Surveillance Protocol for Undifferentiated Pustular / Vesicular Rash Illness

Note: This protocol is designed to assist the investigator in differentiating causes of vesicular/pustular rash illness in the early stages of case or outbreak investigation before the diagnosis is known. The protocol emphasizes identification of febrile rash illness of public health significance. If the case definition for a specific disease is met, please refer to the investigation protocol for that disease.

Public Health Action

1. Identify personnel to investigate a case or outbreak of undifferentiated pustular/vesicular rash illness, and protect employee health. Personnel must have:
   a. Documented immunity to smallpox (successful vaccination within three years). If unvaccinated personnel must be utilized in the response, they must be provided with a fit-tested N 95 mask and have no contraindications to smallpox vaccination (because they will need smallpox vaccine within 72 hours of a confirmed exposure).
   b. Documented immunity to measles, rubella and varicella
   c. Completed training in smallpox investigation and response.

   Also use airborne (N95 mask) and contact precautions (gloves / gown) when diagnosis is unknown.

2. Educate providers to immediately isolate undiagnosed hospitalized patients with acute febrile, generalized pustular/vesicular rash illness, to include:
   a. Airborne precautions (negative pressure isolation of the patient and use of an N-95 mask by the health care worker);
   b. Contact precautions (gloves, gown);
   c. Notification of the Infection Control Practitioner

3. Educate providers to recognize major and minor smallpox diagnostic criteria, as follows:
   a. **Major criteria:**
      i. **Febrile prodrome:**
         (1) occurs 1-4 days before rash onset
         (2) fever $\geq$ 101 F and at least one of the following:
            (a) prostration
            (b) headache
            (c) backache
            (d) chills
            (e) vomiting
            (f) severe abdominal pain
      ii. **Classic smallpox lesions:** deep-seated, firm/hard, round, well-

circumscribed vesicles or pustules; umbilicated or confluent

iii. **Lesions in the same stage of development:** on any one part of the body (e.g., the face or arm) all the lesions are in the same stage of development (i.e., all are vesicles, or all are papules)

b. **Minor criteria:**

i. **Centrifugal distribution**: greatest concentration of lesions on the face and distal extremities

ii. **First lesions** on the **oral mucosa/palate, face, forearms**

iii. **Toxic or moribund** appearance of the patient

iv. **Slow evolution**: lesions evolve from macules to papules then pustules over days (each stage lasts 1-2 days)

v. **Lesions on palms and soles** in the majority of cases

4. Educate hospitals to report cases of acute febrile pustular or vesicular rash illness immediately. Encourage hospitals to report hospitalized cases of varicella immediately.

5. **Triage** reports of pustular / vesicular rash illness according to CDC criteria, as follows:

a. **High risk** of smallpox:

i. Febrile prodrome AND

ii. Classic smallpox lesions AND

iii. Lesions in the same stage of development

b. **Moderate risk** of smallpox:

i. Febrile prodrome AND one other major smallpox criterion OR

ii. Febrile prodrome AND > 4 minor criteria

c. **Low risk** for smallpox, defined as:

i. No/mild febrile prodrome; OR

ii. Febrile prodrome AND < 4 minor criteria (no major smallpox criteria)

6. Investigate reports of vesicular or pustular rash illness as follows:

a. High risk:

i. Contact IDEP emergently (24/7/365.25) to arrange smallpox testing through CDC according to CDC guidelines. IDEP will begin notification through the chain of command according to protocol.

ii. Consider infectious disease and/or dermatology consultation

iii. Consider testing for chickenpox using DFA, if appropriate (contact IDEP urgently at 1-800-4231271 to arrange)

iv. Clinical and epidemiological data may be collected using the Undifferentiated Rash Illness Worksheet - if a specific disease is diagnosed, use the investigation form for that disease.

v. Consider active surveillance for vesicular/pustular rash illness in hospitals and emergency rooms

b. Moderate risk:

i. Consider dermatology and/or infectious disease consultation.
ii. Consider testing for chickenpox (DFA), if appropriate (contact IDEP at 1-800-423-1271 to arrange)
iii. Clinical and epidemiological data may be collected using the Undifferentiated Rash Illness Worksheet - if a specific disease is diagnosed, use the investigation form for that disease.
iv. Recommend additional testing, if indicated

c. Low risk:
i. Consider testing for chickenpox (DFA), if appropriate. Contact IDEP to arrange at 1-800-423-1271.
ii. Clinical and epidemiological data may be collected using the Undifferentiated Rash Illness Worksheet - if a specific disease is diagnosed, use the investigation form for that disease.

