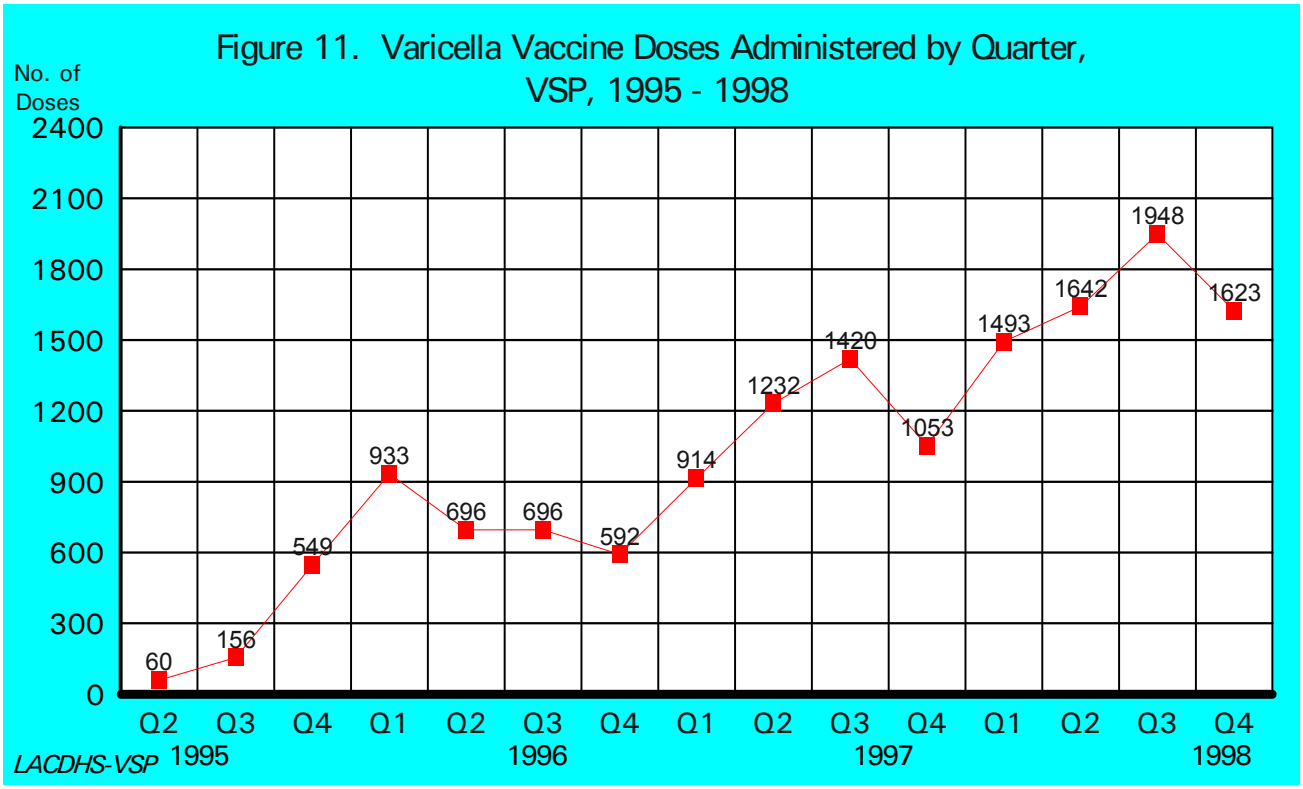
IV. VARICELLA VACCINE IN STUDY POPULATION

Fifty-three reporting sites are currently providing varicella vaccine, up from forty-three in 1997. Reporting site compliance with returning the monthly immunization report to the VSP office during 1998 was 100%. Los Angeles County Clinics began administering the vaccine in March of 1997. The school districts do not require the vaccine for school entry. Although steadily increasing since vaccine licensure, the administered doses experience a dip in Quarter IV each year (Figure 11).



