A Review of Traditional Vaccine-Preventable Diseases and the Potential Impact on the Otolaryngologist

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Abstract

Introduction A majority of otolaryngologists have not had direct experience with many vaccine-preventable diseases since the creation of national vaccination programs. Despite the elimination of endemic transmission of some of these diseases in the United States, outbreaks can occur anywhere and still pose a threat to public health around the world. Recent outbreaks and changing trends in exemption rates indicate that it is important for physicians to maintain a working knowledge of how these diseases present and of the recommended treatment guidelines.

Objectives This review will evaluate the current state of vaccination rates, vaccine exemption rates and disease incidence in the United States and in the world. It will also examine the clinical presentation and treatment recommendations of these diseases.

Data Synthesis United States estimated vaccination rates, vaccine exemption rates and vaccine-preventable disease incidences were obtained from data compiled by the Centers for Disease Control and Prevention. World vaccination rates and disease incidences were obtained from the World Health Organization databases, which compile official figures reported by member states. A PubMed literature review provided information on the current state of vaccination exemptions and outbreaks in the United States.

Conclusion Vaccination and vaccine exemption rates continue to put the United States and many areas of the world at risk for outbreaks of vaccine-preventable diseases. Clinical guidelines should be reviewed in the event of a local outbreak.

Keywords
- vaccine
- otolaryngology
- public health
- disease outbreaks
- disease eradication
- vaccination

Introduction

Vaccines are often considered one of the greatest achievements in medicine and public health, and have helped to greatly reduce the incidence of several historically common infectious diseases. The inclusion of vaccinations in the standard of care guidelines has resulted in record low levels of vaccine-preventable disease (VPD) occurrences in the U.S.[1] The use of vaccines can greatly reduce the risk of contracting one of these diseases at an individual level and when vaccination coverage is high enough,[2,3] it can also confer herd immunity at a community and population level. For most diseases in which vaccinations are regularly used, cases of VPDs in the U.S. have been reduced by 90–100%, with a similar reduction in deaths associated with these diseases.[1] Similar reductions are seen around the world in countries that have developed robust vaccination programs.

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Worldwide progress is evident in the eradication of endemic poliomyelitis in all but three countries and the elimination of both measles and rubella from the World Health Organization (WHO) Region of the Americas in 2002.[4,5] While these are significant advances in public health, most of these diseases are far from complete elimination and still pose a significant threat to all areas of the globe.

Individuals and physicians living in the U.S. and other countries with strong immunization programs are likely to lack any firsthand experience with many VPDs as it has been decades since diseases such as measles, mumps, rubella and diphtheria were commonplace. In the decade preceding the implementation of the national measles vaccine program, in 1963, it was estimated that there were 3 to 4 million cases of measles every year in the U.S., with an average of 500 deaths.[6] Rubella was even more prevalent, with at least 12.5 million cases occurring in the mid-1960s and an estimated 20,000 children born with congenital birth defects as a result.[7] To put this into perspective, the CDC data indicate that the highest reported yearly total of measles cases since the year 2000 is 667, which occurred in 2014.[8] The CDC also reports that there have been less than 100 reported cases of rubella in the U.S. in the past 10 years. This reduction in incidence leads to a decreased perception of the severity and individual susceptibility to these diseases.[9] This distancing from the effects of these diseases may be one of the reasons that nonmedical exemptions (NMEs) are not only increasing, but increasing at a greater rate when compared with data going as far back as 1991.[10] As more individuals choose the route of NMEs, there may be an increased likelihood of outbreaks.

A whole generation of physicians has trained after the time of near-universal vaccinations. Many otolaryngologists, like other physicians, are unlikely to have experience in diagnosing and treating patients with VPDs. As these patients often present with symptoms in the head and neck, it is important that otolaryngologists be reminded of these diseases. This lack of familiarity with these infections and their variable presentations can result in these patients being seen by an otolaryngologist without prior diagnosis. Because these VPDs can occur in both unvaccinated children and adults, patients may present at any age. Therefore, it is important that regardless of the patient population the otolaryngologist serves, familiarity with these diseases is accomplished.

This article will review the current state of vaccination rates and VPD rates in both the U.S. and the world. Additionally, this review will examine how these diseases might present and remind physicians of the current treatment guidelines.

Review of Vaccination Rates and Disease Incidence

The United States childhood vaccination rate estimates for the 19–35 months age group were obtained from data collected by the Centers for Disease Control's (CDC) National Immunization Survey (NIS). National kindergarten vaccination rate data were obtained from publications within the CDC's Morbidity and Mortality Weekly Report (MMWR). World vaccination rates were obtained via annual reports from the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) joint reporting process. The WHO/UNICEF vaccination rate data represent official reports from the 194 WHO member states that participate in the reporting process.

The vaccine preventable diseases incidence data for the U.S. were obtained through the annual Summary of Notifiable Diseases reports from the CDC's National Notifiable Diseases Surveillance System (NNDSS). The international VPDs incidence data were obtained from the WHO/UNICEF database of disease incidence, which collects reported cases from 194 participating WHO member states.

The national and state level vaccine exemption data for kindergarteners were obtained from the CDC's MMWR reports. A literature review of the current state of vaccination exemptions and the reasons parents choose to exempt children in the U.S. was conducted through a PubMed search using the key words "vaccine exemption," "medical exemption" and "nonmedical exemption."

Clinical information regarding the presentation of these diseases and the current treatment guidelines was obtained from the Red Book: Report of the Committee on Infectious Diseases and from the Manual for the Surveillance of Vaccine-Preventable Diseases published by the CDC.