7. Assure collection of appropriate clinical samples for testing:
   a. For varicella: collect a swab sample from the base of a skin lesion, preferably a fresh fluid filled vesicle for DFA [at Office of Laboratory Services].
   b. For measles: collect acute serology for IgM testing at the CDC (testing at commercial reference laboratory is often unreliable) and hold an acute specimen. Sera drawn in the first 72 hours after rash onset maybe IgM negative in up to 20% of cases, and should be repeated.
   c. For smallpox or monkeypox: collect scrapings of skin lesions, papular, vesicular, pustular fluid or crust, blood samples, tonsillar swabbings in consultation with CDC. Instructions are available on the CDC website.
   d. For Herpes simplex, collect a swab of the base of a skin lesion for viral culture at a hospital or reference laboratory or for DFA at OLS.
   e. For Rickettsialpox, contact IDEP.

8. On confirmation of a specific diagnosis, refer to disease specific protocol for public health action.

Disease Control Objectives:

1. To rapidly characterize cases and outbreaks of infectious rash illness so that appropriate control measures can be applied in a timely fashion, preventing additional cases of disease; i.e.:
   a. Prevent community transmission of ***varicella*** from a confirmed case by:
      i. Rapid isolation of the case with airborne and contact precautions;
      ii. Immunization of susceptible eligible individuals within 72 hours of exposure;
      iii. Use of VZIG (within 96 hours) in persons who cannot receive the vaccine and are at risk for serious disease.
   b. Prevent community and nosocomial transmission of ***smallpox*** by:
      i. Rapid isolation of the case with airborne and contact precautions;

ii. Vaccination of contacts to a confirmed case within 4 days of exposure;
iii. Vaccination of household members of *contacts* to minimize the chance of transmission should the contact develop disease – for household members of contacts who cannot be vaccinated due to contraindications, the household member should avoid contact with the contact until the incubation period for the disease has passed (18 days) or until successful vaccination of the contact is established at 14 days.
iv. Vaccination of all health care workers who will be directly involved in evaluating, testing, transporting or interviewing potential smallpox cases;
v. Vaccinating other response personnel who have a reasonable probability of contact with smallpox patients or infected material, e.g., selected law enforcement, emergency response, or military personnel.

c. Prevent community transmission of ***measles*** from a confirmed case by:
i. Isolation of the case using airborne precautions;
ii. Immunization of susceptible eligible individuals within 72 hours of exposure or use of immune globulin (within 6 days) in persons at increased risk for measles who cannot receive the vaccine (susceptible household contacts should receive both the vaccine and immunoglobulin if more than 72 hours have elapsed).

d. Prevent community and nosocomial transmission from a confirmed case of ***monkeypox*** by:
i. Isolation of the case using airborne and contact precautions
ii. Investigation into the source of the outbreak so that further transmission may be prevented.
iii. Protection of persons investigating human or animal cases of monkeypox, to include:
(1) Preferential use of investigators (including veterinarians and animal control personnel) who have been vaccinated against smallpox within the last 3 years AND who have had a confirmed take.
(2) If vaccinated personnel are unavailable, vaccination should be performed immediately before deployment to field investigation.
(3) Unvaccinated investigators employed in field investigation should be vaccinated within 4 days of exposure.

e. Prevent further cases through early identification, investigation and implementation of control measures for other infectious conditions.

Surveillance Objectives

1. To detect suspect cases of smallpox at the earliest possible time.

2. To detect and characterize serious complications of chickenpox and establish whether these are attributable to failure of vaccine (non-preventable causes) or failure to immunize (preventable causes).
3. To identify and characterize outbreaks of vesicular / pustular rash illness
4. To identify cases of other reportable diseases and other diseases of public health importance, e.g., atypical measles, herpes, monkeypox and rickettsialpox.