One year olds represent the largest portion of vaccine recipients (3,139; 47%) in 1998 (Table 36). This represents 63% of the birth co-hort (approximately 5,000). The effect of these vaccinations in lowering incidence of varicella is expected to be seen as these children approach school-age. Of the 19,464 varicella vaccine doses Merck has shipped to the Antelope Valley since vaccine licensure, 15,007 (77%) administered doses have been reported to VSP.

Table 36. Total Varicella Vaccine Doses Administered by Age, Antelope Valley, VSP, 1995 - 1998 and Combined Years

Age (years)	1995 N (%)	1996 N (%)	1997 N (%)	1998 N (%)	Combined Years 1995-1998 N (%)
1	299 (39.1)	1,210 (41.5)	2,138 (46.3)	3,139 (46.8)	6,786 (45.2)
2	123 (16.0)	421 (14.4)	652 (14.0)	654 (9.7)	1,850 (12.3)
3-4	172 (22.5)	553 (19.0)	789 (17.0)	1,211 (18.0)	2,725 (18.1)
5	54 (7.0)	258 (8.8)	425 (9.2)	698 (10.4)	1,435 (9.6)
6-9	71 (9.3)	252 (8.6)	368 (8.0)	509 (7.6)	1,200 (8.0)
10-12	20 (2.7)	78 (2.7)	109 (24.)	259 (3.9)	466 (3.1)
13-19	11 (1.4)	87 (3.0)	73 (1.6)	179 (2.7)	350 (2.3)
>20	15 (2.0)	58 (2.0)	65 (1.4)	57 (0.8)	195 (1.3)
Total	**765 (100)**	**2,917 (100)**	**4,619 (100)**	**6,706 (100)**	**15,007 (100)**

L.A. County public health clinics/Medi-cal providers administered 2,742 (40.9%) of the vaccine doses administered in 1998, followed by HMOs (2,122; 31.6%) and private practice healthcare providers (1,8423; 27.9%; Table 37).

Table 37. Varicella Doses Administered by Provider Type, Antelope Valley, VSP, 1995 - 1998

Provider Type	1995 N (%)	1996 N (%)	1997 N (%)	1998 N (%)
Private Practice Healthcare Providers	144 (19)	940 (32)	1,413 (31)	1,842 (27.9)
HMOs	621 (81)	1,952 (67)	1,770 (38)	2,122 (31.6)
L.A. County Health Clinics & Medi-cal Providers	-----	25 (1)	1,418 (31)	2,742 (40.9)
Total	**765 (100)**	**2,917 (100)**	**4,619 (100)**	**6,706 (100)**

In 1998, of the 8,051 varicella vaccine doses Merck shipped to Antelope Valley providers, 4,006 (50%) were purchased under a CDC contract. Table 38 reflects the 3,965 varicella vaccine doses administered in 1998 by provider type purchasing vaccine exclusively under CDC contract (21 providers in the Antelope Valley).

Table 38. Varicella Doses Administered by Provider Type Purchasing Vaccine Exclusively Under CDC Contract, Antelope Valley, 1997 - 1998

Provider Type	1997 N (%)	1998 N (%)
Private Practice Healthcare Provider	490 (25.8)	1,151 (29.0)
HMO	20 (1.1)	72 (1.8)
L.A. County Health Clinics	1,386 (73.1)	2,742 (69.1)
Total	**1,896 (100)**	**3,965 (100)**

Of the 3,965 varicella vaccine doses purchased under CDC contract and administered, 1,676 (42%) were administered to one-year-olds (Table 39).

Table 39. Age Distribution of Varicella Vaccine Recipients who Received the Vaccine from Providers Obtaining Vaccine Exclusively under CDC contract, Antelope Valley, 1997 - 1998

Age Group (years)	Doses Administered	
	1997 N (%)	1998 N (%)
1	939 (49.5)	1,676 (42.3)
2	271 (14.3)	488 (12.3)
3-4	375 (19.8)	828 (20.9)
5	122 (6.4)	436 (11.0)
6-9	144 (7.6)	298 (7.5)
10-12	36 (1.9)	136 (3.4)
13-19	6 (0.3)	98 (2.5)
>20	3 (0.1)	5 (0.1)
Total	**1,896 (100)**	**3,965 (100)**

EVALUATION

Reporting Completeness

Capture-Recapture.