United States Vaccination Rates

The most recent data from the CDC regarding U.S. vaccination rates for children (19–35 months) for the period of January-December of 2014 contains vaccination rate estimations using NIS results. National and statewide vaccination levels are reported and can be found in ►**Table 1**.

Additional vaccination rate data provided by the CDC's MMWR reports were collected for children enrolled in kindergarten. Both national and statewide vaccination levels were reported and can also be found in ►**Table 1**. Diphtheria, tetanus and pertussis (DTaP) vaccination rates were determined according to individual state regulations of either four or five required doses for enrollment in kindergarten. Data from Pennsylvania was not included as pertussis is not required for kindergarten.

WHO/UNICEF Regional Vaccination Rates

WHO/UNICEF vaccination rate data represent official national reports via the standardized Joint Reporting Form and draws from the most recently updated report released in July of 2015. The data are representative of all age groups. WHO/UNICEF regional vaccination rate estimates are summarized in ►**Table 2**. Countries in the Americas region (North and South America) that had a notably low three dose DTaP vaccination rate were: Ecuador (83%), Venezuela (78%), Guatemala (73%) and Haiti (48%). Two dose measles-containing vaccine (MCV) rates were considerably lower, as over one third of the countries in the region reported a vaccination rate of less than 85%. Haemophilus influenzae type b (Hib) (three doses) vaccination rates were similar to those seen

Table 1 Estimated US vaccination rates for children aged 19–35 months in 2014 and children enrolled in kindergarten for the 2014–2015 school year.

		19–35 months[50]		
State	DTaP 3rd dose (%)	DTaP 4th dose (%)	MMR 1st dose (%)	Hib full series (%)
US National	94.7 ± 0.7	84.2 ± 1.2	91.5 ± 0.9	82.0 ± 1.3
Alabama	92.6 ± 5.7	84.1 ± 7.4	92.0 ± 5.6	85.3 ± 7.0
Alaska	92.5 ± 3.9	78.7 ± 6.3	90.2 ± 4.3	80.8 ± 6.2
Arizona	90.6 ± 5.1	81.4 ± 6.4	84.1 ± 6.3	77.0 ± 7.1
Arkansas	93.8 ± 3.3	80.0 ± 6.8	89.1 ± 5.4	78.3 ± 7.5
California	94.9 ± 3.5	87.3 ± 5.3	90.5 ± 4.7	84.7 ± 6.0
Colorado	94.2 ± 3.8	85.4 ± 4.9	87.4 ± 5.4	85.3 ± 5.3
Connecticut	94.8 ± 4.3	86.0 ± 6.0	93.2 ± 4.6	84.4 ± 6.5
Delaware	95.0 ± 4.0	85.4 ± 6.0	90.8 ± 4.8	84.5 ± 6.1
Dist. of Columbia	92.6 ± 4.3	80.6 ± 6.6	90.9 ± 4.8	80.9 ± 6.9
Florida	98.3 ± 1.5	86.2 ± 6.1	91.2 ± 4.8	84.9 ± 6.3
Georgia	94.9 ± 3.9	85.7 ± 6.2	94.2 ± 3.9	81.1 ± 7.1
Hawaii	94.5 ± 3.3	82.4 ± 5.9	92.5 ± 3.7	84.5 ± 5.1
Idaho	92.2 ± 5.2	77.7 ± 7.2	89.7 ± 5.1	80.4 ± 6.5
Illinois	93.6 ± 3.1	87.8 ± 3.9	93.2 ± 2.8	82.8 ± 4.6
Indiana	94.8 ± 3.7	82.8 ± 5.7	91.5 ± 4.5	82.0 ± 5.7
Iowa	93.4 ± 4.8	87.4 ± 5.7	91.1 ± 5.2	79.8 ± 7.6
Kansas	92.1 ± 5.0	85.3 ± 6.2	93.4 ± 4.0	82.7 ± 6.7
Kentucky	94.6 ± 4.0	83.2 ± 6.5	88.6 ± 5.5	79.7 ± 7.2
Louisiana	95.4 ± 3.5	83.3 ± 5.6	91.8 ± 4.1	81.9 ± 6.4
Maine	97.5 ± 2.0	93.1 ± 3.5	97.2 ± 2.0	90.5 ± 4.1
Maryland	97.0 ± 2.8	85.4 ± 6.4	94.9 ± 3.3	86.2 ± 6.1
Massachusetts	98.2 ± 1.7	89.8 ± 5.0	94.7 ± 3.2	86.8 ± 6.0
Michigan	89.4 ± 6.1	77.7 ± 8.1	87.4 ± 6.5	77.4 ± 7.7
Minnesota	95.3 ± 3.9	87.1 ± 6.2	94.3 ± 4.2	79.9 ± 7.6
Mississippi	96.2 ± 4.0	83.3 ± 7.6	95.0 ± 4.3	80.3 ± 7.9
Missouri	96.8 ± 3.1	79.2 ± 7.3	90.3 ± 4.7	77.6 ± 7.5
Montana	95.9 ± 3.5	83.1 ± 7.0	93.4 ± 4.4	86.4 ± 5.7
Nebraska	97.2 ± 2.6	87.3 ± 5.4	96.0 ± 2.9	87.7 ± 5.0
Nevada	91.4 ± 4.0	81.0 ± 5.8	90.4 ± 4.2	78.8 ± 5.9
New Hampshire	97.8 ± 1.8	91.3 ± 4.2	93.1 ± 3.8	91.9 ± 4.1
New Jersey	97.5 ± 2.1	85.4 ± 5.4	93.3 ± 3.8	80.2 ± 6.1
New Mexico	95.8 ± 2.7	87.5 ± 5.1	94.6 ± 3.0	87.2 ± 5.4
New York	97.6 ± 1.6	85.4 ± 4.0	93.1 ± 2.9	80.5 ± 4.5
North Carolina	96.5 ± 3.5	86.9 ± 5.9	94.3 ± 4.1	89.3 ± 5.4
North Dakota	96.2 ± 3.1	81.8 ± 6.2	94.9 ± 3.3	80.8 ± 6.3
Ohio	95.3 ± 3.1	85.1 ± 6.0	95.6 ± 2.9	81.4 ± 6.6
Oklahoma	93.6 ± 4.7	80.4 ± 7.2	92.0 ± 5.4	84.0 ± 6.6
Oregon	91.8 ± 4.6	80.7 ± 6.8	85.1 ± 6.0	76.4 ± 7.3
Pennsylvania	94.8 ± 2.4	87.0 ± 4.2	92.0 ± 3.3	86.7 ± 4.1
Rhode Island	98.4 ± 2.0	88.8 ± 5.5	94.6 ± 3.7	89.5 ± 5.5
South Carolina	94.0 ± 4.3	85.1 ± 6.3	90.8 ± 5.3	81.8 ± 7.1

