Severe Complications of Varicella in Previously Healthy Children in Germany: A 1-Year Survey

Christine Ziebold, MD, PhD*; Rüdiger von Kries, MD‡; Robert Lang, MD‡; Josef Weigl, MD*; and Heinz J. Schmitt, MD*

ABSTRACT. *Objective.* **Varicella is a common infectious disease, usually benign and self-limited, and complications are believed to be rare. The purpose of this study was to describe the epidemiology of severe varicella complications in immunologically healthy children in Germany.**

Methods. **Information on any admission of children with a severe complication associated with chickenpox was solicited throughout 1997 from all 485 pediatric hospitals in Germany using an established surveillance system. The case definition included nonimmunocompromised individuals who were up to 16 years of age and hospitalized with neurologic complications, bacterial superinfections, or hematologic complications.**

Results. **The response rate to the surveillance questionnaire during the observation period was high: 93.4%. Of the 153 reported cases, 119 met the case definition. There was a seasonal distribution of reported complications with a peak in March. The majority of complications occurred in preschool-age children with a maximum age of 4 years. No gender predominance was found with a distribution of 56 female and 63 male patients. Multiple entries for complications were allowed. The most frequent complications were neurologic, which were reported in 73 children (61.3%); cerebellitis was the leading diagnosis ($n = 48$), followed by encephalitis ($n = 22$), meningitis ($n = 2$), and central facial palsy ($n = 1$). A total of 46 (38.6%) infectious complications were identified. Superinfections of the skin were present in 31 (26.0%), pyogenic arthritis was present in 5 (4.2%), osteomyelitis was present in 4 (3.3%), necrotizing fasciitis was present in 3 (2.5%), orbital cellulitis was present in 2 (1.6%), and pneumonia was present in 1 (0.8%). *Streptococcus pyogenes* was the leading cause of bacterial infections (18 cases [15.1%]), with invasive disease in 6 patients (8.4%) and linked to 4 of 8 cases with defect healing. Infectious complications were reported in the majority in younger children up to 4 years of age, whereas neurologic complications occurred more frequently in an older age range. Five children experienced thrombocytopenia or severe anemia. There was no bleeding disorder, no fatality, and no case of Reye syndrome reported during the 1-year observation period. In total, 8 (6.7%) of 119 patients reported having long-term sequelae, 6 attributable to infectious complications and 2 to persistent deficits after neurologic complications.**

Conclusion. **This is the first prospective nationwide study of severe complications of varicella in immunologically healthy children. Related to 14 025 867 children up to the age of 16, a crude incidence of severe chickenpox complications of 8.5/100 000 could be calculated. The actual hospitalization rate attributable to complicated chickenpox is probably much higher, because this calculation refers to a population theoretically at risk and not the truly susceptible individuals. The results of this study demonstrate considerable morbidity with a comparatively high rate of encephalitis, osteomyelitis, and pyogenic arthritis. Although infectious complications were present in only 38.6% of the reported cases, they contributed disproportionately to the cases with chronic sequelae. Looking at these cases in more detail, *S pyogenes* involvement was identified as the major risk factor for invasive disease with an unfavorable long-term outcome.** *Pediatrics* **2001;108(5). URL: http://www.pediatrics.org/cgi/content/full/108/5/e79; *varicella-zoster virus, chickenpox/epidemiology, chickenpox/complications, encephalitis, cellulitis, osteomyelitis, necrotizing fasciitis, group A β-hemolytic streptococci, Europe.***

ABBREVIATIONS. GABHS, group A β-hemolytic streptococci; ESPED, "Erhebungseinheit für Seltene Pädiatrische Erkrankungen in Deutschland"; VZV, varicella-zoster virus.

Varicella is usually a self-limited disease and not reportable in Germany. In Germany, there are no data collections or epidemiologic surveys regarding varicella from which overall or specific incidences could be calculated. Varicella occurs seasonally and in epidemics. According to US data, approximately 95% of cases, 66% of hospitalizations, and 45% of varicella-related deaths occur among people who are younger than 20 years, with most cases occurring in children who are younger than 10 years.[1] Despite a public perception of varicella infection as being a harmless childhood affliction, different complications may occur.[2] The range of complications was previously thought to depend on the immune status and underlying diseases, such as chronic cutaneous or pulmonary disorders and immunosuppressive therapies. Immunocompromised individuals, especially those with T-cell defects, are at increased risk of dissemination of the virus to the internal organs, including lungs, liver, brain, heart, and kidneys. However, healthy individuals may experience complications as well, and not limited to infection beyond adolescence, as forthcoming re-

From the *Pediatric Infectious Diseases, Zentrum für Präventive Pädiatrie, Johannes Gutenberg University Mainz, Mainz; and ‡Institute for Social Pediatrics and Adolescent Medicine, University of Munich, Munich, Germany.

