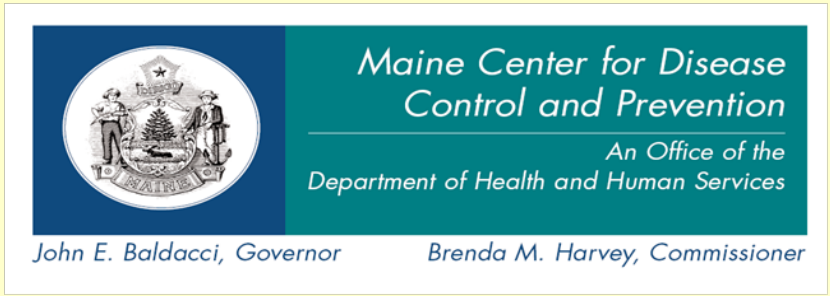
Mumps 101: A Brief Update for Clinicians



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Outline

- Characteristics of Mumps Virus
- Diagnosing Mumps
  - Clinical Presentation
  - Laboratory Tests
  - Differential Diagnosis
- Management
- Recommendations for Vaccine

- Mumps is a single-stranded RNA virus in the paramyxoviridae family.

- There is only 1 serotype, but 10 distinct genotypes have been identified in the small hydrophobic protein in the viral envelope. The genotypes show distinct geographic clustering. [1]

- Humans are the only natural hosts.

- Mumps virus replicates in the epithelial cells of the nose and upper respiratory tract, then spreads to regional lymph nodes. Viremia results in spread to salivary glands and other organs.

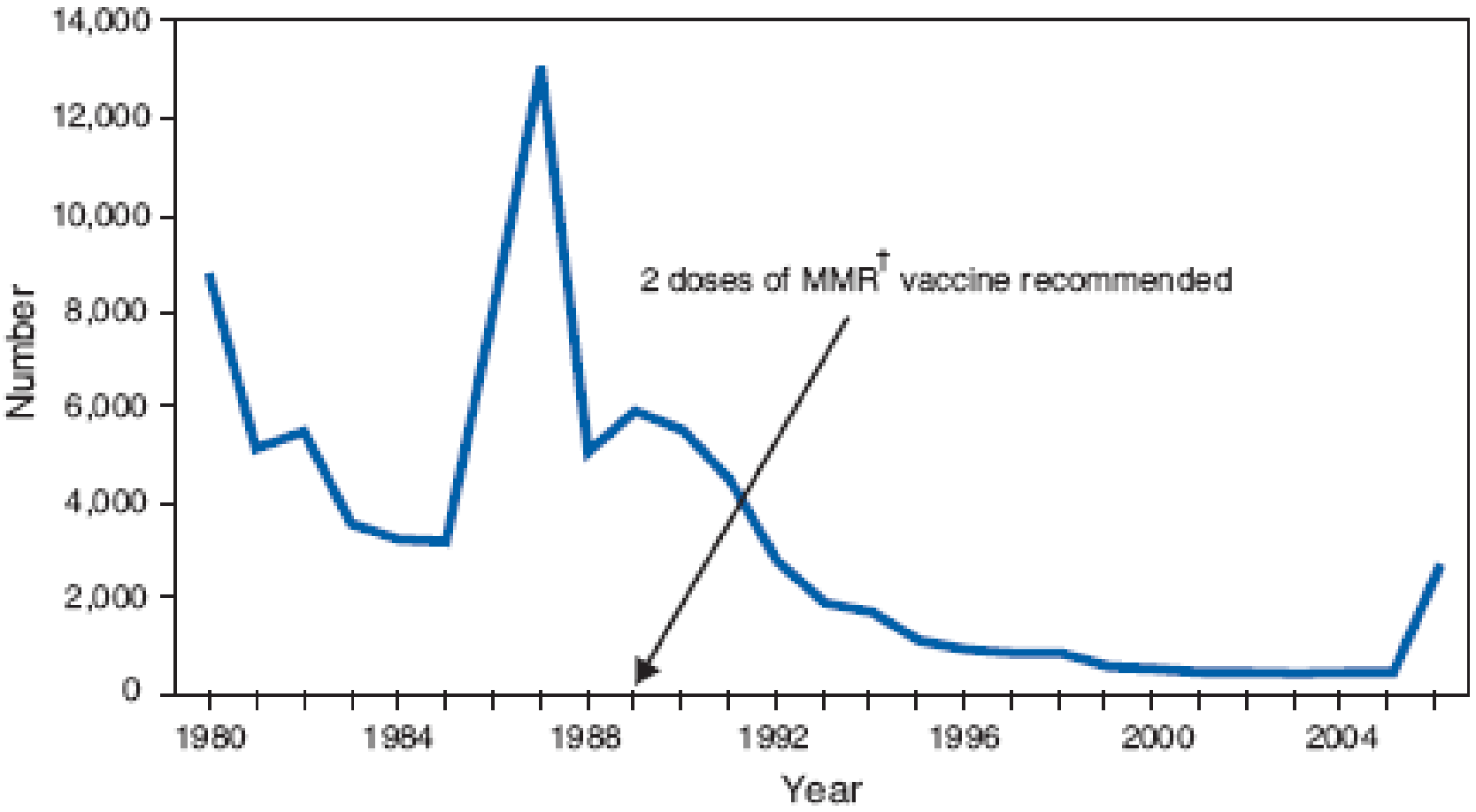
- The virus demonstrates glandular and nervous system tropism.