(*Continued*)

Table 1 (*Continued*)

		19–35 months[50]		
State	DTaP 3rd dose (%)	DTaP 4th dose (%)	MMR 1st dose (%)	Hib full series (%)
South Dakota	98.5 ± 2.1	87.8 ± 6.5	94.1 ± 4.2	89.0 ± 5.9
Tennessee	96.6 ± 2.4	80.7 ± 7.2	95.8 ± 2.4	80.5 ± 7.1
Texas	93.1 ± 2.9	78.2 ± 4.9	90.4 ± 3.2	76.2 ± 4.9
Utah	90.7 ± 4.9	81.9 ± 6.5	85.3 ± 6.4	78.8 ± 6.9
Vermont	96.1 ± 2.8	86.1 ± 5.4	93.2 ± 3.4	86.9 ± 5.5
Virginia	91.5 ± 5.8	87.2 ± 6.7	91.5 ± 5.1	87.5 ± 6.3
Washington	93.0 ± 4.8	81.6 ± 6.7	86.3 ± 6.2	75.6 ± 7.5
West Virginia	92.1 ± 5.0	77.2 ± 7.2	88.9 ± 5.4	78.4 ± 7.0
Wisconsin	94.9 ± 3.4	84.4 ± 5.8	93.2 ± 4.2	80.4 ± 6.7
Wyoming	93.1 ± 4.7	72.8 ± 8.7	90.4 ± 5.0	75.1 ± 8.2

			Kindergarten[19]	
State	Varicella (%)	Pneumococcal full series (%)	MMR* (%)	DTaP* (%)
US National	91.0 ± 0.9	82.9 ± 1.3	94.7**	95**
Alabama	92.1 ± 5.6	84.3 ± 7.3	≥ 93.5	≥ 93.5
Alaska	88.4 ± 4.7	79.8 ± 6.3	92.7	92.7
Arizona	84.6 ± 6.2	79.8 ± 6.7	94.2	94.3
Arkansas	91.1 ± 4.5	78.9 ± 7.0	88.4	85.6
California	90.3 ± 4.8	84.1 ± 6.1	92.6	92.4
Colorado	87.9 ± 5.1	84.8 ± 5.3	86.9	84.3
Connecticut	93.1 ± 4.5	84.2 ± 6.6	97	97
Delaware	90.2 ± 4.9	85.9 ± 5.8	97.8	97.7
Dist. of Columbia	92.4 ± 4.3	84.3 ± 6.3	90.4	90.2
Florida	92.4 ± 4.8	81.6 ± 8.0	≥ 93.3	≥ 93.3
Georgia	94.5 ± 3.8	81.3 ± 7.2	≥ 94.0	≥ 94.0
Hawaii	90.0 ± 4.4	86.3 ± 4.8	NA	NA
Idaho	90.0 ± 5.0	83.6 ± 6.2	89.5	89.4
Illinois	92.8 ± 2.6	80.9 ± 4.9	94.7	94.9
Indiana	89.7 ± 4.8	80.1 ± 6.2	89.3	92.7
Iowa	86.4 ± 6.2	84.2 ± 6.6	≥ 91.9	≥ 91.9
Kansas	95.0 ± 3.3	85.9 ± 6.2	89.2	89.6
Kentucky	92.4 ± 4.4	84.5 ± 6.8	92.7	94.4
Louisiana	91.4 ± 4.1	83.4 ± 5.3	96.8	98.3
Maine	94.5 ± 2.8	91.4 ± 3.9	92.1	95.4
Maryland	94.8 ± 3.7	87.5 ± 6.2	99.1	99.6
Massachusetts	93.6 ± 3.9	88.6 ± 5.3	94.7	92.9
Michigan	85.3 ± 6.7	74.4 ± 8.1	94.3	95.1
Minnesota	91.2 ± 5.2	86.3 ± 6.8	93.5	93.7
Mississippi	92.0 ± 6.0	82.8 ± 7.4	≥ 99.2	≥ 99.2
Missouri	89.8 ± 4.7	82.6 ± 6.4	95.8	96
Montana	90.9 ± 4.8	82.4 ± 6.6	94.6	94.6

Table 1 (*Continued*)

