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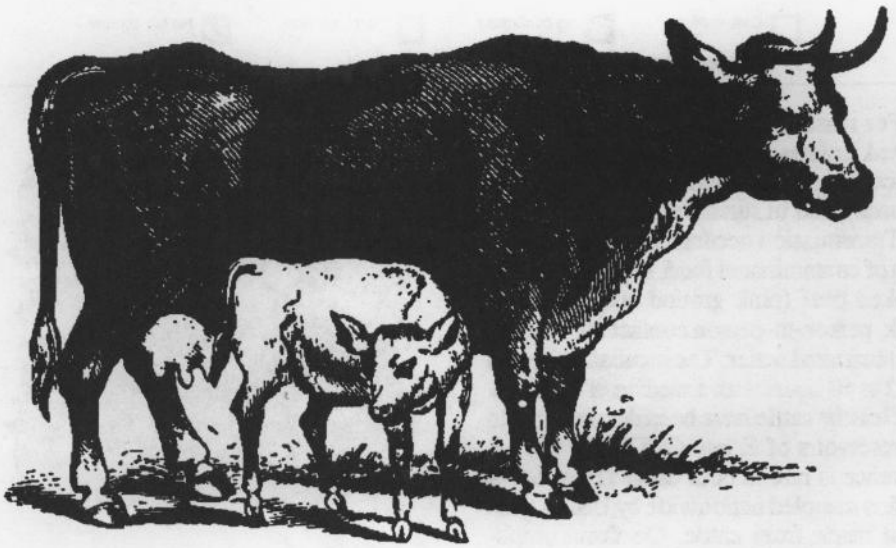
Escherichia coli O157:H7 Infections

Current Trends

During January 1-29, 1993, 230 persons with culture-confirmed infection with *Escherichia coli (E. coli)* O157:H7 resulting in bloody diarrhea and, in some cases, hemolytic uremic syndrome (HUS) were reported in the state of Washington.[1] Culture results were pending for many others with similar illnesses. Two deaths have since been reported in affected children.

Preliminary investigations by public health agencies linked cases to consumption of hamburgers from one fast-food restaurant chain. *E. coli* O157:H7 was isolated from epidemiologically implicated lots of ground beef and an interstate recall was initiated by the restaurant on January 18. Meat from the same lots of ground beef had been distributed to at least three other western states in which increased numbers of cases of bloody diarrhea have been reported. One lot contained 597,600 patties and represented one afternoon's production from a California processing plant. The Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture, state and county health departments, and state agriculture investigators have been investigating whether cases of bloody diarrhea in the other states are linked to consumption of meat from the same lots of ground beef and are determining the possible sources of the contaminated meat.

In This Issue:



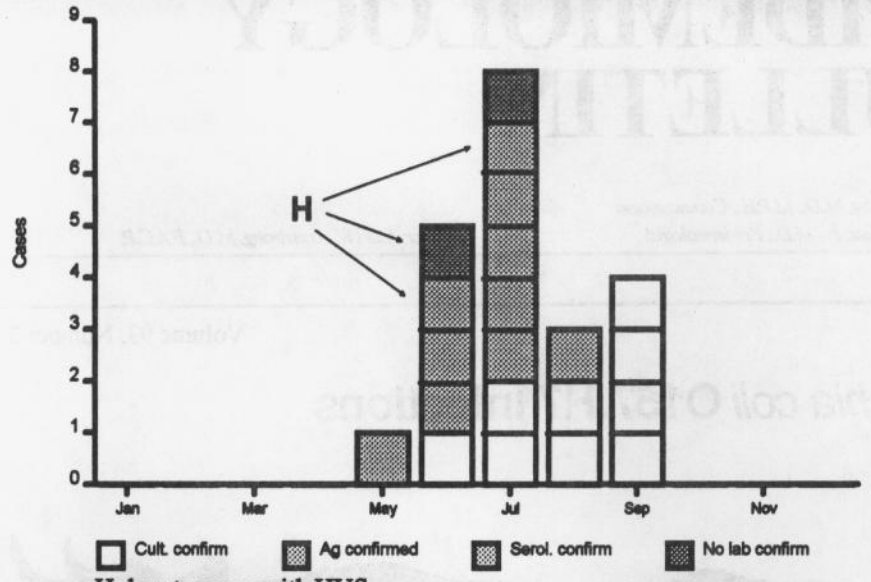
In Virginia, 21 cases of hemorrhagic colitis, including three with HUS, were reported to the Office of Epidemiology during 1992. All except two had laboratory evidence of *E. coli* O157:H7 infection. Of the two without such confirmation, both had classic symptoms, one had HUS and the other was epidemiologically linked to a culture-positive case. Onsets clustered during the summer months (Figure 1) and children were more commonly affected than other age groups (Figure 2). Ten of the 21 cases were investigated because of geographic clustering in the greater Richmond metropolitan area (see the August 1992 issue of the *Bulletin*).

Epidemiology

E. coli O157:H7 is the most commonly isolated strain of enterohemorrhagic *E. coli* (EHEC), the most recently identified of several pathogenic *E. coli* strains (see accompanying boxed text). It was first associated with a multistate community outbreak in 1982, when investigators found that illness was associated with eating hamburgers at restaurants belonging to the same fast-food chain in Oregon and Michigan.[2] Since then, outbreaks have been documented in nursing homes, daycare centers, and schools.