- The incubation period is 16 – 18 days (range 12 – 25 days).

- Virus is transmitted by respiratory droplets, fomites, or direct contact.

- The period of maximum communicability is from 2-3 days before onset of parotid swelling to 5-9 days after onset of parotid swelling. Viral shedding also occurs in infected persons with subclinical disease.

FIGURE 4. Number of reported mumps cases, by year — United States, 1980–2006*



* Data for 2005 and 2006 are provisional.
† Measles, mumps, and rubella.

Source: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm55d518a1.htm. Accessed 11/30/07.

- There have been several notable mumps epidemics in recent years, both in the U.S. and internationally.

- Most notably, there was a large multi-state outbreak of mumps in the U.S. in 2006. The outbreak involved 2,597 cases in 11 mid-western states during the period January 1 – May 2, 2006. This was the largest outbreak in the U.S. since the MMR vaccine was introduced.

- 57% of cases were reported in Iowa.
- The median age of cases was 21 years. [4]
- Vaccination Status:
  - 65% of cases had documentation of 2 doses of vaccine
  - 14% had documentation of 1 dose of vaccine
  - 6% no doses
  - 14% vaccine status could not be documented. [4]

- Parotitis was reported in 66% of cases.
- Complications: 27 reports of orchitis, 11 reports of meningitis, 4 reports of encephalitis, 4 reports of deafness, 1 report of oophoritis, 1 report of mastitis, and 1 report of pancreatitis. [4]

4 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5513a3.htm. Accessed 11/30/07.

Why have we seen a resurgence of mumps?

- Post-licensure studies in the U.S. demonstrated vaccine efficacy ranging from 78-91% with the Jeryl Lynn live, attenuated vaccine.[7]

- Why is the vaccine not 100% effective?

  No vaccine is 100% effective.

[7] http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5522a4.htm. Accessed 11/30/07.

8 Watson-Creed, G., et al. Two successive outbreaks of mumps in Nova Scotia among vaccinated adolescents and young adults. CMAJ. 2006; 175: 483 – 488.

Possible hypotheses to explain the resurgence in disease

- The immune response directed against one genotype may not provide absolute protection against infection with other genotypes.[8]

- Outbreaks among persons who have received 1 or 2 doses of vaccine have resulted in questions about vaccine failure. Primary vaccine failure is the failure to respond appropriately to a vaccination. Primary vaccine failure would be expected to occur primarily among singly vaccinated individuals. Primary vaccine failure can also occur due to inappropriate storage and handling of vaccine. Interruption of the cold chain, delay in use after reconstitution > 30 minutes, and exposure to light can all decrease vaccine potency.[5]

- Our population of young adults and adolescents represents a high-risk population for several reasons. This population is a “lost cohort” that only received one dose of vaccine in childhood. In addition, young adults often share close living quarters and have many close contacts as compared to older adults and young children, which can facilitate transmission of disease. Adults are also more likely to have sub-clinical infection as compared to younger children, and can unknowingly transmit infection.

How is mumps diagnosed?

Clinical Presentation of Mumps

- Presentation is highly variable. Subclinical infection occurs in as many as 1/3 of patients, and 1/3 of patients may present with mild non-specific symptoms, such as URI symptoms. [9]
- 1/3 of patients have the classic presentation, with prodromal symptoms (headache, low-grade fever, malaise, anorexia), followed by onset of salivary gland swelling within 1-3 days.
- Salivary gland swelling peaks within 3-5 days, and resolves within 7-10 days.
- Location of salivary gland swelling: [10]
  - 75% of cases: bilateral parotitis
  - 25% of cases: unilateral parotitis
  - 10% of cases: swelling of submandibular and/or sublingual gland

9 Kancherla VS and Hanson, IC. Mumps resurgence in the U.S. J. Allergy and Clinical Immunology; 118: 938 – 941.
10 http://www.cdc.gov/print.d0?url=http://www.cdc.gov/vaccines/vpd-vac/mumps/outbreak. Accessed 11/30/07.