			Kindergarten[19]	
State	Varicella (%)	Pneumococcal full series (%)	MMR* (%)	DTaP* (%)
Nebraska	95.1 ± 3.2	90.2 ± 4.5	96	96.4
Nevada	89.7 ± 4.3	78.8 ± 5.8	94	93.2
New Hampshire	94.5 ± 2.9	90.6 ± 4.5	≥ 91.4	≥ 91.4
New Jersey	92.1 ± 4.0	84.5 ± 5.8	≥ 92.3	≥ 92.3
New Mexico	92.4 ± 4.0	86.3 ± 5.6	97.7	96.4
New York	91.7 ± 3.2	84.9 ± 3.9	98.2	97.5
North Carolina	94.9 ± 3.9	87.2 ± 6.1	98.5	98.4
North Dakota	92.2 ± 4.1	84.3 ± 5.9	89.8	89.6
Ohio	92.9 ± 3.6	83.3 ± 6.4	91.9	92.2
Oklahoma	92.2 ± 5.1	83.4 ± 6.6	90.3	90
Oregon	83.3 ± 6.2	77.4 ± 7.2	94.1	93.8
Pennsylvania	92.8 ± 3.1	87.5 ± 3.9	91.7	NReg
Rhode Island	93.9 ± 4.0	88.9 ± 5.3	95.7	96.1
South Carolina	91.5 ± 5.0	81.6 ± 7.2	96.5	97.2
South Dakota	92.6 ± 4.4	87.2 ± 6.8	97.1	97.2
Tennessee	92.4 ± 4.0	85.5 ± 6.1	≥ 95.1	≥ 95.1
Texas	89.9 ± 3.3	78.6 ± 4.7	97.4	97.2
Utah	86.3 ± 6.0	80.0 ± 6.9	94	93.8
Vermont	87.0 ± 4.6	86.1 ± 5.3	92.7	93.2
Virginia	92.2 ± 4.7	83.2 ± 7.6	93.4	97.4
Washington	86.7 ± 5.8	79.5 ± 6.9	89.4	90.7
West Virginia	87.1 ± 5.5	77.7 ± 7.0	97.6	97.6
Wisconsin	91.7 ± 4.1	86.4 ± 5.2	91.6	96.5
Wyoming	86.4 ± 6.3	80.3 ± 7.2	96.8	96.7

Abbreviations: DTaP, diphtheria, tetanus and pertussis; Hib, haemophilus influenzae type b; MMR, measles-mumps-rubella; NA, not available; NReg, no registry.
*Kindergartners were considered up to date if they received all doses required for school entry in their jurisdiction.
**National Median.

in DTaP, with Ecuador (83%), Panama (80%), Venezuela (78%), Guatemala (73%), and Haiti (48%) reporting the lowest rates.

In the European region (►**Table 2**), countries reporting DTaP (three doses) rates below 85% were: Austria (83%), San Marino (80%) and Ukraine (76%). Countries with MCV (two doses) rates below 85% were: Denmark (84%), Greece (83%), San Marino (76%), France (74%), Austria (64%) and Ukraine (54%). Countries reporting Hib (three doses) below 85% were: Austria (83%), Bulgaria (83%), Ukraine (83%), San Marino (79%), Bosnia and Herzegovina (79%), Russian Federation (31%) and Belarus (20%).

Regional vaccination rate data from the Eastern Mediterranean, Africa, Southeast Asia and West Pacific regions are also summarized in ►**Table 2**. Individual country vaccination rates data can be found on the WHO website.[11]

Global and U.S. Reported Disease Incidence

Global VPD incidence data represent official figures reported to WHO/UNICEF through the Joint Reporting Form for 2014, and was last updated in January of 2016. WHO/UNICEF region incidence data are summarized in ►**Table 3** and the U.S. incidence data for 2005-2014, 2000 and 1995 are displayed in ►**Table 4**. WHO/UNICEF reports that there were 7,324 reported cases of diphtheria in 2014, worldwide; this number increased significantly from 2013. According to the most recent data, there have been only two cases (2012, 2014) of diphtheria in the U.S. over the past 10 years. Diphtheria cases appear to be heavily concentrated in India (6094 cases) and Nepal (1079).

In 2014, there were 267,582 reported cases of measles worldwide, and 667 cases in the U.S. The reported cases of measles were highest in Africa and Asia, with the greatest

Table 2 World Health Organization regional average estimated vaccination coverage for 2014[51]

		Vaccine	
WHO Region	**DTaP 3rd dose (%)**	**MCV 2nd dose (%)**	**Hib 3rd dose (%)**
African	77	11	77
Americas	90	51	90
Eastern Mediterranean	82	66	72
European	95	84	85
South East Asia	84	59	30
Western Pacific	96	93	21
Global	86	56	56

Abbreviations: DTP, diphtheria, tetanus and pertussis; Hib, haemophilus influenzae type b; MCV, meningococcal vaccine.

Table 3 World Health Organization 2014 regional vaccine-preventable disease incidence data[34]

	Disease			
WHO Region	**Diphtheria**	**Measles**	**Mumps**	**Rubella**
African	1	73914	7	7402
Americas	9	1966	15643	10
Eastern Mediterranean	40	18080	9608	2945
European	35	14176	10807	653
South East Asia	7217	28403	34623	9263
Western Pacific	22	131043	234473	12814
Global	7324	267582	305161	33087

Table 4 Annual US national vaccine reportable disease incidence from the CDC's Summary of Notifiable Diseases reports

	Vaccine-Preventable Diseases Incidence				
Year	**Diphtheria**	**Measles**	**Mumps**	**Rubella**	**Haemophilus Type B***
2014[8]	1	667	574	2	40
2013[8]	0	187	584	9	31
2012[8]	1	55	229	9	30
2011[8]	0	212	370	4	14
2010[8]	0	63	2612	5	23
2009[52]	0	71	1991	3	38
2008[53]	0	140	454	16	30
2007[54]	0	43	800	11	22
2006[55]	0	55	6584	11	29
2005[56]	0	66	314	11	9
2000[57]	1	86	338	176	NA**
1995[58]	0	309	906	128	NA**