Received for publication Mar 13, 2001; accepted Jun 20, 2001.

Reprint requests to (H.J.S.) Zentrum Präventive Pädiatrie, Johannes Gutenberg Universität, Langenbeckstraβe 1, 55101 Mainz, Germany. E-mail: schmittj@kinder.klinik.uni-mainz.de

search from the United States is showing. The more common and comparatively benign complications include otitis media, subclinical hepatitis, cerebellar ataxia, and bacterial superinfection of the rash. The last can be troubling if group A β-hemolytic streptococci (GABHS) are inoculated into the skin break, leading to cellulitis, an increased chance of systemic spread with bacteremia, and occasionally necrotizing fasciitis. Recent observations of the epidemic nature of invasive disease attributable to GABHS after varicella in child care centers have been reported from the United States.[3] Transient bacteremia may cause pneumonia, pyogenic arthritis, and osteomyelitis. Rare complications of varicella in immunologically healthy hosts include encephalitis, myocarditis and pericarditis, pancreatitis, orchitis, bleeding diatheses, and nephritis.

This study was conducted to collect data regarding the epidemiology of severe varicella complications in immunologically healthy children through an established reporting system. To our knowledge, this is the first prospective nationwide survey on the frequency of severe varicella complications in immunologically healthy children.

METHODS

Case Finding

The "Erhebungseinheit für Seltene Pädiatrische Erkrankungen in Deutschland" (ESPED) is a German adaptation of the British Pediatric Association Surveillance Unit. Established in 1992 to study the epidemiology of rare childhood diseases, the ESPED is run under the auspices of the German Society for Pediatrics and Adolescent Medicine. Details have been described elsewhere.[4] In brief, a report card is mailed each month to all 485 pediatric department heads in Germany to determine whether a patient who was up to 16 years of age and had a defined rare illness was hospitalized. If a case is reported, then a follow-up questionnaire and request for the discharge letter is mailed. Severe varicella complications were included in the catalog of the regular ESPED query for the calendar year 1997. In most instances, no case was observed and a "zero option" (no case seen) was marked before the card was returned to ESPED.

Questionnaire and Case Definition

A multiple-choice questionnaire collected patient demographics, diagnoses at discharge, immune status of the patient, information on 3 categories of varicella complications, and the outcome (resolution, incomplete resolution/chronic sequelae, death). Discharge letters were used to supplement this information. The use of acyclovir to treat varicella in immunologically healthy children in Germany is negligible. Similarly, although varicella vaccine is available in Germany, there is no general recommendation to use it and thus it is not regularly paid for by health insurance companies. At $50 (US) per dose, it is hardly ever used in a population where all health care expenditures are usually paid for. Information regarding treatment with immune γ globulin and acyclovir and previous vaccination, therefore, was not sought. Varicella vaccine was licensed in 1994 and is recommended only for special risk groups. Information regarding treatment with those drugs or previous vaccination, therefore, was not sought. A case of severe varicella complication was defined as an individual who was up to 16 years of age and had an onset of varicella between January 1 and December 31, 1997, confirmed by a pediatrician. The child was not known to have or suspected of having an immune defect or receiving immunosuppressive therapy and had at least 1 of the following complications (multiple entries possible):

- Neurologic complication: if present, the next question was whether abnormal electroencephalogram, magnetic resonance imaging, altered level of consciousness, seizures, or focal neurologic deficits were present. When cerebrospinal fluid was examined, cell count and percentage of lymphocytes were requested. When myelitis was present, a description of the clinical picture was requested.
- Bacterial superinfection: if affirmed on the questionnaire, the following clinical diagnoses were accepted: cellulitis, abscess, necrotizing fasciitis, sepsis, pyogenic arthritis, pneumonia, and osteomyelitis. Also, the offending organisms were requested.
- Hematologic complication: if affirmed, the details of the clinical diagnosis were requested: thrombopenia ($<30\,000/\mu l$), granulocytopenia ($<500/\mu l$), anemia requiring transfusion, and arterial or venous thrombosis.

