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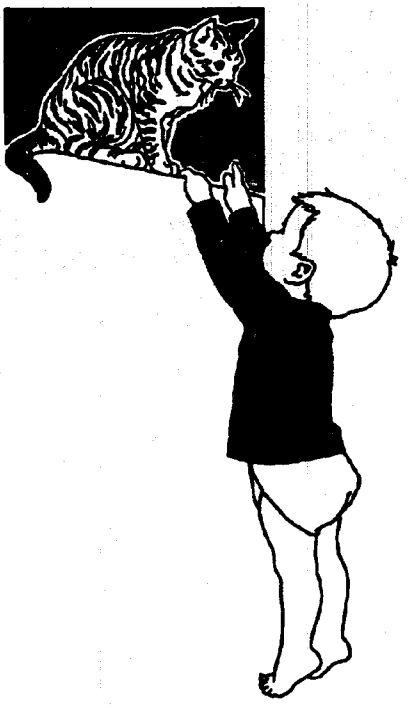
Rubella Prevention

Excerpts of Recommendations of the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service*

Before licensure of rubella vaccine, rubella was a common childhood rash disease. Currently, it can be often overlooked or misdiagnosed because its signs and symptoms vary. The most common manifestations—postauricular and suboccipital lymphadenopathy, arthralgia, transient erythematous and sometimes pruritic rash, and low fever—may not be recognized as rubella. Similar exanthematous illnesses are caused by adenoviruses, enteroviruses, and other common respiratory viruses. Moreover, up to 30% of infections are subclinical and many are unrecognized. Transient polyarthralgia and polyarthritis sometimes accompany or follow rubella.

By far the most important consequences of rubella are the miscarriages, stillbirths, fetal anomalies, and therapeutic abortions that result from rubella infection in early pregnancy, especially in the first trimester. Preventing fetal infection and consequent congenital rubella syndrome (CRS) is the objective of rubella immunization programs.

The most commonly described anomalies associated with CRS** are auditory (sensorineural deafness), ophthalmic (cataracts, microphthalmia, glaucoma, chorioretinitis), cardiac (patent ductus arteriosus, pulmonary artery stenosis, atrial or ventricular septal defects), and neurologic (microcephaly, meningoencephalitis, mental retardation). In addition, infants with CRS frequently are retarded in growth and have radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, and purpuric skin lesions (blueberry-muffin appearance). Moderate and severe cases of CRS are readily recognizable at birth; mild cases (e.g., those with only slight cardiac involvement or deafness) may not be detected for months or years after birth or not at all. Inapparent maternal rubella infection can result in congenital malformations.



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Vaccine Use

The live rubella virus vaccine currently distributed in the United States is prepared in human diploid cell culture. The vaccine is produced in monovalent form (rubella only) and in combinations: measles-rubella (MR), rubella-mumps, and measles-mumps-rubella (MMR) vaccines.

In clinical trials, 95% of susceptible persons who received a single dose of rubella vaccine when they were 12 months of age developed antibody. Clinical efficacy and challenge studies have shown that 90% of vaccinees have protection against both clinical rubella and viremia for at least 15 years. Available follow-up studies indicate that vaccine-induced protection is long-term, probably lifelong; therefore, a history of vaccination can be considered presumptive evidence of immunity.

Some vaccinees intermittently shed small amounts of virus from the pharynx 7-28 days after vaccination. However, studies of 1,200 susceptible household contacts and experience gained over 20 years of vaccine use failed to identify transmission of vaccine virus. These findings indicate that vaccinating susceptible children whose mothers or other household contacts are pregnant does not pre-

sent a risk. Rather, vaccination of such children provides protection for these pregnant women.

Persons can be considered immune to rubella only if they have documentation of a) laboratory evidence of rubella immunity or b) adequate immunization with at least one dose of rubella vaccine on or after the first birthday. Many persons will receive two doses of rubella vaccine as a result of the new two-dose schedule for MMR vaccination, which is recommended to improve control of measles. Clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status.

Persons 12 months of age should be vaccinated, unless they are immune. All children, adolescents, and adults—particularly females—are considered susceptible and should be vaccinated if there are no contraindications. Those who should be vaccinated include persons who may be immune to rubella but who lack adequate documentation of immunity. All vaccinations should be documented in the patient's permanent medical record.