Abbreviation: NA, not available.
* The National Notifiable Diseases Surveillance System (NNDSS) only requires Haemophilus serotype reporting in those $<$ 5 years of age
** Serotype reporting not required in 2000 or 1995

Table 5 Estimated percentage of children enrolled in kindergarten in the US with medical and nonmedical vaccination exemptions by state for the 2014–15 school year[19]

State	Kindergarten Exemption Rates	
	Medical (%)	Nonmedical (%)
US National Median	0.2	1.5
Alabama	0.1	0.7
Alaska	1.3	4.5
Arizona	0.1	4.6
Arkansas	< 0.1	1.2
California	0.2	2.5
Colorado	< 0.1	5.4
Connecticut	0.3	1.6
Delaware	0.4	0.9
Dist. of Columbia	0.6	0.5
Florida	0.3	1.8
Georgia	0.1	2.0
Hawaii	< 0.1	3.3
Idaho	0.3	6.2
Illinois	NA	NA
Indiana	0.5	0.8
Iowa	0.3	1.4
Kansas	0.3	1.1
Kentucky	0.2	0.7
Louisiana	0.1	0.6
Maine	0.5	3.9
Maryland	0.4	0.8
Massachusetts	0.3	1.1
Michigan	0.3	5.0
Minnesota	NA	NA
Mississippi	< 0.1	NA
Missouri	NA	NA
Montana	0.3	3.6
Nebraska	0.6	1.1
Nevada	0.3	1.1
New Hampshire	0.2	2.7
New Jersey	0.2	1.6
New Mexico	0.1	1.2
New York	0.1	0.7
North Carolina	0.1	0.9
North Dakota	0.3	2.4
Ohio	0.3	1.8
Oklahoma	0.1	1.4
Oregon	0.2	5.8
Pennsylvania	0.3	1.8
Rhode Island	0.2	0.9
South Carolina	0.1	1.0
South Dakota	0.2	1.5
Tennessee	0.2	0.9
Texas	NA	1.3
Utah	0.2	4.1
Vermont	0.2	5.9
Virginia	0.3	0.8
Washington	1.2	3.5
West Virginia	0.2	NA
Wisconsin	0.4	4.9
Wyoming	NA	NA

Abbreviation: NA, not available.

number of cases occurring in the Philippines (58,848), China (52,628), the Democratic Republic of the Congo (33,711), India (24,977), Vietnam (15,033), Ethiopia (12,739), Angola (11,699) and Somalia (10,229). There were 21 countries that had over 1,000 reported cases.

Mumps cases worldwide in 2014 were noted to be 305,161, with 574 occurring in the U.S. The greatest incidence was reported in China (187,500), Japan (46,340), Nepal (34,034), Egypt (7,626), Colombia (7,368), Mexico (4,143) and the United Kingdom (2,958).

Worldwide, there were 33,087 reported cases of rubella, and two cases in the U.S. The countries with the highest reported cases were China (11,793), India (4,870) and Indonesia (3,267).

Specific country-level reported disease incidence data can be found on the WHO website.[12]

Discussion

The recent outbreaks of measles in California, and of mumps at numerous college campuses in 2015 serve as a reminder that even countries with relatively high vaccination rates remain at risk for future outbreaks. Despite the elimination of endemic measles from the U.S. in 2000,[13] 2014 saw the highest levels of measles cases over the past two decades. While this incidence increase has several likely contributing factors, it has brought an alarming trend of vaccine avoidance and exemption to the national spotlight.

Parental concerns about vaccine safety have increased over the past 15 years, and more parents are choosing to seek alternative vaccination plans or forgo vaccination altogether.[14] All 50 states have a set of vaccination requirements that children must meet before enrollment in school. Because laws regarding vaccination are determined at a state level, regulations differ from state to state. All states allow for medical exemptions when vaccinations are medically contraindicated and all but three states, Mississippi, West Virginia and California, allow some form of NME.[15,16] As of October of 2016, 47 states allow for a religious exemption, while only 18

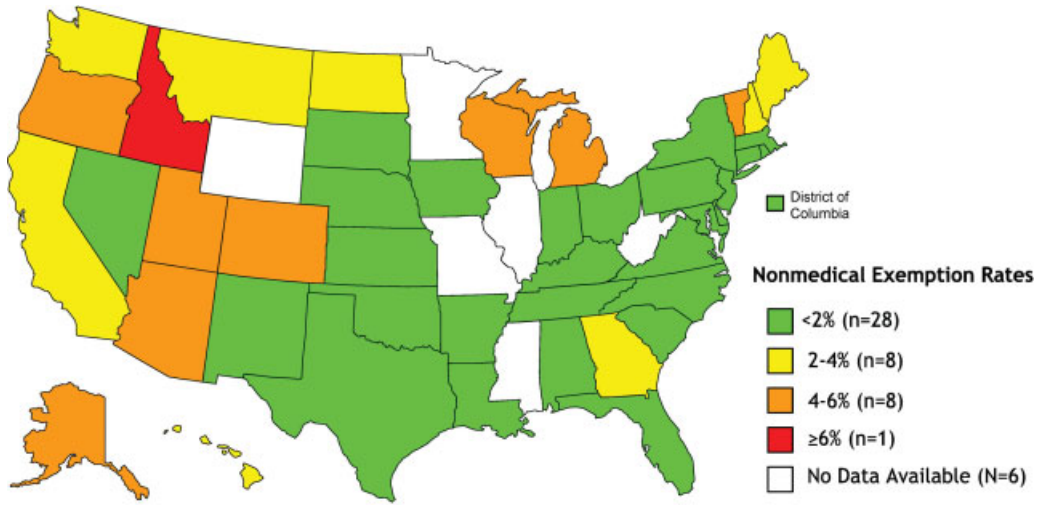

Fig. 1 Estimated percentage of children enrolled in kindergarten in each state that obtained a nonmedical exemption from receiving one or more vaccines in the United States for the 2014–2015 school year.