Disease Prevention Objectives

1. Prevent varicella through appropriate use of the varicella vaccine.
2. Prevent measles through appropriate use of the measles vaccine.
3. Prevent monkeypox and rickettsialpox through control of the animal reservoir.

Public Health Significance

One of the most significant developments in public health during the last century was the eradication of smallpox declared world wide in 1980. With this event came the promise of worldwide eradication of other vaccine diseases such as Polio, and the disease elimination efforts in the United States which have focused on Measles, Mumps, Rubella, *Haemophilus influenzae* type b in children under 5 years, tetanus in children under 15 years, and Diphtheria.

Tragically, smallpox is now considered a potential “level A” bioterrorist weapon because of the potential for dissemination through aerosol, and the high morbidity and mortality associated with the disease. Deliberate reintroduction of smallpox would undoubtedly cause widespread panic and social disruption. Obviously no one knows whether a bioterrorist attack with smallpox is likely or not however planning has begun in earnest after the deliberate use of anthrax as a bioweapon in the fall of 2001.

The Centers for Disease Control and Prevention has published a triage algorithm for acute generalized vesicular or pustular rash illness. The algorithm assumes that the first case of smallpox will be missed until day 4-5 because maculo-papular rashes will be excluded from consideration. It is further likely that an atypical case of smallpox will be missed if it is the first case.

It likely that this highly specific detection algorithm will be challenged if a suspect or confirmed case is reported anywhere in the world. For that reason, physicians and public health officials must familiarize themselves both with the highly specific algorithm and a much broader differential diagnosis of the many maculopapular and papulovesicular rash illnesses.

In addition, public health officials should keep in mind the public health significance of other vesiculopustular rash illnesses. Varicella and measles are vaccine-preventable diseases. Cases of measles should be investigated urgently to confirm the diagnosis and prevent spread. Cases of varicella resulting in hospitalization or death should be

investigated to identify vaccine failure or missed opportunities to vaccinate. Rickettsialpox and monkeypox are zoonoses, and identification of human cases indicates a need to identify and eliminate the animal reservoir.

Clinical Description

The differential diagnosis of pustular/vesicular eruptions includes many agents. Those of most concern to public health because of their potential for airborne transmission include: Atypical Measles, Chickenpox, Smallpox and monekeypox; however disseminated Herpes simplex infections, generalized vaccinia or eczema vaccinatum, and rickettsialpox also have substantial public health significance.

The New England Journal of Medicine (Vol 346, pp 1300) listed this differential diagnosis for papulovesicular rashes:

- Atypical measles (rubeola)
- Acne
- Chickenpox
- Coxsakievirus infection (hand-foot-and-mouth disease and consackievirus A16)
- Dermatitis herpatiformis
- Drug eruptions
- Eczema herpeticum (herpes simplex virus)
- Generalized vaccinia and eczema vaccinatum (vaccinia)
- Impetigo
- Insect bites
- Molluscum contagiosum
- Monkeypox
- Papular urticaria
- Pemphigus
- Rickettsialpox (*Rickettsia akari*)
- Shingles (varicella-zoster virus)
- Yaws (*Treponema pallidum*, subspecies *pertenue*)
- Smallpox (*Variola major* and *V minor*)

In addition, pemphigoid and disseminated fungal infections might also be considered. A table with summary information on each syndrome follows. For additional detail on each of these agents, see the disease-specific protocol and the references cited at the end of this protocol.

Some definitions:
Prodrome: An early or premonitory symptom of a disease.
Enanthem: A mucous membrane eruption, especially one occurring in connection with one of the exanthemas.
Exanthem: 1. A skin eruption occurring as a symptom of an acute viral or coccal disease; e.g., scarlet fever or measles; 2. An acute disease, e.g., scarlet fever or measles, accompanied by an eruption on the skin.

