella pneumonia complicating pregnancy: report of a case and review of literature. Obstet Gynecol **1965**;25:734–40.
4. Brousard RC, Payne DK, George RB. Treatment with acyclovir of varicella pneumonia in pregnancy. Chest **1991**;99:1045–7.
5. Smego RA Jr, Asperilla MO. Use of acyclovir for varicella pneumonia in pregnancy. Obstet Gynecol **1991**;78:1112–6.
6. Ellis ME, Neal KR, Webb AK. Is smoking a risk factor for pneumonia in adults with chickenpox? Br Med J **1987**;294:1002.
7. Grayson ML, Newton-John H. Smoking and varicella pneumonia [letter]. J Infect **1988**;16:312.
8. Haake DA, Zakowski PC, Haake DL, et al. Early treatment with acyclovir for varicella pneumonia in otherwise healthy adults: retrospective controlled study and review. Rev Infect Dis **1990**;12:788–98.
9. Mermelstein RH, Freireich AW. Varicella pneumonia. Ann Intern Med **1961**;55:456–63.
10. Brown HL, Pastorek JG II. Varicella complicating pregnancy. Infect Med **1990**;7:20–3.
11. Stagno S, Whutley RJ. Herpesvirus infection of pregnancy. II. *Herpes simplex* and varicella-zoster virus infections. N Engl J Med **1985**;313:1327–30.
12. Landesberger EJ, Hager WD, Grossman JH. Successful management of varicella pneumonia complicating pregnancy: a report of three cases. J Reprod Med **1986**;31:311–4.
13. Nilsson A, Ortqvist A. Severe varicella pneumonia in adults in Stockholm County 1980–1989. Scand J Infect Dis **1996**;28:121–3.
14. Miller E, Marshall R, Vurdien J. Epidemiology, outcome and control of varicella-zoster virus infection. Rev Med Microbiol **1993**;4:222–30.
15. Gray GC, Palinkas LA, Kelly PW. Increasing incidence of varicella hospitalizations in the United States army and navy personnel. Pediatrics **1990**;86:867–73.
16. Weber GM, Pellechia JA. Varicella pneumonia: study of prevalence in adult men. JAMA **1965**;192:572–3.
17. Baren JM, Henneman PL, Lewis RJ. Primary varicella in adults: pneumonia, pregnancy and hospital admission. Ann Emerg Med **1996**;28:165–9.
18. Davidson RN, Lynn W, Savage P, et al. Chickenpox pneumonia: experience with antiviral treatment. Thorax **1988**;43:627–30.
19. Esmonde TF, Herdman G, Anderson G. Chickenpox pneumonia: an association with pregnancy. Thorax **1989**;44:812–5.
20. Donnan MGF. Varicella pneumonia in adults. J College Radiol Aust **1965**;9:49–51.