We estimated (1) the number of varicella cases among children two to eighteen years of age missed by the surveillance system and (2) the true number of varicella cases in that same age group, by analyzing the degree of overlap between two incomplete lists of cases (two-source capture-recapture methods) as originally described by Chapman. The two ascertainment sources used were 'schools' (elementary, middle and secondary schools, preschools, and daycare facilities), and 'healthcare providers' (physicians, clinics, hospitals, and health maintenance organizations). We limited the analysis to children two to eighteen years of age to decrease heterogeneity of the two ascertainment sources; fewer than 10% of children under two years of age in the study population attend a child care facility with an enrollment of 12 or more (data not shown). Considering all surveillance unit types, dual reporting of 253 cases two- to eighteen-years-old occurred in 1998 (Table 40).

Table 40. Source of Report for Varicella Cases 2 - 18 years old, by Surveillance Unit Type, VSP, 1998

Surveillance Unit Type	Households	Health Providers	Schools	Day cares	Others	Total
Households	314	15	47	4	9	384
Providers		129	124	24	3	180
Schools			670	16	6	692
Day cares				90	5	95
Others					34	34
Total						**1,390**

*The values along the diagonal designate cases reported by one surveillance unit type. The 253 cases off the diagonal were reported by more than one surveillance unit type. Eleven cases not included in table were reported by three different unit types.

In this model, *a* is the number of cases reported by both sources, *b* is the number of cases reported by source x only, *c* is the number of cases reported by source y only, and *d* is the number of cases missed by both ascertainment sources. In our calculations we included an adjustment for small samples that yields a nearly unbiased estimator (NUE) for unascertained cases and total cases in the population, as described by Chatham, Witte, and Hook and Regal.

Thus, the nearly unbiased estimator of total cases in children aged two- to eighteen-years-old not ascertained by school or providers *(d_{nue})* is given by (bc)/(a+1), and the total cases in the population with varicella in this age group *(p_{nue})* is given by [(a+b+1) (a+c+1)/(a+1]-1 (Table 41)

.

Table 41. Structure of Population with Two Sources of Ascertainment

		Cases reported in source Y (schools)		
		yes	no	
Cases reported in source X (healthcare providers)	yes	a	b	a+b
	no	c	d=?	
		a+c		P=a+b+c +d

We evaluated bias of the data due to dependence of the two sources by computing *r*, a relative odds ratio that if a case is reported in one source, it is reported in the other, equal to (ad)/(bc). We evaluated possible within-source variation in probability of ascertainment by stratifying by age, race, and overall disease severity. We calculated 95% confidence intervals for p_{nue} using goodness-of-fit.

Using only two ascertainment sources, we estimate 60% completeness during 1998 in the two- to eighteen-year-old age group (Table 42). However, considering cases from all surveillance units including those outside the selected ascertainment sources (i.e. households), overall completeness percentages are 68%, 70%, 74% and 78% for 1995, 1996, 1997, and 1998, respectively.

Table 42. Capture-Recapture Estimates of Two- to Eighteen-Year-Olds Based On Two Ascertainment Groups, 'Schools' and 'Providers', VSP, 1995 - 1998 and Combined Years

Time Period	Reported by both, a	Providers Only, b	Schools Only, c	Cases Missed by both groups, d_{nue}	Varicella Cases p_{nue} (95% Confidence Interval)	Actual Reported Cases a+b+c	Percentage Complete	Odds Ratio r
1995	222	310	1,297	1,803	3,632 (3,330-4,009)	1,829	50.4	0.995
1996	161	193	1,188	1,415	2,957 (2,680-3,319)	1,542	52.1	0.994
1997	197	234	964	1,139	2,534 (2,323-2,803)	1,395	55.0	0.995
1998	161	148	859	785	1,953 (1,785-2,173)	1,953	59.8	0.994
'95-'98	741	885	4,308	5,138	11,072 (10,561-11,651)	6,023	53.6	0.999