Clinical features and epidemiology of selected agents causing a pustular / vesicular rash illness in humans

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Atypical measles	Incubation 1-2 weeks in persons who received formalin-inactivated measles vaccine (1963-1967) Spread airborne Association travel or link to an imported case of measles Vaccine Live / attenuated	Prodrome high fever, headache, abdominal pain, myalgia, and cough; Exanthem urticarial, maculopapular, petechial, hemorrhagic, vesicular or some combination -- occasionally pruritic Location eruption on the extremities with spread centripetally over the next 2-3 days Enanthem ^^ Duration week to 10 days Systemic illness may occur, including elevated hepatocellular enzymes, nodular pneumonia with pleural effusion. Peripheral edema may also be present.	IgM capture ELISA 72 hours to 30 days after rash onset / CDC	*Emergency* to 1)confirm the case 2)vaccinate susceptible contacts
Acne	Onset at puberty; may, however appear at age 25 years or older Association lithium, hydantoin, topical and systemic glucocorticoids, oral contraceptives, androgens Positive family history in persons with cystic acne	Prodrome none Rash Comedones, papules, papulopustules with or without inflammation, nodules, noduloulcerative lesions or cysts, scars Location face, shoulders, upper back Mucous membranes unaffected Duration chronic Systemic illness none	N/A; usually clinical	Rule out

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Chickenpox	Incubation 14-15 days (range 10-21 days) Spread Direct contact, droplet or airborne spread from vesicles or lesions in the respiratory tract Seasonality Winter and early spring Vaccine live, attenuated	Prodrome Fever 100 to 103, and constitutional symptoms may precede the rash by 1-3 days (in a few). Exanthem macules, papules, vescicles, crusts in various stages of evolution - 'dewdrop on a rose petal' is the classic lesion Location Begins on face and scalp, spreading inferiorly to trunk and extremities; highest density on trunk and face, less on extremities; palms and soles usually spared Enanthem Vesicles and shallow erosions most commonly on the hard palate, but also on nasal mucosa, conjunctivae, pharynx, larynx, trachea, GI tract, urinary tract, vagina. Duration crusts fall off in 1-3 weeks, leaving a pink somewhat depressed base Systemic illness rare in the immunocompetent host; however liver, lung and CNS involvement can occur	DFA / OLS, Ruby Hospital, CAMC, Cabell-Huntington Hospital PCR/ Virginia State Public Health Laboratory (through OLS)	*Urgent* to 1) confirm the case 2) offer vaccine to susceptible contacts Priority Investigations: Deaths Hospitalized cases or those with severe complications Primary surveillance objective: differentiate vaccine failure versus failure to vaccinate

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Coxsackievirus	Incubation 3-5 days Spread by direct contact with nose and throat discharges and feces of infected persons Seasonality Summer and early Autumn	Prodrome none Exanthem classic 'hand, foot and mouth' (HFM) disease manifests with painful papules and clear vesicles on an erythematous base located on hands, feet. Generalized vesicular eruptions may also occur - in crops of lesions similar to HFM and without evolution to pustules and scabs Location HFM on hands, feet, with painful ulcers in the mouth; Generalized eruptions occur on the head, trunk, and extremities. Enanthem painful ulcers in the mouth Duration 5-10 days Systemic illness Fever accompanies the rash; enterovirus infections may result in aseptic meningitis, encephalitis, pneumonia, and other syndromes.	N/A Culture of vesicle / hospital or reference laboratory	Rule out; investigate outbreaks
Dermatitis herpetiformis	Onset age 20-60 years; most commonly age 30-40 Association gluten sensitive enteropathy and circulating IgA immune complexes	Prodrome Intense, episodic pruritis or burning or stinging of the skin precedes the skin lesions by 8-12 hours Rash erythematous papules or wheal-like plaques; tiny firm-topped vesicles, sometimes hemorrhagic; occasionally bullae; arranged in groups Location Extensor areas - elbows, knees, buttocks, scapular and sacral areas. Scalp, face, hairline Mucous membranes lesions not described Duration chronic Systemic illness No systemic symptoms	N/A Skin biopsy / immuno-fluorescent stain for IgA in perilesional skin/ hospital or reference laboratory	Rule out