Incidence

The crude incidence of severe varicella complications was calculated using population figures provided by the German census bureau.[5] The case number was divided by the population of the respective age group.

RESULTS

The response rate to the monthly postcards during the period of observation was 93.4%. A total of 153 cases were reported. Thirty-four reports were excluded; the remaining 119 cases—56 girls and 63 boys—were analyzed.

The reasons for exclusion were as follows: Four centers did not return the follow-up questionnaire; therefore, only 149 cases could be evaluated. Four were reported twice. Thoroughness of reporting was good; very few cards were incomplete with additional information sought in the discharge letter, which was available for 58 patients (48.7%). Twenty-six reports did not match the case definition: onset of varicella was outside the period of observation (n = 12), patient was immunosuppressed, did not have varicella, was older than 16 years, or had minor complications such as a febrile seizure only (n = 14). Cerebellar ataxia was reported in 48 children, although it had not been specifically requested, and entered into the analysis.

There was no gender difference except in musculoskeletal infections (see below).

In 1997, there were 14 025 867 children up to 16 years of age living in Germany. The crude incidence of all severe complications was 8.5/100 000 population per year.

Seasonal Distribution

Complications followed a normal distribution, with a peak in March, and declined gradually to a nadir in September (Fig 1).

Age varied according to the type of complication (Fig 2): all infectious complications were most prev-

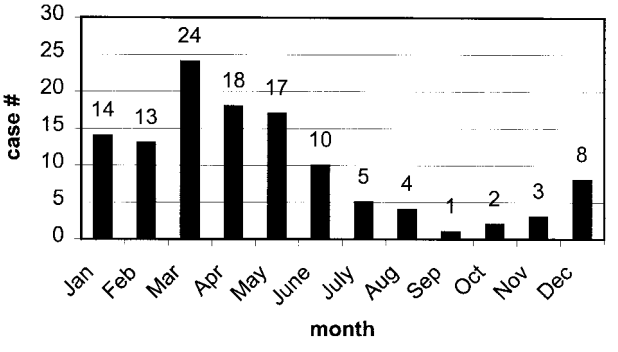

Fig 1. Seasonal distribution of 119 VZV complications.

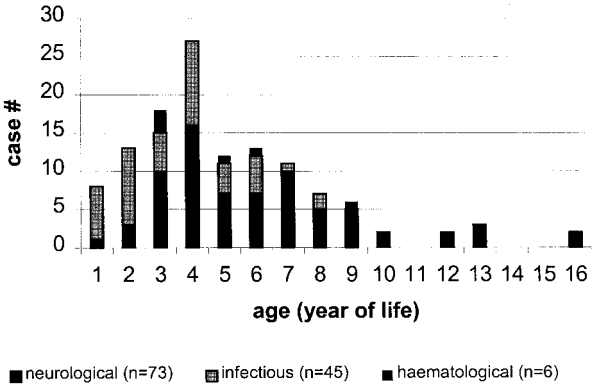

Fig 2. Age distribution by type of complication.

alent in children who were younger than 4 years and much less frequent thereafter. Encephalitis was seen throughout the ages of 1 to 13 years with a peak in the seventh year of life (median age: 6.4 years). The age distribution of cerebellitis, in contrast, resembled that of the infectious complications, with a sharp peak at 4 years of age (Fig 3) and a median age of 4.8 years. The 6 children with hematologic complications were between 3 and 9 years of age.

Neurologic complications constituted the largest group of children (n = 73 [61.3%]). Of 22 confirmed cases of encephalitis, 15 had an abnormal electroencephalogram, 8 had altered level of consciousness, 6 had cerebral magnetic resonance imaging abnormalities, and 3 had seizures. Two children with encephalitis also had concomitant ataxia. Focal neurologic deficits other than ataxia developed in 7 children: 3 with facial nerve palsy, 1 with concomitant hemiplegia, 2 with paresis of the arm, 1 with radiculitis resulting in paresis of the leg, and 1 with abducens nerve palsy. Two children were reported to have had isolated meningitis; the remaining 12 reports of meningitis were classified under encephalitis or cerebellitis. One child had isolated central nerve palsy. Myelitis was not reported. Of all 73 children with neurologic complications, 71 were discharged without sequelae. One child experienced persistent paralysis of the arm, and another had abducens nerve palsy.