allow for a philosophical exemption.[17] An increasing amount of literature has been published in recent years in an attempt to quantify and understand trends in NMEs. On a national level, NMEs have shown a general increase over the last decade, with states such as Arkansas, California and Oregon tripling their NME rate between 2005 and 2013.[18] Kindergarten vaccine exemption rates are compiled yearly using CDC data and are summarized in ►**Table 5** and presented in ►**Fig. 1**. The data show that while the national median NME rate is only 1.7, states such as Idaho, Vermont, Oregon and Colorado have NME rates of over 5.0%.[19] This regional disparity is backed by several sources that identify the clustering of exemptions across state and even county lines.[20–22] When communities of any size experience higher clusters of NMEs and lower vaccination rates, herd immunity can be compromised and the risk of VPD outbreaks can increase. Herd immunity relies on the reduction of susceptible persons in the population and works to reduce the efficiency with which a microbe is transmitted from one person to another. When there are enough immune individuals to stop effective transmission, outbreaks no longer occur. Several studies have shown a strong association between small regional clusters of NMEs and higher risks of pertussis and measles outbreaks.[23,24] Increased attention to the effects of NMEs on preventable disease incidence is necessary to better explain these changes and their effects on public health.

A subset of the literature attempts to explain the increasing trend in NMEs. Traditionally, under-vaccination was associated with lower access to health care and it was more prevalent among the impoverished, inner city ethnic and racial minorities, and those with a lower level of education.[25,26] However, increasingly, under-vaccination is resulting from higher NME rates reported among white, highly educated and wealthier populations.[20,27,28] The most prevalent concerns voiced by parents are associated with vaccine safety and common themes include the potential for adverse reactions, developmental problems, dangerous vaccine ingredients and the need for too many shots at one time under the national guidelines.[18,29,30] Other sources have mentioned an inverse relationship between the difficulty of receiving an exemption and NME levels,[15] and an additional analysis shows a greater increase in NMEs in states where both religious and philosophical exemptions are allowed.[10] It is clear that legislation can have an impact on vaccination rates.

Families who choose to not vaccinate or intentionally under-vaccinate their children rely on herd immunity to protect their children from VPDs. For herd immunity to be established, there must be enough protected individuals in a population to exceed the herd immunity threshold, which is defined as the fraction of a population that must be immune to confer herd immunity on those not protected from a disease.

Table 6 Estimated herd immunity thresholds and critical vaccination coverage using generally accepted reproductive numbers for common vaccine-preventable diseases

Vaccine-Preventable Disease	R_0 *[59,60]	Herd Immunity Threshold (%)[31]	Critical Vaccination Coverage** (%)[31]
Diphtheria	4 to 5	75–80	79–84
Measles	11 to 18	91–94	96–99
Mumps	7 to 14	86–93	90 to 98
Rubella	6 to 14	83–94	87 to 99

*R_0 values indicate the number of individuals that can be directly infected by one infectious case. Herd immunity thresholds are a function of this value.
**herd immunity thresholds are adjusted to account for vaccine effectiveness.

An important objective of the public health departments is to meet vaccination rate goals that are likely to ensure herd immunity. Although critical vaccination coverage values have been identified for common VPDs, it is important to note that the heterogeneity of populations, vaccine effectiveness and virus strain reproductive numbers (R_0) cause significant variation in the critical vaccination coverage values over time and in different populations.[31] Ranges of some of the more accepted herd immunity thresholds and critical vaccination rates can be seen in ►**Table 6**. Based on the CDC's estimated vaccination rate data for 19–35-month-olds, there are currently 19 states that are right at or below the lower bound of estimated herd immunity threshold for measles (91%). There are also nine states that are at or below estimated herd immunity thresholds based on the CDC's kindergarten data. While this type of analysis is useful in determining trends, both datasets are estimates based on telephone and immunization program surveys and reporting/sampling bias could be a factor in overestimating rates.

In most cases, the sources of U.S. outbreaks have been linked to international travel and immigration. This is especially true in the case of measles. A recent MMWR report looking at measles cases in the first half of 2014 indicated that 97% of 288 cases were associated with importation from 18 countries.[32] Forty-five of these cases were reported to be direct importation and half were travelers returning from the Philippines, where a large outbreak was occurring. Of those who became infected, 69% were unvaccinated and 20% had an unknown vaccination status. The remaining importations were spread relatively evenly amongst the WHO world regions. A similar analysis was performed on the 911 confirmed cases of measles in the U.S. between 2001 and 2011.[33] A total of 801 (88%) of these cases were determined to be import-associated from a total of 57 countries. China, Japan, India, Italy, the Philippines and the U.K. were all shown to be associated with 20 or more of these imported cases. Unsurprisingly, the Philippines, China and India were countries reporting a high incidence of measles in 2014.[34]

In an increasingly interconnected world, the chances for exposure to infectious diseases grow and vaccination rates in developed and developing countries directly affect each other. An estimated 1.9 million U.S. children travel overseas each year, often to countries where these diseases are still endemic.[35] It is highly recommended that parents consult their physicians about vaccination recommendations before taking children abroad. In some cases, it is even recommended that children receive vaccines ahead of schedule to protect them from exposure abroad.[36]

Disease Presentation and Clinical Guidelines

Many of these commonly vaccinated diseases have not been seen in the U.S. in large numbers and, therefore, are unlikely to have been encountered during physician training or practice. With the possibility of encountering these diseases both at home and abroad and the likelihood of head and neck presentations, the following review of clinical presentations and treatment guidelines will serve as a guide to VPDs that may present to the otolaryngologist.