The capture-recapture results in this report differ from the 1997 annual report in that

verified cases associated with 'schools' and 'healthcare providers' that closed were inadvertently excluded from the capture-recapture analysis. This problem was revealed during a quality study performed in August of 1998 and corrected by electronically mapping the deleted sites to their proper category of 'schools' or 'healthcare providers' and manually comparing the list of surveillance units for their inclusion. This improved the percentage complete by 1.2% in 1995 and 1.7% in 1996. Coincidently, a quality control study of the Fourth Quarter 1997 did not reveal this problem as none of the Fourth Quarter cases made reference to closed or deleted surveillance site.

Under-reporting of Known Cases.

This method of estimating under-reporting focuses on those cases in all age groups that should have been reported by surveillance units (pre-schools/day cares, schools and healthcare providers). To obtain this information, the Varicella Case Report form contains an Under-reporting Survey which includes the following questions:

1) Did case attend preschool? If yes, specify: _____
2) Did cases attend day care? If yes, specify: _____
3) Did case attend school? If yes, specify: _____
4) Did case consult a healthcare provider by telephone? If yes, specify:
5) Did case see a healthcare provider in the office? If yes, specify:
6) Was case out of session (off-track, summer break, spring break, etc.) when they had varicella?

After collecting the above answers, varicella surveillance staff determine whether or not the specified preschool/day care, school or healthcare provider is a surveillance unit. Under-reporting by surveillance units can be estimated by ascertaining whether or not the case was known to surveillance units other than the one that initially identified (or reported) the case.

The Varicella Surveillance Project began collecting this information June 1, 1996. Generally, this study shows that schools, daycares and healthcare providers report 65% of the varicella cases they encounter (Table 43). Specifically, daycares report 78% - 83%, schools report 75% to 81% and healthcare providers report 34% to 54% of the cases they encounter. The reporting by schools has improved with each successive year.

Table 43. Cases Known and Reported or Not Reported by Surveillance Unit Type, VSP, 1996 - 1998

Cases	Daycare/Preschools N (%)	Schools N (%)	Healthcare Providers N (%)	Combined Types
		1996		
Not Reported	31 (16.7)	165 (24.2)	390 (65.3)	586 (40.0)
Reported	154 (83.2)	518 (75.8)	207 (34.7)	879 (60.0)
Total Potential Reports	185 (100)	683 (100)	597 (100)	1,465 (100)
		1997		
Not Reported	62 (21.2)	257 (21.0)	552 (47.9)	871 (32.7)
Reported	230 (78.8)	965 (79.0)	600 (52.0)	1,795 (67.3)
Total Potential Reports	292 (100)	1,222 (100)	1,152 (100)	2,666 (100)
		1998		
Not Reported	29 (16.6)	206 (18.9)	473 (54.5)	708 (33.3)
Reported	145 (83.3)	880 (81.1)	395 (45.5)	1,420 (66.7)
Total Potential Reports	174 (100)	1,086 (100)	868 (100)	2,128 (100)
		COMBINED YEARS 1996-1998		
Not Reported	122 (18.7)	628 (21.0)	1,415 (54.0)	2,165 (34.6)
Reported	529 (81.3)	2,363 (79.0)	1,202 (46.0)	4,094 (65.4)
Total Potential Reports	651 (100)	2,991 (100)	2,617 (100)	6,259 (100)

Quality Control.

When the reported cases from the Varicella Case Logs are received in the office and entered into the database, the case demographics are printed onto the Varicella Case Report. The handwritten Varicella Case Log is then highlighted when the reported demographics compare accurately to the computer generated Varicella Case Report. After collection and entry of clinical variables, the same manual verification procedure is followed. Any noted data entry errors are immediately corrected at that time and re-verified.