What are the clinical characteristics of mumps parotitis?

- **Nonsuppurative** inflammation
- Tenderness and swelling **in front of the lower ear**, that extends forward and downward as fluid builds in tissue
- Characteristically **pushes the ear up and out**, and may **obscure the angle of the jaw**
- Onset may occur in one side before the other

Mumps Parotitis

Courtesy of Centers for Disease Control and Prevention

What should be considered in the differential diagnosis of unilateral or bilateral parotid swelling?

- **Lymphadenitis**: Can be differentiated from mumps by well-defined borders for lymph nodes, location behind the angle of the jaw bone, the lack of ear protrusion or obscuring the angle of the jaw.

- **Viral Parotitis**: Common viral etiologies include Parainfluenza Virus Types 1 and 3, Influenza A, EBV, Coxsackie viruses, Adenovirus.

- **Acute Suppurative Parotitis**: Usually unilateral, but may be bilateral in 15-25% of cases.[11] The most frequent organism is penicillin-resistant Staphylococcus aureus, but Strep Viridans, Strep pneumoniae, and anaerobes may also be seen.

- **Salivary Duct Calculi**

11 Mandel, Louis and Surattanont, Farisa. Bilateral Parotid Swelling: A Review. 2002; 93(3): 221 – 237.

- **Drug reaction:** Iodides, thiouracil, phenylbutazone

- **Sialadenosis:** Seen in metabolic disorders such as diabetes, malnutrition, and alcoholism.

- **Other etiologies:**
  - Masseteric Hypertrophy
  - Bulimia
  - HIV
  - Recurrent Parotitis in Children/Adults
  - Sjogren's Syndrome
  - Wegener Granulomatosis
  - Sarcoidosis
  - Polycystic Parotid Disease
  - Warthin Tumor

What are potential complications of mumps?

- CNS involvement is very common.
  - 50% of patients present with asymptomatic mononuclear pleocytosis. [3] CSF analysis may show slightly elevated protein, and normal or depressed glucose levels.
  - Up to10% of patients have aseptic meningitis.[3] Symptoms include severe headache aggravated by movement, photophobia, and neck stiffness. Patients recover without complications.
  - 0.02 -0.3% of patients have encephalitis. Associated symptoms include focal neurologic signs, emotional lability, irritability, and change in consciousness. 75% of patients with mumps encephalitis are below 15 years of age. [3]
  - Neurologic symptoms usually present about 5 days after onset of parotitis, but they can occur in the absence of parotitis.

- Epididymo-orchitis is the most common complication, and may occur in up to 25% of post-pubertal males. [3]
  - Orchitis is usually unilateral, but may be bilateral in 17-38% of cases. [3]
  - Orchitis usually appears a week after onset of parotitis, but it can appear in the absence of parotitis.
  - Presentation is sudden onset of testicular pain, with associated headache, vomiting, chills, and fever.
  - Physical exam reveals erythema of the scrotum, tenderness of the testis, and can result in testicular atrophy and in rare cases, infertility.
  - Fever usually abates within 5 days, and gonadal pain and swelling usually resolve in 1-2 weeks.
  - Persistent testicular atrophy is seen in 30-50% of cases, and may result in cosmetically apparent change in testicular size. [13] Impaired fertility (oligospermia, azospermia, asthenospermia) is estimated to occur in about 13% of patients, and can be transient or permanent. [13] Sterility is a rare complication.

13 Masarani, M., Wazait, H., Dinneen, M. Mumps Orchitis. The Journal of the Royal Society of Medicine. 2006; 99: 573- 575.

- Oophoritis may occur in up to 5% of post-pubertal females. [1] Patients present with pelvic pain and tenderness, nausea, and vomiting. Oophoritis is not associated with infertility.

- Mastitis may occur in up to 5% of women with mumps. [1]

- Pancreatitis may occur in up to 2-5% of cases. [1]

- Transient or permanent sensorineural hearing loss may occur in up to 4% of cases. [3]

- Spontaneous abortion may occur if infection occurs during the first trimester of pregnancy.

- Other complications are less common, and include myocarditis, mild polyarthritis, mild renal function abnormalities, EKG abnormalities, hepatitis, and death (death occurs in < 2% of encephalitis cases).

What laboratory tests does the MeCDC recommended to diagnose mumps?