Forty-six infectious complications were observed in 42 children (35.2%). Thirty-one were superinfections of the skin with cellulitis as the most common diagnosis (n = 18). Ninety-three percent of children with skin complications were younger than 5.5 years. The age distribution of cellulitis and abscess cases

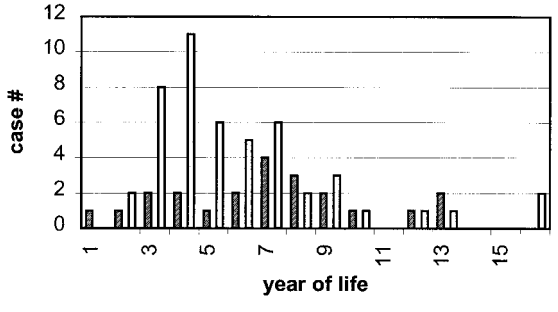

Fig 3. Age distribution of varicella encephalitis and cerebellitis.

were clearly distinct. The median age of the children with cellulitis was 1.58 years, with two thirds younger than 24 months (n = 12). The offending organism(s) could be isolated in 12 patients with cellulitis (Table 1). One patient had been on antibiotics, and in 5 cases no information regarding culture was given. The leading cause of cellulitis was GABHS (n = 8), isolated from blood in 3 cases, followed by *Staphylococcus aureus* (n = 3), isolated from blood in 1 case, and *S epidermidis* from the blood in 1 case. The wound culture of 1 child with cellulitis-associated scarlet fever grew both *S aureus* and GABHS. In another child with cellulitis-associated scarlet fever, GABHS was not isolated. Cellulitis-associated coinfections were reported in 1 each of pyogenic arthritis, cerebellitis, and necrotizing fasciitis with concomitant osteomyelitis.

The next most common infectious complication was abscess (n = 13). The median age for children with an abscess was 3.9 years with 10 between 3 and 5 years of age (no infant case). Culture was successful less often than in cellulitis (7 cases). Three abscesses could be attributed to GABHS, 3 to *S aureus*, and 1 to both (Table 1). In contrast to cellulitis, only 1 invasive case was associated with an abscess: GABHS grew from blood in a child with an abscess, erysipelas, and febrile seizure. In 5 of 7 children, when this information was provided, the abscess was located in the inguinal region, including thigh and genitalia; 2 had an abscess of the lower arm or rib.

Pyogenic arthritis was seen in 5 boys only (median age: 2.5 years), and none had concomitant osteomyelitis. Four of them were monoarticular. Multiple joints were involved in 1 case with invasive GABHS infection. GABHS was isolated from the throat of 1 child with concomitant pharyngitis and *S epidermidis* from another. The remaining 2 cases of pyogenic arthritis had previous antibiotics; 1 also had cellulitis.

Osteomyelitis was reported in 4 children (median age: 1.5 years); 3 were boys. Blood culture grew GABHS in 2 cases both with hip and "knee" (exact location not reported) involvement. No organism could be identified in the other 2 cases. *S aureus* was isolated from the wound in only 1 case. Three boys developed necrotizing fasciitis attributable to GABHS; 1 child had associated osteomyelitis. GABHS grew from the wound in 2 cases and from the blood culture in 1 case. Orbital cellulitis was observed in 2 boys with 1 secondary to GABHS. Pneumonia with pneumococcal bacteremia was reported in 1 child.

Six patients had chronic sequelae after infectious complications. One child was discharged with a residual hip defect after necrotizing fasciitis. Another child had severe calcifications in multiple joints after sepsis and pyogenic arthritis. Disfiguring cosmetic results, extensive scar formation, or other skin defects were seen in 4 children after an abscess or incision.