At the end of a day, a program (called PRINTCD) generates a computer printout of each case not previously printed for which clinical data was collected and entered. Those cases linked to a household are automatically labeled as either primary (the first individual

who introduces the disease into the family), co-primary (occurring ten or fewer days after the primary case) or secondary (occurring more than ten days after onset of varicella in the index case). The computer-generated printout is manually compared with the original, handwritten, clinical data collection sheet to ensure that computer entered data matches.

Once having entered the demographic information for one individual within a household, a shortcut exists for applying the same demographic information to other household members without retyping. This minimizes errors especially with regard to the street address. At the end of a day or session of data input, a program (called PRINTIND) scans the data base and generates a report that links household cases.

The computer detects duplicate cases by comparing the first five digits of the street address and the date of birth (the individual's name is not considered). A provision exists to override the duplicate detection mechanism if twins are encountered within a household. If two different reporting sites should report the same individual, but provide either a different address or different date of birth for the individual, this duplicate case initially goes undetected. At the end of a day, a program (called PRINTALP) places all names of varicella cases in an alphabetized list. By comparing duplicate (or near duplicate) last names, along with comparisons of date of births, addresses, and phone numbers, it is often possible to resolve cases that are duplicates, despite inconsistent demographic information pertaining to address or date of birth.

Another program (called ENTERADD) can be used to list the names of all cases at a given address (or partial address). This proves useful for resolving cases reported with either different last names that reside at the same address and/or minor inconsistencies in the recorded street addresses (such as Avenue instead of Street, a missing apartment number, etc.).

Since capture-recapture depends on the determination of the type of surveillance unit reporting each case, we manually checked the categories assigned to each reporting site. This revealed that closed sites no longer reporting cases were improperly assigned at 'other' rather than 'schools' or 'healthcare providers' they actually represented.

VI. PRIOR VARICELLA STUDY

In 1998, a study was conducted to gather additional information on those individuals reporting multiple cases of varicella (Attachment 7). Interviews were successfully conducted on 102 individuals with the goal of ascertaining the likelihood of their multiple varicella cases by collecting data concerning the rash description/location and whether or not (1) the varicella had been diagnosed by a physician and (2) there were other concurrent outbreaks of varicella within the same household or perhaps some other known exposure (such as at school/daycare). The raw data, along with a summary of the collected responses were provided in an electronic format to CDC for their further study and evaluation.

VII. CHRONOLOGICAL SUMMARY OF WORK COMPLETED IN 1998

January 1998:

1) Slide presentation on project results to date presented to Westside Union School District nurses and health clerks.

2) Slide presentation on project results to date presented to Eastside Union School District nurses and health clerks.

3) Thirty-six reporting sites visited.

4) Review of the medical staff roster from three local hospitals for new physicians practicing in the Antelope Valley.

5) Monthly surveillance report prepared.

February 1998:

1) Quarterly Newsletter, Vol. 4, #1, was prepared and mailed to reporting sites and other interested parties.

2) Slide presentation on project results to date presented to Lancaster Union School District Nurses and health clerks.

3) Six reporting sites visited.

4) Began 16-bit Turbo Pascal code conversion to the 32-bit Delphi Windows '95 platform.

5) Monthly surveillance report prepared.

March 1998:

1) Nine reporting sites visited.

2) State of California, Department of Social Services, Community Care Licensing Division, Licensing Directory were reviewed for newly licensed child care facilities in the Antelope Valley.

3) Developed computer program to resolve duplicate cases through a secondary check by date of birth or telephone number.

4) Slide presentation on project results to date presented to Antelope Union High School District nurses.

5) Computer program developed to compare four years of data by quarter or by year (Attachment 8).

6) Evaluation of capture-recapture data base accuracy performed by comparing cases reported by site via the case logs with case and site numbers recorded in the data base.

7) Monthly surveillance report prepared

April 1998:

1) 1997 Annual Report prepared and submitted to CDC.

2) Nine reporting sites visited.

3) Collected clinical data on hospitalized case.