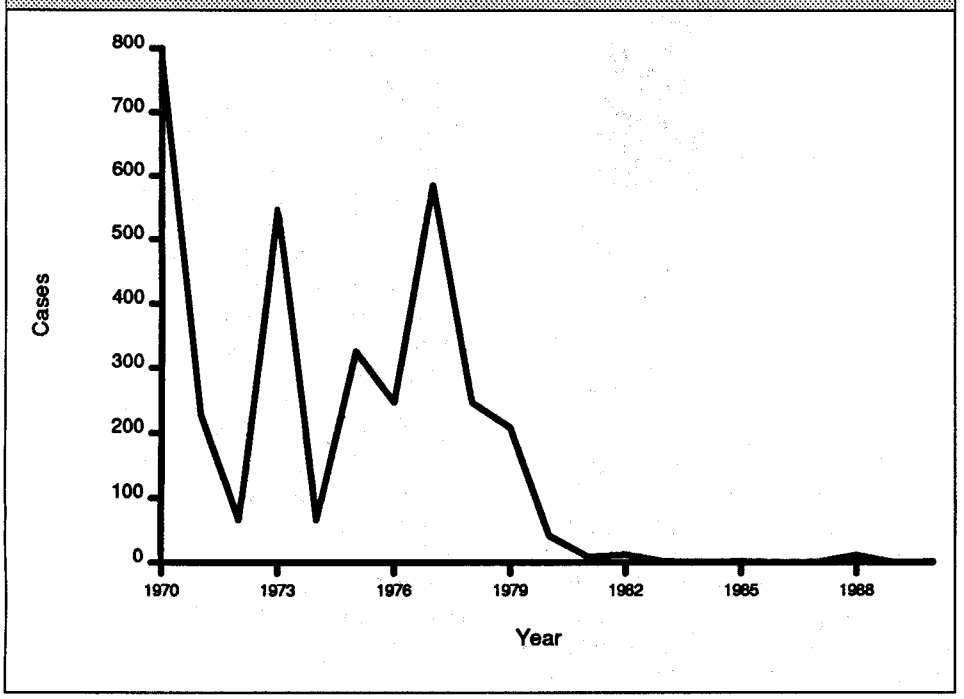
Vaccinating susceptible individuals both protects them against rubella and prevents their spreading the virus. Vaccinating susceptible postpubertal females confers individual protection against rubella-induced fetal injury. Vaccinating adolescents or adults in high-risk population groups, such as those in colleges, places of employment, or military bases, protects them against rubella and reduces the chance of epidemics.

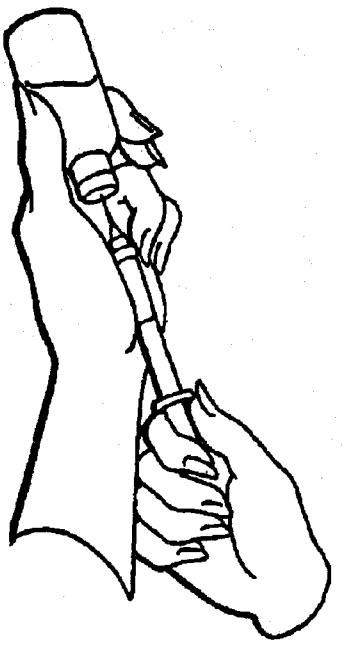
The **dose** of 0.5 ml of reconstituted vaccine (whether as a monovalent product or, preferably, in combination with measles and mumps antigens) should be administered subcutaneously.

Live rubella virus vaccine is recommended for all children 12 months of **age**. It should not usually be given to younger infants, because persisting maternal antibodies may interfere with seroconversion. When the rubella vaccine is part of a combination that includes the measles antigen, the combination vaccine should generally be given to children at 15 months of age to maximize measles seroconversion. A second dose of MMR is recommended at school entry, although in some localities the decision may be made to administer the second dose at older ages (e.g., entry to middle or junior high school). Initial vaccination with MMR may be given at 12 months of age to children living in areas at high risk for measles transmission among preschool-age children.

Older children who have not received rubella vaccine should be vaccinated promptly. Because a history of rubella illness is not a reliable indicator of immunity, all children should be vaccinated unless there are contraindications.

Cases of Rubella Reported in Virginia, 1970-1990.