Of the 6 children with hematologic complications, 5 had thrombocytopenia. This persisted in 1, which required continued steroid therapy and was considered an incomplete recovery. One child developed

TABLE 1. Organisms Identified in 46 Infectious Complications of 42 Patients* After Varicella

	GABHS*	*S aureus*†	Both†	Other†	Negative Culture	Negative Culture and on Antibiotics	No Information
Cellulitis (n = 18)	8 (3)	2 (1)	1 (0)	1 (1)	0	1	5
Abscess (n = 13)	3 (1)	3 (0)	1 (0)	0	3	1	2
Osteomyelitis (n = 2)	1 (1)	0	1 (1)	0	0	0	2
Necrotizing fasciitis (n = 3)	3 (1)	0	0	0	0	0	0
Pyogenic arthritis (n = 5)	2 (1)	0	0	1 (1)	0	0	2
Orbital cellulitis (n = 2)	1 (1)	0	0	0	0	0	1
Pneumococcal pneumonia (n = 1)	0	0	0	1 (1)	0	0	0
Total (n = 6)	18 (8)*	5 (1)	3 (1)	3 (1)	3	2	12

* Three patients had >1 infectious complication.
† Invasive cases are in parentheses.

anemia and neutropenia for at least 3 months. No bleeding disorder, fatality, or case of Reye syndrome was reported during the period of observation.

DISCUSSION

Varicella is managed on an outpatient basis in the German health care system, if medical treatment is sought at all. We surmised that severe complications of varicella would lead to hospital admission, and, therefore, cases would be presented to the ESPED. However, cases with a rapidly fatal outcome and less severe complications may have remained undetected by this reporting system. We believe that our numbers are a fairly accurate reflection of the true frequency of severe complications of varicella during 1997 for 3 reasons: 1) all 416 German pediatric departments and children's hospitals with their 485 pediatric chiefs are included in the ESPED registry, 2) the response was excellent, and 3) thoroughness of reporting was good. Still, without a second independent reporting system, the completeness of reporting cannot be verified. Confirming case ascertainment by surveying hospital discharge diagnoses is not possible in Germany.

The only figures of public surveillance for varicella may be found in the Federal Register of Death Certificates, the equivalent of the British coroner forms. For 1997, 3 fatalities associated with varicella in children who were younger than 15 years were listed[5] with an average of 2.9 fatalities per year during the past 10 years.[5,6] It remains unclear whether these 3 fatalities would have fulfilled our case definition, because underlying diseases and/or immunosuppression are not reported.

The validity of our data may be confirmed in the demonstrated seasonal and age distribution. Complications peaked in spring, paralleling the highest incidence of disease, as has been described in studies from Israel, Switzerland, the United States,[7–10] and Germany[11] when optimal climatic conditions for varicella-zoster virus (VZV) transmission, such as low temperature and high humidity, prevail. Complications occurred more commonly in preschool children, who have the highest age-specific incidence rates[12,13] because of "favorable" conditions for transmission and absent herd immunity.

Because of the short period of observation, our case numbers are only a clue to the magnitude of the problem. A longer period of observation would reflect the true situation more adequately because the incidence of varicella may peak every 3 to 5 years.[2] Ongoing surveillance through ESPED is desirable.

The spectrum of complications in our study was different from other studies because minor complications had been excluded. Of 11 studies of complications after varicella infection, all but 1 were retrospective[14] and only 3 involved immunologically healthy children.[15–17] The remainder included mixed populations of previously ill and immunologically healthy children.[8–10,18,19] Most studies used hospital admission as the sole criterion for severity of the complication and inclusion in their studies[9,10,17,19]; there less serious complications, such as gastrointestinal or respiratory complications, rank second or third most common.

The crude incidence of complications is a minimum figure because it refers to the maximum population of all children who are younger than 16 years and theoretically at risk. The truly susceptible group is a much smaller fraction, because most children will have seroconverted to VZV much earlier. A 16-month prospective study of varicella and zoster in Ansbach, Germany, found that 400 of 437 varicella cases of all ages occurred in children who were younger than 10 years.[11] This is similar to what has been reported from the United Kingdom[12] and the United States.[13,20,21] There are no varicella incidence figures or hospitalization rates from Germany. The crude incidence cannot be compared easily with rates in other studies. Jaeggi et al[9] published a hospitalization rate of 92 cases/100 000 for varicella complications, which is closest to our figure. It is 10-fold higher because a much wider case definition was used and 22% of cases were immunocompromised. Similarly, Peterson et al[10] calculated an estimated risk of 1 in 550 cases of varicella with a much wider case definition used and nearly half of the patients previously ill. A surveillance of varicella and associated complications encountered in French general practices during a 5-year period listed only 96 skin superinfections (0.6% of varicella cases) and 21 neurologic sequelae (0.13%) with only 6 cases of encephalitis or cerebellitis in all age groups.[18] These figures seem to underestimate significantly the over-

all case load. No other comparative European incidence figures of varicella complications have been published, including the most recent studies from Italy and Spain.[14,22]