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Drug eruptions; e.g., Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN)	Onset 1-3 weeks after institution of medication Association Sulfa drugs, allopurinol, hydantoins, carbamazepine, phenybutazone, piroxicam, chlormenazone, amithiozone, aminopenicillins, others	Prodrome fever, influenza-like symptoms 1-3 days prior to rash Rash begins as a morbilliform eruption progressing to necrotic epidermis (macular areas with crinkled surface that enlarge and coalesce), followed by sheet-like loss of epidermis. Epidermal sloughing results in large denuded areas, resembling a second-degree burn. Raised flaccid blisters that spread with lateral pressure or pressure on the blister (Nikolsky's sign) Location Initial erythema is on face and extremities, becoming confluent over a period of hours or days. Denudation most pronounced over pressure points. Scalp, palms, soles may be less severely involved or spared. SJS: widely distributed with prominent involvement of trunk and face TEN: generalized, universal Mucous membranes painful, tender mouth lesions Duration average duration of progression is less than 4 days; resolution is dependent on extent of skin necrosis with course of illness similar to thermal burns Systemic illness complications may include azotemia due to fluid loss, and secondary bacterial infection	N/A Skin biopsy / hospital or reference laboratory withdrawal of drug	Rule out

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Eczema herpeticum	Incubation 2-12 days for primary infection with herpes simplex Spread by direct contact with saliva or by sexual contact Association underlying disease, especially atopic dermatitis	Prodrome none; Rash umbilicated lesions evolve into punched out erosions. Erosions may become confluent. Larger crusted lesions with staphylococcal superinfection may occur. Successive crops of new vesicles may occur. Location Vesicles are first confined to eczematous skin and are disseminated. Common sites are face, neck, trunk; may later spread to normal-appearing skin. Duration 2-6 weeks Systemic illness fever and other systemic symptoms accompany the rash; aseptic meningitis, encephalitis, pneumonitis, hepatitis, etc. may occur due to dissemination, especially in an immunocompromised host.	DFA/ OLS PCR, antigen detection / hospital or reference laboratory Also: tissue culture, dermatopathology,	Assure that individual is in contact isolation to prevent spread
Fungal disease, disseminated; e.g. Histoplasmosis, Cryptococcosis, Coccidiomycosis	Incubation N/A Spread likely autoinfection as mold and fungi are ubiquitous in the environment Association severely immunocompromised patients Travel to California for Coccidiomycosis	Prodrome often presents in the context of clinical syndrome of acute septicemia or high fever Rash variable; may include – papules, nodules, pustules, ulcers, etc. Location generalized Duration dependent on treatment and course of underlying illness Systemic illness Disseminated fungal infection can affect the brain, lungs, and other organs	*Histoplasmosis:* touch preparation stained with Giemsa stain *Cryptococcosis:* touch preparation stained with KOH / hospital or reference laboratory	Report and investigate underlying HIV infection if applicable.

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Generalized vaccinia & eczema vaccinatum	Incubation 5 days after vaccination Spread by direct contact with vesicles Seasonality N/A	Prodrome none; severe constitutional symptoms and fever may accompany rash Rash papules evolve to vesicles and later pustules. Location widespread Duration scabs form at 14 to 21 days Systemic illness multiple complications of vaccination have rarely been reported, including overwhelming viremia, myocarditis, thrombocytopenia, arthritis and pericarditis	PCR / State of Virginia Public Health Laboratory (through OLS)	Priority investigation: Report as a vaccine adverse event. Contact isolation.
Impetigo	Incubation variable, commonly 4-10 days Spread autoinfection in a colonized person or direct contact with a colonized or infected person Seasonality warm weather	Prodrome none Rash non-bullous: transient superficial small vesicles or pustules rupture, resulting in erosions, which in turn become surmounted by a crust / bullous: vesicles and bullae containing clear yellow or slightly turbid fluid. With rupture, bullous lesions decompress. If roof of bulla is removed, shallow moist erosion forms. Location most common in intertriginous areas Duration days to weeks Systemic illness none	gram stain, culture, dermatopathology / hospital or reference laboratory	Rule out Investigate and apply control measures in outbreaks
Insect bites, e.g., bullous lesions; see also papular urticaria	incubation hours to days after the bite	Prodrome none Rash *Bullous lesions* are tense bullae with clear fluid on an erythematous base; excoriation results in large erosions Location more common on exposed skin Duration days, weeks, months Systemic illness varied; associated with toxic or allergic reaction to substance injected during the bite	usually clinical, at times confirmed by dermatopathology / hospital or reference laboratory	Rule out