Measles[37,38]

Measles is an acute viral infection characterized by the prodrome of fever (as high as 105), malaise, cough, coryza and conjunctivitis followed by a maculopapular rash. The rash starts $\sim$ 14 days after exposure, starts on the head and spreads to the trunk and extremities. Measles can result in complications such as pneumonia, encephalitis and death, with a death rate of 2–3/1000.

The average incubation period is 14 days with a range of 7–21 days. Patients are considered infectious from 4 days before to 4 days after the onset of the rash. Laboratory testing is required for all suspected cases of measles and includes measles-specific immunoglobulin M (IgM) antibodies and measles ribonucleic acid (RNA) detection by real-time polymerase chain reaction (RT-PCR). These samples are obtained via a serum sample and throat swab. Virus isolation and RNA detection are much more likely to be successful early in the infection (first 3 days of rash) but may be successfully isolated up to 10 days after the start of the rash.

Patients should be isolated for 4 days post rash onset. Airborne precautions should be instituted in a hospital setting. Measles, mumps and rubella (MMR) vaccine, if administered within 72 hours of initial measles exposure, and immunoglobulin (IG), if administered within 6 days of exposure, may provide some protection or modify the clinical course of the disease. Individuals who are at high risk for severe disease and complications from measles (infants aged $<$ 12 months, pregnant women without evidence of measles immunity and severely immunocompromised persons) should receive IG.

Children who are malnourished are at a much higher risk of severe complications. In the developing world, this population has a death rate as high as 10%. The WHO recommends two doses of vitamin A (separated by 24 hours) to infected children in the developing world. This has been shown to not only reduce blindness but it can also cut the death rate by 50%.

Mumps[39,40]

Mumps is an acute viral illness caused by a paramyxovirus. The classic symptom of mumps is parotitis lasting at least 2 days and it may persist for longer than 10 days. The parotitis typically develops 16 to 18 days after exposure and is present in 31–65% of cases. Non-specific symptoms may precede the parotitis by a few days, including low-grade fever, myalgia, anorexia, malaise and headache. Mumps may also present as a nonspecific respiratory infection or subclinical infection. Fifty percent of individuals with mumps have cerebrospinal fluid pleocytosis, but fewer than 10% have symptoms of central nervous system infection.

In the pre-vaccine era, unilateral deafness caused by mumps occurred in 1 in 20,000 infected individuals and orcheitis presented in 11.6–66% of infected post-pubertal males. The virus is known to cross the placenta but has not been associated with any known congenital defects.

Mumps viral count is highest around the time of onset of parotitis and decreases rapidly after that. Most transmission likely occurs before and within 5 days of parotitis onset.

If mumps is suspected, laboratory tests should be performed. Acute mumps infection can be detected with serum levels of IgM (enzyme immunoassay is preferred over immunofluorescence assay), a significant rise in immunoglobulin G (IgG) titers, positive mumps viral culture or detection of the virus by RT-PCR. Parotid duct swab yields the best sample, especially when the gland area is massaged for 30 seconds prior to collection. Samples should be collected as close to the onset of parotitis as possible.

There are currently no medications that have been shown to treat the mumps virus. Treatment is focused on relieving symptoms and preventing its spread. This includes pain control, hydration, warm or cold compresses to the parotid region, soft diet and isolation for 5 days.

Rubella[41,42]

Rubella is caused by the Rubivirus and is characterized by a generalized erythematous maculopapular rash. Children usually develop no constitutional symptoms but adults may experience headaches, malaise, mild coryza and conjunctivitis. Postauricular, occipital and posterior cervical lymphadenopathy is characteristic and precedes the rash by 5–10 days. The transient polyarthralgia is rarely present in children but is more common in adolescents and adults. Encephalitis and thrombocytopenia are rare complications. Congenital rubella has much more common and severe complications including miscarriage, fetal death and congenital anomalies. The classical presentation of congenital rubella includes ophthalmologic issues, cardiac defects, sensorineural hearing loss, and neurological issues. Mild forms of the disease may be associated with few obvious abnormalities but more outward presentations include purpuric skin lesions (blueberry muffin appearance), thrombocytopenia, hepatosplenomegaly and radiolucent bones. The severity of these anomalies is often associated with the gestational age at onset of infection, with a much higher rate of a clinically significant effect in infants infected in the first 4 weeks of gestation.

Maximal contamination period is from a few days before to 7 days after the presentation of the rash. A small number of infants with congenital rubella may shed the virus for up to a year in their nasopharyngeal secretions and urine. The incubation period for postnatal infection is from 14 to 23 days.

The clinical diagnosis of rubella is unreliable; therefore, cases must be confirmed by laboratory testing. The rubella virus can be detected from nasal, throat, blood, urine and cerebrospinal fluid (CSF) specimens. Throat swabs and urine sample collected for RT-PCR are recommended. Cerebrospinal fluid testing should be reserved for patient suspected to have rubella encephalitis. Enzyme immunoassays (EIAs) can be used to detect IgG and IgM antibodies. This test is sensitive and relatively easy to perform. Because this disease is rare in the U.S., a high proportion of IgM-positive tests will be false positives.