The high number of encephalitis cases is surprising, because we excluded children with underlying disease in which this is more frequently seen.[10,19] A possible explanation is that some may have been cerebellitis cases and were misclassified, because the reports together with the discharge letter served as the only confirmation of the physician's classification. Encephalitis was observed throughout all age groups and with a similar mean age as in the study of Fleisher et al.[19] To our knowledge, our study is the first to show the same age distribution in patients with cerebellitis and suppurative complications, paralleling general disease incidence.

The number of cases with osteomyelitis and pyogenic arthritis was comparably high. Other studies do not differentiate between them and may have underreported these complications, not including the respective *International Classification of Diseases, Ninth Revision* codes in their automated search of cases.[8–10,22,23] Although hematogenous osteomyelitis is a known complication of varicella, adjacent cellulitis as in 1 of our cases with middle finger osteomyelitis has been described only twice in the literature.[24]

Infectious complications are known to occur mostly in infants and toddlers,[9–11,22,23] with infections of the skin being the most common complication of varicella in most published articles.[2,8,10,17,18,23] This may have been underestimated in this study, because uncomplicated courses often are not admitted to the hospital. Remarkably, in two thirds of all bacteriologically confirmed infections (n = 27), GABHS was involved (15.1% of all cases). This corresponds with 12.2% for the period after 1993 in study by Peterson et al[10] from the United States. Superinfection with GABHS makes an invasive course of GABHS infection more likely[25] and has been recognized to be an increasing problem.[15,25,26] Six children in our study had invasive GABHS (6%), mostly after cellulitis, corresponding with 6.7% in the US literature.[10]

Long-term outcome and disability often are not reported, which hampers comparison. Also, incomplete reporting is likely because of the brief reporting interval between data collection and period of observation. Eight of our cases (6.7%) had long-term sequelae. Four children with invasive disease developed chronic sequelae, which is half of all of the children with chronic sequelae (n = 8), confirming the major role of *S pyogenes* as a risk factor for this outcome.

The public health significance of varicella in Germany differs from the United States and other countries. Important factors to immunize against varicella are lacking, explaining the relatively low use of vaccine. First, in the context of other vaccine-preventable diseases with a higher morbidity and mortality, such as measles, varicella has a lower priority in the public health pursuit in Germany as compared with the United States, Japan, or South Korea, where there are universal immunization recommendations. Varicella vaccine was licensed in 1994 in Germany and is recommended (and free of charge) only for people who are at special risk. Second, child care use in Germany is still much lower than in the United States, for example.

In conclusion, we found 119 immunocompetent children with severe varicella complications by using a population-based, prospective surveillance system during a 1-year period in Germany. This resulted in a crude incidence of 8.5/100 000 population at risk. To our knowledge, this is the first pertinent incidence figure in Germany published to date. Neurologic complications were found in 61%, infectious in 38%, and hematologic in 5%. Seven percent of cases had long-term sequelae, and there was no fatality. *S pyogenes* was the leading cause of bacterial infections with a considerable proportion of invasive disease and link to chronic sequelae.