The Immunization Practices Advisory Committee (ACIP) has weighed several factors in developing recommendations for vaccinating **women of childbearing age** against rubella. The risk of vaccine-associated defects is negligible and should not ordinarily be a reason to consider interruption of pregnancy. However, because birth defects, one-third of which are serious, are noted in 3% of all births, confusion about the etiology of birth defects may result if vaccine is administered during pregnancy.

The continuing occurrence of rubella among women of childbearing age and the lack of evidence for teratogenicity from the vaccine strongly indicate the need to continue vaccination of susceptible adolescent and adult females of childbearing age. However, because of concern about risk for the fetus, women of childbearing age should receive vaccine only if they state that they are not pregnant and are counseled not to become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against rubella, reasonable practices in a rubella immunization program include a) asking women if they are pregnant, b) excluding those who state that they are, c) explaining the concern about risk for the fetus to the others, and d) explaining the importance of not becoming pregnant during the 3 months following vaccination.

Immune globulin (IG) given after exposure to rubella will not pre-

vent infection or viremia, but it may modify or suppress symptoms and create an unwarranted sense of security. The routine use of IG for postexposure prophylaxis of rubella in early pregnancy is not recommended.

Vaccine should be administered approximately 2 weeks before or deferred for approximately 3 months after receipt of IG, because passively acquired antibodies might interfere with the response to the vaccine. However, previous administration of anti-Rho (D) IG (human) or blood products does not generally interfere with an immune response and is not a contraindication to postpartum vaccination. In this situation, persons who have received the globulin or blood products should be serologically tested 6-8 weeks after vaccination to assure that seroconversion has occurred. Obtaining laboratory evidence of seroconversion in other vaccinees is not necessary.

During **storage**, before reconstitution, rubella vaccine must be kept at a temperature of 2 C-8 C (35.6 F-46.4 F) or colder. It must also be protected from light, which may inactivate the virus. Reconstituted vaccine should be discarded if not used within 8 hours. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice.

Adverse events

Vaccinees can develop low-grade fever, rash, and lymphadenopathy after vaccination. Arthralgia and transient arthritis occur more frequently in susceptible adults than in children, and more frequently in susceptible postpubertal females than in susceptible men. Arthralgia or arthritis are rare following vaccination of children with RA 27/3 vaccine. By contrast, approximately 25% of susceptible postpubertal females develop arthralgia following RA 27/3 vaccination, and approximately 10% have been reported to have arthritis-like signs and symptoms. Rarely, transient peripheral neuritic complaints, such as paresthesia and pain in the arms and legs, have occurred.

When joint symptoms occur, or when pain and/or paresthesia not associated with joints occur, they generally begin 1-3 weeks after vaccination, persist for 1 day-3 weeks, and rarely recur. Adults with joint symptoms following rubella vaccination usually have not had to disrupt work activities.

The mechanism for joint abnormalities after vaccination is unclear. Joint destruction rarely has been reported.

Available published data indicate that only susceptible vaccinees have side effects of vaccination. There is no conclusive evidence of an increased risk of these reactions for persons who are already immune when vaccinated.

Precautions and Contraindications

Pregnant women should not be vaccinated with rubella vaccine. If a pregnant woman is vaccinated or if she becomes pregnant within 3 months after vaccination, she should be counseled about the concern for the fetus, but rubella vaccination during pregnancy should not ordinarily be a reason to consider interruption of pregnancy.

Vaccination of persons with severe **febrile illness** should be postponed until recovery. However, susceptible children with mild illnesses, such as upper respiratory infection, should be vaccinated. Considering the importance of protecting against rubella, medical personnel should use every opportunity to vaccinate susceptible individuals.

Hypersensitivity reactions rarely follow the administration of live rubella vaccine. Most of these reactions are considered minor and consist of wheal and flare or urticaria at the injection site. Live rubella vaccine is produced in human diploid cell culture. Consequently, a history of anaphylactic reactions to egg ingestion needs to be taken into consideration only if measles or mumps antigens are to be included with rubella vaccine.

Since rubella vaccine contains trace amounts of neomycin (25 ug), persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive rubella vaccine. Most often, neomycin allergy is manifested as a contact dermatitis, which is a delayed-type (cell-mediated) immune response, rather than anaphylaxis. In such individuals, the adverse reaction, if any, to neomycin in the vaccine would be an erythematous, pruritic nodule or papule at 48-96 hours. A history of contact dermatitis to neomycin is not a contraindication to receiving rubella vaccine. No preparations of live rubella vaccine contain penicillin.