4) Evaluation of capture-recapture formula accuracy performed by checking each case for grouping in 'provider', 'school' or both categories using the cases in Quarter IV 1997.

5) Review of Merck report delineating varicella vaccine doses shipped to the Antelope Valley by zip code, to determine any new vaccine providers.

6) Monthly surveillance report prepared.

7) Initiated evaluation study to confirm accuracy of vaccine doses reported by large HMO.

May 1998:

1) First Quarterly Report of 1998 prepared and submitted to CDC.

2) Heath care providers not providing varicella vaccine surveyed to determine if they implemented a varicella vaccination program yet.

3) Since duplicate cases occasionally occur because they are reported with different addresses, telephone numbers and/or date of birth, a computer program developed to list cases with similar names.

4) Computer program developed to monitor vaccine doses administered by reporting site and month.

5) Monthly surveillance report prepared.

June 1998:

1) Quarterly Newsletter, Vol. 4, #2, was prepared and mailed to reporting sites and other interested parties.

2) Office procedure manual reviewed and revised.

3) Reporting site directory and mailing lists updated.

4) Prepared for CDC site visit on varicella modeling.

5) Grant renewal application prepared and submitted.

6) Varicella Case Report form revised to collect varicella vaccination history at the end of the clinical interview.

July 1998:

1) Semi-Annual Report of 1998 submitted to the CDC.

2) Prior Varicella study questionnaire planned and developed.

3) Data base for Prior Varicella study developed in 32-bit Delphi Windows '95 platform.

4) Six reporting sites visited.

5) Month Surveillance Report Prepared.

August 1998:

1) Clinical variables for Prior Varicella study collected via telephone.

2) Clinical variables from Prior Varicella study entered into computer database.

3) Eight reporting sites visited.

4) Office procedure manual reviewed and revised.

5) Antelope Valley Map Book updated and revised.

September 1998:

1) Prior Varicella study continued with collection of clinical variables via telephone.

2) Varicella Case Logs for 1999 prepared for distribution to reporting sites.

3) Varicella Immunization Reports for 1999 prepared for distribution to reporting sites.

4) Prior Varicella database submitted to Susan Hall at CDC.

5) Four reporting sites visited.

6) State of California, Department of Social Services, Community Care Licensing Division, Licensing Directory was reviewed for newly licensed child care facilities in the Antelope Valley. Two newly licensed daycares were added as surveillance units.

7) California Private School Directory prepared by the Department of Education was reviewed for newly licensed private schools. Two new private schools (K-12) were added as surveillance units.

October 1998:

1) Rating system for Prior Varicella study developed but not utilized.

2) Eighty-four reporting sites visited with delivery of 1999 case logs.

November 1998:

1) One hundred thirty-seven reporting sites visited with delivery of 1999 case logs.

2) Third Quarterly Report of 1998 prepared and submitted to CDC.

December 1998:

1) Quarterly Newsletter, Vol. 4, #3, was prepared and mailed to reporting

sites and other interested parties.

2) Forty-nine reporting sites visited with delivery of 1999 case logs.

VIII. PROJECTIONS

After four full years of data collection, it appears that utilization of the varicella vaccine is having an impact on the reduction of varicella cases in the population. Investigation of vaccine break-through cases and failures will continue to be of increasing concern. In 1999-2000, the Varicella Surveillance Project will continue the following activities:

1) Collect and analyze demographic and clinical data and trends as additional varicella cases are reported.
2) Identify dramatic changes in the epidemiology of varicella due to widespread vaccination and analyze vaccine status of cases as the level of vaccine coverage increases.
3) Design and implement additional evaluation studies as needed.
4) Maintain the current level of reporting site participation and reporting accuracy.
5) Continue assessment of level of vaccine coverage in the study area.
6) Continue with Capture-Recapture methodology and Under-reporting study.
7) Repeat Knowledge, Attitude and Practice Survey among healthcare providers of the Antelope Valley in early 1999.
8) Continue joint investigation, with John Glasser of the CDC, to determine the role ambient air temperature and school enrollment plays in the transmission of varicella.