Presentation	Serum for IgM and IgG	Buccal Swab for RT-PCR and/or culture	NP Swab for other viral illnesses	Urine for RT-PCR and/or culture
Initial patient visit is </= 5 days after onset of parotitis	Yes	Yes	Optional	No
Initial patient visit is 6-13 days after onset of parotitis	Yes	Yes	No	Optional
Initial patient visit is >/= 14 days after onset of parotitis	Yes	No	No	No
Patient with orchitis (no parotitis)	Yes	Yes	No	Optional
Follow-up testing for a patient who did not have a buccal swab collected at initial visit	Yes; IgG collected 14-21 days after onset	No	No	Optional; collected 10-14 days after onset
Follow-up testing for a patient who is mumps IgM positive during acute phase, and PCR and culture negative	Yes; IgG collected 14-21 days after onset	No	No	Optional; collected 10-14 days after onset

FAQ’s about laboratory testing for mumps

How do I take the buccal swab?

- Use a non-cotton swab (rayon or dacron)
- Massage the parotid area for 30 seconds, and then swab the area around Stenson’s duct
- Send to the MeCDC Health and Environmental Testing Lab using viral transport medium (golden top used for HSV or Influenza). The NP and Buccal swabs may be sent in the same tube.

When is the best time to collect a clinical specimen?

- Serum and buccal swabs should be collected within 2 – 3 days of symptom onset for maximum sensitivity.
- In persons with 1 or more doses of MMR, virus may be cleared rapidly.
- Specimen may be collected as long as 10 days after symptom onset, but will have decreased sensitivity.

How common are false-negative and false–positive results for IgM antibodies?

- In unvaccinated persons, IgM is present by day 5, peaks at week one, and can be present for 6 weeks.
- Serum IgM may be false-negative in 50-60% of patients who have been fully immunized, so a negative test can't be used to rule out acute mumps.[14]
- Parainfluenza viruses 1 and 3 may interfere with serologic testing and may produce false-positive results. [14]

14 http://www.cdc.gov/vaccines/vpd-vac/mumps/outbreak/ Accessed 11/30/07.

Why isolate the mumps virus?

- Virus can be detected by PCR or culture when IgM is not detected.
- Viral isolation provides virus that can be used for sequence studies. The sequence information is helpful to identify the source of infection, and can provide confirmation of suspected epidemiologic links.

If specimen are negative for PCR and culture, does this rule out infection?

- No. The specimen could be negative because the amount of virus shed at the time of sample collection was low, or because of inadequate specimen collection, processing, shipping, or storage.

How are patients with mumps managed?

- Supportive care
- There is no post-exposure prophylaxis for close contacts.
- Vaccine is indicated to protect contacts who are not immune from future disease.
- Isolation:
  - Patients with mumps should be excluded from social events, school, and employment for 9 days after onset of illness.

Current Recommendations for MMR Vaccine from Maine CDC

(as of 1/1/08)

MMR vaccine in the pediatric population

- MMR vaccine is recommended for children at ages 12-15 months, followed by a second dose at 4-6 years.
- During an outbreak setting, providers may be advised to accelerate the vaccine schedule, and to provide a second dose to children 28 days after the first dose.
- Maine CDC recommendations as of 1-1-08 are not to accelerate the vaccine schedule, since we are not in a outbreak setting.

Vaccine recommendations for non-immune students in public and private schools in Maine

- If there is no disease activity in a specific school, students should be allowed to return to school immediately after receiving the MMR vaccine.

- If there is mumps activity identified in a school, students who have never been vaccinated with MMR must be excluded for 18 days after the last case of mumps was diagnosed in the school. For students updating their MMR with a second shot, the 18-day rule shall not be applied because they are already primed from their first shot.

Vaccine recommendations for college students

- On 11/29/07, Maine CDC implemented an emergency rule requiring all post-secondary students born in 1957 or later to have documentation of 2 doses of MMR vaccine, unless they have documentation of immunity. Students include full-time and part-time students who are degree candidates.

- Students whose vaccination status is not updated should be notified that they will be excluded from school if they do not come into compliance and if there is an outbreak of mumps on campus.

Vaccine recommendations for Healthcare Workers (HCW)

- Current recommendations from the Maine CDC are for hospital HCW's born before 1957 who do not have evidence of immunity should receive 1 dose of MMR vaccine. Hospital HCW's born during or after 1957 who do not have evidence of immunity should receive 2 doses of MMR.

- Recommendations for non-hospital HCW's have not changed. HCW's born before 1957 are considered immune. HCW's born during or after 1957 are not routinely considered immune, and should provide documentation of immunity due to prior history of disease, or should receive 2 doses of MMR.