REFERENCES

1. Centers for Disease Control and Prevention. Evaluation of Varicella Reporting to the National Notifiable Disease Surveillance System—United States, 1972–1997. *MMWR Morb Mortal Wkly Rep.* 1999;48:55–58
2. Preblud SR. Varicella: complications and costs. *Pediatrics*. 1986;78:728–735
3. Centers for Disease Control and Prevention. Outbreak of invasive group A streptococcus associated with varicella in a child care center—Boston, Massachusetts, 1997. *MMWR Morb Mortal Wkly Rep.* 1997;46:944–948
4. Schmidt E, von Kries R, Herzig P. Die Erhebungseinheit für pädiatrische Erkrankungen in Deutschland (ESPED). Teil I: Angebot eines Instrumentes für epidemiologische Forschung. *Monatsschr Kinderheilkd*. 1993;141:758–759
5. Sterbefälle nach Todesursachen. Einzelnachweis für ICD 052 (Varizellen) Statistisches Bundesamt. Zweigstelle Bonn; 1997
6. Anzahl der Gestorbenen für ICD 052 Varizellen nach IDG—Altersklassen 1987–1997. Statistisches Bundesamt. Zweigstelle Bonn; 1997
7. Guess HA, Broughton DD, Melton LJD, Kurland LT. Population-based studies of varicella complications. *Pediatrics*. 1986;78:723–727
8. Maharshak N, Somekh E. Hospitalization for varicella in central Israel. *Acta Paediatr*. 1999;88:1279–1283
9. Jaeggi A, Zurbruegg RP, Aebi C. Complications of varicella in a defined central European population. *Arch Dis Child*. 1998;79:472–477
10. Peterson CL, Mascola L, Chao SM, et al. Children hospitalized for varicella: a prevaccine review. *J Pediatr*. 1996;129:529–536
11. Paul E, Thiel T. Zur Epidemiologie der Varizella-Zoster-Infektion. Ergebnisse einer prospektiven Erhebung im Landkreis Ansbach. *Hautarzt*. 1996;47:604–609
12. Yawn BP, Yawn RA, Lydick E. Community impact of childhood varicella infections. *J Pediatr*. 1997;130:759–765
13. Fairley CK, Miller E. Varicella-zoster virus epidemiology: a changing scene? *J Infect Dis*. 1996;74:314–319
14. Deguen S, Chau NP, Flahault A. Epidemiology of chickenpox in France (1991–1995). *J Epidemiol Community Health.* 1998;52(suppl):46S–49S
15. Manfredi R, Chiodo F, Titone L, et al. Chickenpox complications among immunocompetent hospitalized children in Italy. Acyclovir-Chickenpox Italian Study Group. *Pediatr Med Chir*. 1997;19:99–104
16. Bullowa JGM, Wishik SM. Complications of varicella: I. Their occurrence among 2534 patients. *Am J Dis Child*. 1935;49:923–926
17. Jackson MA, Burry VF, Olson LC. Complications of varicella requiring hospitalisation in previously healthy children. *Pediatr Infect Dis J*. 1992;11:441–445
18. Riaza Gomez M, de la Torre Espi M, Mencia Bartolome S, et al. Complications of varicella in children. *An Esp Pediatr*. 1999;50:259–262
19. Fleisher G, Henry W, Mc Sorley M, Arbeter A, Plotkin S. Life threatening complications of varicella. *Am J Dis Child*. 1981;135:896–899
20. Kouwabunpat D, Hoffman J, Adler R, et al. Varicella complicated by group A streptococcal sepsis and osteonecrosis. *Pediatrics*. 1999;104:967–969
21. Finger R, Hughes JP, Meade BJ, Pelletier AR, Clarkson TP. Age-specific incidence of chickenpox. *Public Health Rep*. 1994;109:750–755
22. Aebi C, Ahmed A, Ramilo O. Bacterial complications of primary vari-

cella in children. *Clin Infect Dis*. 1996;23:698–705
23. Choo PW, Donahue JG, Manson JE, Platt R. The epidemiology of varicella and its complications. *J Infect Dis*. 1995;172:706–712
24. Aebi C, Ramilo O. Metacarpal osteomyelitis complicating varicella-associated cellulitis of the hand: report of 2 cases. *Scand J Infect Dis*. 1998;30:306
25. Doctor A, Harper MB, Fleisher GR. Group A beta-hemolytic streptococcal bacteremia: historical overview, changing incidence, and recent association with varicella. *Pediatrics*. 1995;96:428–433
26. Vugia DJ, Peterson CL, Meyers HB, et al. Invasive group A streptococcal infections in children with varicella in Southern California. *Pediatr Infect Dis J*. 1996;15:146–150

Severe Complications of Varicella in Previously Healthy Children in Germany: A 1-Year Survey

Christine Ziebold, Rüdiger von Kries, Robert Lang, Josef Weigl and Heinz J. Schmitt

Pediatrics 2001;108;e79

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Severe Complications of Varicella in Previously Healthy Children in Germany: A 1-Year Survey

Christine Ziebold, Rüdiger von Kries, Robert Lang, Josef Weigl and Heinz J. Schmitt

Pediatrics 2001;108;e79