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Molluscum contagiosum	Incubation 7 days to 6 months Spread skin to skin contact; fomite spread suspected Association with HIV infection in persons with multiple facial mollusca	Prodrome none Rash 1-2 mm papules, 5-10 mm nodules. White or skin colored. Round, oval, hemispheric or umbilicated. Single, multiple, scattered discrete or confluent mosaic plaques. Location exposed skin sites in children; genital region, thighs, abdomen in adults; multiple facial mollusca in HIV-infected individuals. Duration up to six months in immunocompetent individuals; may persist and disseminated in HIV-infected persons Systemic illness none	usually clinical; dermatopathology if disseminated fungal disease is in the differential / hospital or reference laboratory	Rule out Investigate and report underlying HIV disease, if applicable
Monkeypox	Incubation 7-17 days Spread Contact with squirrels or monkeys from West or central Africa. Western Hemisphere transmission associated with Gambian rats or prairie dogs Human to human transmission (by ? large respiratory droplets) Travel to West or central Africa Etiology orthopox virus	Prodrome fever, headache, muscle aches, backache, swollen lymph nodes, discomfort and exhaustion lasting 1-3 days Rash develops through macules, papules, vesicles, pustules, and crusts that evolve in the same stage over 14-21 days, similar to smallpox.. Location head, trunk and extremities; satellite and initial lesions on palms, soles, and extremities. disseminated in some patients. Duration 2-4 weeks Systemic illness one case of encephalitis described in the recent series. There is limited information on the clinical manifestations of this disease; however, most sources state that the illness is 'clinically indistinguishable' from smallpox or 'smallpox-like.' The major difference is the presence of lymphadenopathy in persons with monkeypox.	PCR / CDC	Emergency investigation: Identify and eliminate animal source of infection. Assure isolation of an infected individual using airborne and contact precautions. Assure vaccination of health care workers and investigators of human and animal cases. Vaccinate close contacts (> 3 hours of direct exposure within 6 ft.

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Papular urticaria	Incubation hours to days after an insect bite Etiology hypersensitivity reaction to substance injected during bite	Prodrome none Rash urticarial papules, often surmounted by a vesicle, usually < 1 cm. Superinfection and excoriation are common. Location more common on exposed skin Duration days, weeks, months Systemic illness varied; associated with toxic or allergic reaction to substance injected during the bite	Usually clinical, at times confirmed by dermatopathology / Hospital or reference laboratory	Rule out
Pemphigus vulgaris; variants include: Pemphigus vegetans, Drug-induced pemphigus, Pemphigus foliaceus is a closely-related variant	Onset age 40-50 Etiology Autoimmune	Prodrome none Rash round or oval vesicles and bullae with serous content, easily ruptured and weeping arising on normal skin. Erosions are painful. Pressure on bullae leads to lateral extension Location Scalp, face, chest, axillae, groin, umbilicus; back of bedridden patient Mucosal lesions Disease usually starts in the oral mucosa with painful erosions, and months may elapse before skin lesions occur Duration chronic Systemic illness not prominent	N/A Dermatopathology, immunofluorescence	Rule out

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Pemphigoid	Onset at ages 60 to 80 years Autoimmune	Prodrome none Rash Erythematous, papular or urticarial-type lesions may precede bullae formation by months. Bullae, large, tense, firm-topped, oval or round may arise in normal or erythematous skin and contain serous or hemorrhagic fluid. Location generalized or localized with axillae, medial aspects of thighs, groin, abdomen, flexor aspects of forearms, lower legs most likely to be affected. Mucosal lesions mouth, anus, and rarely the vagina. Less severe and painful than in pemphigus, the bullae are less easily ruptured. Duration chronic Systemic illness not prominent	N/A dermatopathology, immunopathology / hospital or reference laboratory	Rule out
Rickettsialpox (*Rickettsia akari*)	Incubation 9 -14 days Spread from rodents to humans via the bites of a mite *(Liponyssoides sanguineus)*	Prodrome headache, myalgia, fever occurring 1-5 days prior to rash Rash papulovesicle at the site of inoculation 4-7 days prior to the onset of a papulovesicular eruption - 5 to 30 lesions Location scattered on the face, trunk, and extremities Enanthem not described Duration one week Systemic illness not described	N/A DFA of parafin-embedded tissue / ?CDC	Assure appropriate therapy and report and investigate as an unusual health condition of public health significance