Replication of vaccine viruses can be enhanced in persons with immune deficiency diseases and in persons with **immunosuppression**, as occurs with leukemia, lymphoma, generalized malignancy, or resulting from therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids. Although there is no evidence that wild rubella or rubella vaccine virus causes serious illness in immunocompromised persons, concern exists about the risk of any live virus vaccine, including rubella vaccine, for such persons. Therefore, such patients should not be given live rubella virus vaccine—except persons with symptomatic infection with human immunodeficiency virus (HIV), who can receive MMR (see below).

Patients with leukemia in remission who have not received chemotherapy for at least 3 months may be vaccinated with live virus vaccines. Short-term (2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy (e.g., nasal, skin), long-term alternate-day treatment with low to moderate doses of short-acting systemic steroids, and intraarticular, bursal, or tendon injection of corticosteroids are not immunosuppressive in their usual doses and do not contraindicate rubella vaccine administration.

The growing number of infants and preschoolers with HIV infection has directed special attention to the appropriate immunization of such children. Asymptomatic children do not need to be evaluated and tested

for HIV infection before decisions concerning vaccination are made. Asymptomatic HIV-infected persons in need of MMR should receive it. MMR should be considered for all symptomatic HIV-infected children, including children diagnosed as having acquired immunodeficiency syndrome (AIDS), because measles disease in these children can be severe. Limited data on MMR vaccination among asymptomatic and symptomatic HIV-infected children indicate that MMR has not been associated with serious or unusual adverse events, although antibody responses have been variable.

The administration of high-dose intravenous immune globulin (IGIV) to HIV-infected children at regular intervals is being studied to determine whether it will prevent a variety of infections. For those children who have received IGIV within the 3 months preceding vaccination, MMR vaccine may be ineffective.

Simultaneous Administration of Certain Live Virus Vaccines

In general, the simultaneous administration of the most widely used live and inactivated vaccines does not impair antibody responses or increase rates of adverse reactions. The administration of MMR vaccine yields results similar to that of individual measles, mumps, and rubella vaccines at different sites or at different times.

Equivalent antibody responses and no clinically important increases in the frequency of adverse events occur when diphtheria-tetanus-pertussis vaccine (DTP), *Haemophilus influenzae* b conjugate vaccine (HbCV), oral polio vaccine (OPV), or inactivated polio vaccine (IPV) are administered with MMR either simultaneously at different sites or at separate times. Routine simultaneous administration of MMR, DTP, HbCV, and OPV (or IPV) to all children 15 months who are eligible to receive these vaccines is recommended. Vaccination with MMR and HbCV at 15 months, followed by DTP and OPV (or IPV) at 18 months remains an acceptable alternative for children whose parents/caregivers are known generally to follow health-care recommendations. If the child might not be brought back for future immunizations, simultaneous administration of all vaccines (including DTP, OPV, MMR, and HbCV) appropriate to the age and previous vaccination status of the recipient is recommended.

Strategies for Eliminating CRS

The primary strategy for eliminating CRS in the United States is to interrupt rubella transmission by achieving and maintaining high immunization levels among all children. To hasten the elimination of CRS, continued effort should be directed toward vaccinating susceptible women of childbearing age. A multifaceted approach is necessary.

If it is practical and if reliable laboratory services are available, women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility (so that vaccine is given only to proven susceptible women) can be effective but is expensive. Also, two visits to the health-care provider would be necessary—one for screening and one for vaccination. Accordingly, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing—and may be preferable, particularly when costs of serology are high and follow-up of identified susceptible women for vaccination is not assured. Vaccinated women should be counseled to avoid becoming pregnant for a 3-month period following vaccination. Routine serologic screening of men is not recommended.

Routine **premarital testing** for rubella antibody identifies many susceptible women before pregnancy. Documented histories of rubella vaccination or serologic evidence of immunity should be considered acceptable proof of immunity. To ensure a significant reduction in susceptibility through premarital screening, more aggressive follow-up of women found to be susceptible is required.

Prenatal screening should be carried out on all pregnant women not known to be immune. Women who have just delivered babies should be vaccinated before discharge from the hospital, unless they are known to be immune. Although such women are unlikely to become pregnant, counseling to avoid conception for 3 months following vaccination is still necessary. It is estimated that postpartum vaccination of all women not known to be immune could have prevented approximately 40% of recent CRS cases. Breast-feeding is not a contraindication to vaccination, even though virus may be excreted in breast milk, and infants may be infected. Women attending abortion clinics should be vaccinated after termination of pregnancy.