Patients with rubella should be isolated for 7 days after rash onset. All persons who are at risk and cannot provide evidence of vaccination should be revaccinated. There is no effective antiviral treatment for rubella. Immunoglobulins are sometimes used in pregnant women who have been exposed.

Diphtheria[43,44]

Diphtheria is caused by the toxigenic strains of gram-positive *Corynebacterium diptheriae*. Diphtheria typically presents with a sore throat, difficulty swallowing, malaise and low-grade fever. The hallmark of respiratory diphtheria is the gray-whitish pseudomembrane over the tonsils, pharynx or larynx that bleeds when removed. Swelling of the cervical lymph nodes gives rise to a "bull-neck" appearance. As the pseudomembrane extends from the pharynx to the larynx, it may cause obstruction of the airway and if left untreated may be fatal with a case fatality rate of 10%. Diphtheria toxin can also cause systemic complications with damage to the myocardium, nervous system and kidneys. Cutaneous diphtheria is usually mild, typically consisting of non-distinctive sores or shallow ulcers and it rarely causes toxic effects (1–2%).

Diagnostic tests used to confirm diphtheria include isolation of the bacteria in culture and toxigenicity testing. There are no other commercially available tests but the CDC can perform polymerase chain reaction (PCR) tests on clinical specimens. Clinical specimens for culture should be taken from the nose or nasopharynx and throat from all persons with suspected cases and those in close contact with them. Material should be taken from the pseudomembrane or the area just below the pseudomembrane. Toxigenicity testing using the Elek test should be done to determine whether the organisms produce diphtheria toxin.

The mainstay of treatment is prompt administration of diphtheria antitoxin in suspected cases, even before laboratory confirmation. The amount of antitoxin used depends on the extent of the disease. To obtain the antitoxin, the clinician should contact the CDC Emergency Operations Center (770–488–7100). In addition, the patient should receive antibiotics with erythromycin or penicillin administered as a 14-day course. Droplet precautions are recommended until two nasal and pharyngeal cultures are negative.

Haemophilus influenzae Infection[45,46]

Haemophilus Influenzae (*H. influenzae*) is an invasive disease caused by the gram-negative coccobacillus bacterium *haemophilus influenzae*. The bacteria may either be encapsulated (types a-f) or non-encapsulated (non-typeable). Invasive *H. influenzae* may cause meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis and cellulitis. Before effective vaccination, Hib was the cause of more than 95% of all invasive *haemophilus* infections. Meningitis occurred in more than two thirds of the cases of Hib disease with resulting hearing impairment or severe permanent neurological sequelae, paralysis in 15–30% of survivors and 4% of all cases were fatal.

Gram stain of infected fluid may demonstrate small gram-negative coccobacilli suggestive of invasive *haemophilus* disease and positive culture establishes the diagnosis. All isolates of *H. influenzae* should be serotyped. Antigen

testing of body fluid may be performed in addition to cultures in those patients who have received antimicrobial therapy.

Treatment includes either a third-generation cephalosporin (cefotaxime or ceftriaxone) or chloramphenicol in combination with ampicillin. Ampicillin-resistant strains of Hib are now common, so Ampicillin should not be used as a monotherapy. Patients showing signs of airway obstruction should be given supplemental oxygen and taken to the operating room (OR) for management of the airway according to the local hospital's epiglottitis protocol.

Final Comments

The recent rise in NMEs in school-age children has led to a higher risk of VPD occurrence. This trend coincides with an increase in the severity and risk of outbreaks within the U.S. Increasing global mobility allows for ease of disease transmission and limits the extent to which outbreaks can be contained. Most otolaryngologists have not cared for patients with these diseases and this paper serves as a review of the clinical presentations and treatment guidelines for these VPDs.

Due to the increased chance of exposure to patients with VPDs and their presentation in the head and neck, it is recommended that otolaryngologists familiarize themselves with these disease processes, their treatment, and the agencies involved in reporting occurrences. Each state and country maintains its own set of reportable diseases and mandates reporting to the respective department of health. Physicians should familiarize themselves with reportable diseases in their state of practice and identify the forms necessary for notification. The VPDs discussed in this article are included on most state's reportable disease lists.

The misconception is often that these diseases only present in young unvaccinated children. The recent 2015 measles outbreak in California showed that 40% of the intentionally unvaccinated patients who contracted measles were adults.[47] Similarly, recent outbreaks of mumps in college campuses are primarily affecting students in their late teens and early twenties. However, certain VPDs are more likely to present in early childhood. Children under the age of 18 comprise 30–35% of the patient population of general otolaryngologists and most children receiving otolaryngologic care in the US receive care from a general otolaryngologist.[48]

While the likelihood that an individual otolaryngologist will see one of these VPDs is small, as global mobility increases and social changes affect the number of patients choosing not to vaccinate, exposure may increase with time. With this increased likelihood of exposure, otolaryngologists need to be aware of the variable presentations of these diseases and include them in their differential diagnosis where appropriate.

While the majority of work otolaryngologists perform is in the diagnosis and management of diseases of the head and neck, they do play a role in disease prevention by recommending vaccinations. Otolaryngologists often recommend immunization for influenza to prevent recurrent ear and sinus infections in susceptible populations. They also recommend pneumococcal vaccinations to prevent increased risk of meningitis in patients undergoing cochlear implantation. More recently, otolaryngologists are playing a larger role in recommending HPV vaccines to prevent oropharyngeal cancer. Data consistently suggests that the more patients and families are encouraged to vaccinate, the more likely they are to actually undergo vaccinations.[49] As part of the medical community, otolaryngologists who treat children and adults should encourage routine vaccinations.

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Conflict of Interest
None

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