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Shingles (varicella-zoster virus)	Etiology reactivation of varicella infection Association elderly or immunosuppressed individuals	Prodrome neuritic pain or paresthesia for 2-3 weeks Rash painful papulovesicular rash Location dermatomal distribution; may widely disseminate in the immunocompromised host Duration crust formation: days to 2-3 weeks; post-herpetic neuralgia: months to years Systemic illness Fever and constitutional symptoms may accompany the prodrome and early rash formation. Dissemination and internal organ involvement may occur	DFA / OLS	Investigate and report as a vaccine adverse event in persons who have received the varicella vaccine
Yaws (*Treponema pallidum*, subspecies *pertenue*)	Incubation 3-5 weeks Spread when traumatized skin comes in contact with infectious exudate from active yaws lesions Travel to humid tropical areas of Africa, South America, Southeast Asia and Oceania	Prodrome none Rash *primary lesion*: papule that enlarges and erodes *secondary lesion:* papules, nodules - do not ulcerate unless secondarily infected. *late stage:* cutaneous plaques, nodules and ulcers, hyperkeratoses of palms and soles Location *primary lesion:* usually on the lower extremities. *secondary and late lesions:* generalized Duration chronic with multiple relapses Systemic illness *secondary stage:* osteitis and periosteitis. *late stage:* gummatous lesions of skull, sternum, tibia, or other bones	Darkfield microscopy/ on-site; limited availability VDRL, FTA / ?CDC	Assure complete treatment and institution of contact precautions

Disease	Epidemiology	Clinical features	Rapid Diagnostic test / Availability	Public Health Implications
Smallpox (*Variola major* and *V minor*)	Incubation 7-19 days; usually 10-14 days Spread airborne or direct nasal innoculation from contaminated hands; inhaled dust from contaminated bedlinen Priority Single confirmed case is an international public health emergency	Prodrome Sudden onset of fever, prostration, headache, backache, vomiting, beginning about 3 days prior to the rash Exanthem Progression from macules (1-2 days) => papules (1-2 days) => vesicles (2-3 days) => pustules (5-8 days) =>crusts (5-7 days) => desquamation (weeks) Location Most dense on the face; more dense on the extremities than the trunk; one the extremities; more dense on the distal parts than on the proximal, on the extensor than the flexor surfaces, and on the convexities than on the concavities. Palms and soles are involved in most cases. Enanthem first to appear; may result in complaint of sore throat - red macules. Duration about three weeks Systemic illness	PCR / CDC	International public health emergency. Contact Bureau for Public Health day or night

Differentiation of Smallpox and Chickenpox (NEJM, 2002; 346:1300.)

Diagnostic Criteria	Smallpox	Chickenpox
History		
Recent contact with smallpox	Yes	No
Recent contact with chickenpox	No	Yes
Prior vaccination against smallpox	In some cases	In some cases
Prior vaccination against chickenpox	In some cases	No
Incubation period (days)	10-12 (range, 7-17)	14-16
Prodromal phase		
Duration (days)	2-4	0-2
Fever	Yes	In some cases
Headache, backache	Yes	In many cases
Muscle pain, malaise	Yes	In some cases
Pallor, transient rash	In some cases	No
Physical examination		
Scar from smallpox vaccination	In some cases	In some cases
Skin lesions		
Distribution	Centrifugal	Central
Peak	7-10	3-5
Evolution	Same Stage	Different stages
Diameter	4-6	2-4
Shape	Round	Oval
Depth	Deep	Superficial
Desquamation (days after onset of eruption)	14-21	6-14
Lesions on palms and soles	Common	Uncommon
Complications		
Skin infection	In some cases	In some cases
Facial scarring	In some cases	In some cases (superficial)
Pneumonia	In some cases	Rare
Blindness	In some cases	No
Encephalitis	In some cases	Rare
Case-fatality rate		
Chickenpox		<1 (2-3 / 100,000)
Variola major	30	
V minor	<1	
Laboratory diagnosis		
Antigen or nucleic acid detection	Variola virus	Varicella-zoster virus
Electron-microscopical findings	Poxvirus particles	Herpesvirus-varicella virus
Results of culture of chorioallantois	Characteristic pocks	No growth
Serologic findings	Increase in antibody to orthopoxvirus	Increase in antibody to varicella virus

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