Vaccination of susceptible women of childbearing age should be part of routine **general medical and gynecologic outpatient care**, should take place in all family-planning settings, and should become routine before discharge from a hospital for any reason, if there are no contraindications. Vaccination should be offered to adults, especially women of childbearing age, any time that contact is made with the health-care system, including when children are undergoing routine examinations or immunizations.

Medical personnel, both male and female (e.g., volunteers, trainees, nurses, physicians), who might transmit rubella to pregnant patients or other personnel, should be immune to rubella. Consideration should be given to making rubella immunity a condition for employment. All medical personnel who have patient contact and who are beginning employment should have proof of rubella immunity or prior vaccination.

Ascertainment of rubella-immune status and availability of rubella immunization should be components of **employee health-care programs** in places hiring women of childbearing age (e.g., day-care centers, schools, colleges, prisons, companies, government offices, and industrial sites).

Colleges are high-risk areas for rubella transmission because of large concentrations of susceptible persons. Proof of rubella as well as measles immunity should be required for attendance for both male and female students. All students born in or after 1957 who enter institutions of post-high-school education should have documentation of receipt of two doses of measles vaccine (preferably given as MMR) and at least one dose of rubella vaccine or other evidence of measles and rubella immunity.

Surveillance

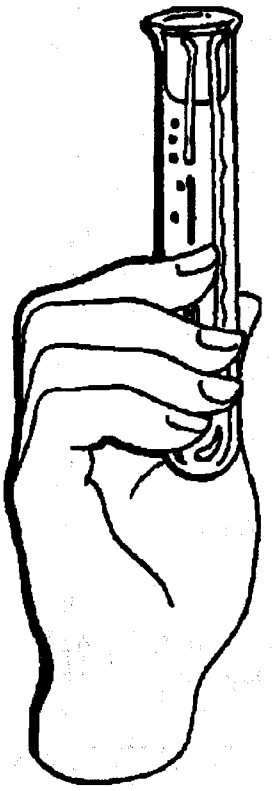
Surveillance of rubella and CRS has three purposes: a) to provide important data on program progress and long-term trends, b) to help define groups in greatest need of vaccination and in turn provide information for formulation of new strategies, and c) to evaluate vaccine efficacy, duration of vaccine-induced immunity, and other issues related to vaccine safety and efficacy.

As the rates of rubella and CRS decline in the United States, effective surveillance becomes increasingly important. Known or suspected rubella cases should be reported immediately to local health departments.

Laboratory Diagnosis

The diagnosis of **acute rubella** should be confirmed serologically. The presence of IgM antibody or a significant rise in IgG or total antibody levels is evidence of acute rubella infection. For HI assays, a fourfold rise in the titer of antibody indicates recent infection; for other types of assays, the criteria for a significant rise in antibody level vary by type of assay and by laboratory. The acute-phase serum specimen should be drawn as soon after rash onset as possible, preferably within the first 7 days. The convalescent-phase serum specimen should be drawn 10 or more days after the acute-phase serum specimen. If the acute-phase serum specimen is drawn more than 7 days after rash onset, a significant rise in antibody titer may not be detected by most commonly used tests. In this case, complement fixation (CF) testing may be especially useful, because CF antibodies appear in serum later than HI, EIA, or IFA antibodies. The acute- and convalescent-phase serum specimens should be tested simultaneously in the same laboratory.

Occasionally, significant rises may not be detected, even if the first specimen is drawn within the first 7 days after rash onset. Rubella infection may also be serologically confirmed by demonstrating rubella-specific IgM antibody. If IgM is to be determined, one serum specimen should be drawn between 1 week and 2 weeks after rash onset. Although rubella-specific IgM antibody may be detected shortly after rash onset, IgM antibody is less likely to be detected if the specimen is drawn earlier than 1 week or later than 4-5 weeks following rash onset. False-negative IgM antibody test results may sometimes occur even when the specimen is appropriately drawn. False-positive IgM test results may also occur.



In the absence of rash illness, the diagnosis of **subclinical cases** of rubella can be facilitated by obtaining the acute-phase serum specimen as soon as possible after **exposure**. The convalescent-phase specimen should then be drawn 28 or more days after exposure. If acute- and convalescent-phase paired sera provide inconclusive results, rubella-specific IgM antibody testing can be performed, but results should be interpreted cautiously. Expert consultation may be necessary to interpret the data.

Confirmation of rubella **infection in pregnant women** of unknown immune status following rash illness or exposure may be difficult. A serum specimen should be obtained as soon as possible. Unfortunately, serologic results are often nonconfirmatory. Such situations can be minimized by performing prenatal serologies routinely. In addition, health providers should request that laboratories performing prenatal screening retain such specimens until delivery so that retesting, if necessary, can be done.

Suspected cases of CRS should be managed with contact isolation (see CDC "Guidelines for Isolation Precautions in Hospitals"). While diagnostic confirmation is pending, children with suspected CRS should be cared for only by personnel known to be immune. Confirmation by attempting virus isolation can be done by using nasopharyngeal and urine specimens. Serologic confirmation can be obtained by testing cord blood for the presence of rubella-specific IgM antibodies. An alternative but less rapid serologic method is to document persistence of rubella-specific antibody in an infant with suspected CRS, age 3 months or older, at a level beyond that expected from passive transfer of maternal antibody, i.e., a rubella antibody level in the infant that does not decline at the expected rate (the equivalent of one twofold dilution in HI titer per month). However, some infected infants may lose antibody because of agammaglobulinemia or dysgammaglobulinemia.

In some infants with CRS, virus can persist and be isolated for the first year of life. CRS precautions need to be exercised through the first year of life, unless nasopharyngeal and urine cultures are negative for rubella virus.

** Excerpts from: Centers for Disease Control. Rubella prevention: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1990;39 (no. RR-15):(1-18).*

***A confirmed case has at least one defect in categories A or B and laboratory confirmation of rubella infection. A compatible case has any two complications listed in A or one from A and one from B without laboratory confirmation.*
A. Cataracts / congenital glaucoma (either or both count as one), congenital heart disease, loss of hearing, pigmentary retinopathy.
B. Purpura, splenomegaly, jaundice, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease.

Cases of Selected Notifiable Diseases, Virginia, March 1 through March 31, 1991.

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	83	5	34	9	13	22	180	155	93
Campylobacter	25	3	8	7	5	2	74	112	89
Gonorrhea~	1954	-	-	-	-	-	4216	4898	4249
Hepatitis A	21	1	12	0	1	7	47	52	59
Hepatitis B	30	0	10	6	7	7	66	60	81
Hepatitis NANB	3	0	1	1	0	1	6	9	14
Influenza	23	5	0	10	6	2	556	739	1906
Kawasaki Syndrome	5	0	2	2	0	1	10	5	5
Legionellosis	1	0	1	0	0	0	3	5	3
Lyme Disease	5	3	2	0	0	0	7	7	2
Measles	14	0	6	0	6	2	14	19	12
Meningitis, Aseptic	23	2	8	3	2	8	50	50	39
Meningitis, Bacterial*	11	2	2	3	2	2	38	43	52
Meningococcal Infections	4	0	0	1	2	1	11	16	22
Mumps	9	0	4	2	2	1	19	19	14
Pertussis	2	0	0	2	0	0	4	7	11
Rabies in Animals	27	4	8	4	4	7	49	48	68
Reye Syndrome	1	0	1	0	0	0	1	0	<1
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	<1
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	79	19	15	7	16	22	208	225	224
Shigellosis	42	1	4	31	6	0	69	36	66
Syphilis (Primary/ Secondary)~	117	1	17	6	34	59	266	210	137
Tuberculosis	52	10	20	3	5	14	76	82	85

Localities Reporting Animal Rabies: Albemarle 1 raccoon; Essex 1 fox; Fairfax 1 bat, 3 raccoons; Gloucester 2 raccoons; Hanover 2 raccoons; Loudoun 4 raccoons; Lunenburg 1 raccoon; Madison 1 skunk; Middlesex 1 raccoon; Montgomery 1 fox, 1 skunk; Newport News 3 raccoons; Shenandoah 1 skunk; Surry 1 raccoon; Warren 1 skunk; Washington 1 fox, 1 skunk.

Occupational Illnesses: Asbestosis 64; Carpal Tunnel Syndrome 34; Coal Workers' Pneumoconiosis 26; Loss of Hearing 11; Mesothelioma 1; Repetitive Motion Disorder 4.

~Total Cases Reported now include military cases to make the data consistent with reports of the other diseases.

*other than meningococcal

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