E. coli O157:H7 is also a cause of sporadic illness, and in some areas a more common enteric pathogen than *Salmonella* or *Shigella*. Most cases have occurred in North America and Europe; it has only been identified in developed nations. Its importance as a human pathogen appears to be increasing. In the few population-based studies conducted to date, the incidence of laboratory-confirmed infection has ranged from 2-8 per 100,000 persons per year.[3]

Figure 1. Reported cases of hemorrhagic colitis with or without hemolytic uremic syndrome (N=21), by month of onset and status of laboratory confirmation for *E. coli* O157:H7, Virginia, 1992



H denotes case with HUS

For reasons that are not clear, most reported isolates and outbreaks have tended to occur in northern states (many bordering Canada), and in summer months.[4]

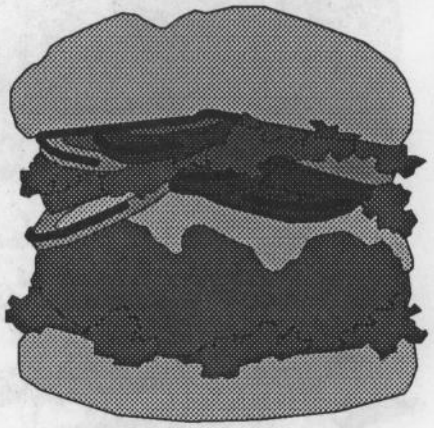
Transmission occurs through the ingestion of contaminated food, typically poorly cooked beef (pink ground beef) and raw milk, person-to-person contact and, rarely, contaminated water. The incubation period is 12 to 60 hours with a median of 48 hours.

Healthy cattle have been documented to be reservoirs of *E. coli* O157:H7,[5] but occurrence is rare in both cattle (25 of 6,894 heifers sampled nationwide by USDA) and meat made from cattle. On farms implicated in outbreaks of human illness the isolation rate from cattle is higher, especially among heifers and calves. Calves can develop hemorrhagic colitis from *E. coli* O157:H7. In some areas *E. coli* O157:H7 has been found in 3-4% of ground beef samples.[3]

Clinical Manifestations

Typical illness is characterized by severe abdominal pain with cramps and watery diarrhea followed, in two to three days, by grossly bloody diarrhea. Vomiting occurs in about one half of patients. The patient is usually afebrile. Average duration of symptoms is around eight days.[6] Tissue pathology shows evidence of ischemic colitis without enteroinvasion of the intestinal mucosa.

There appears to be a spectrum of illness severity with some patients (25-50%) having only watery diarrhea without progression to bloody diarrhea.[7] Secondary cases



resulting from person-to-person contact usually have this milder form of illness.

Hemolytic uremic syndrome (HUS) may develop in 2-7% of infected persons, especially children. HUS is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal failure, and carries a 10% mortality if untreated. *E. coli* O157:H7 may be the major cause of HUS; it was isolated from 46% of Minnesota children with HUS when stool specimens were appropriately tested for the organism.[8] Other studies have found isolation rates as high as 75%.[9] HUS from *E. coli* O157:H7 is usually, but not always, preceded by diarrhea containing blood.

Thrombotic thrombocytopenic purpura (TTP) is also associated with *E. coli* O157:H7, and this may be especially true in the elderly.[3] TTP is characterized by microangiopathic hemolytic anemia, thrombocytopenia, renal failure, neurologic manifestations and fever.

Diagnosis

Physicians who have patients with severe bloody diarrhea of unknown etiology or HUS should consider infection with *E. coli* O157:H7 and should request the appropriate cultures be done. Fecal leukocytes may be present in a minority of patients (30% of cases in one series).

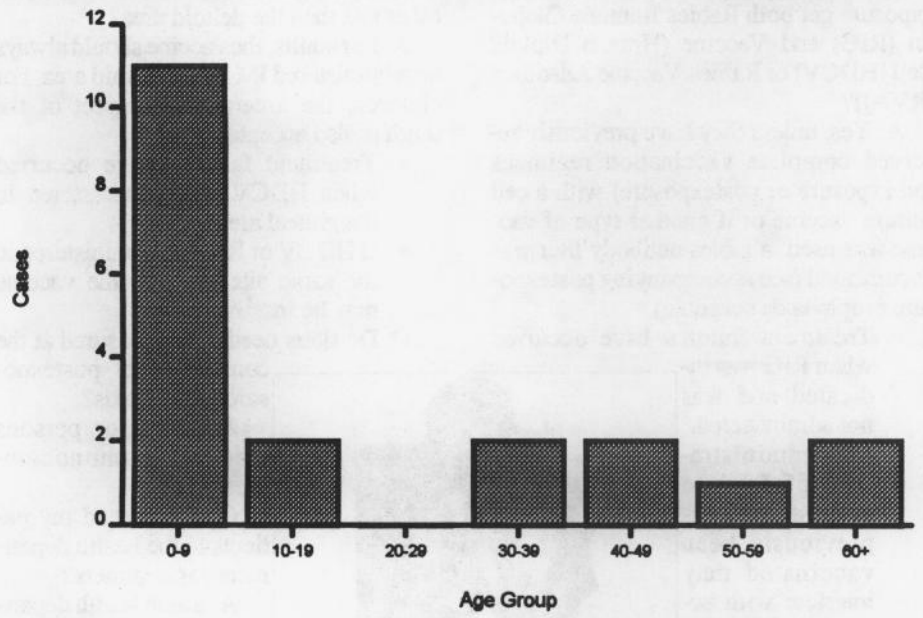
The organism is not normally detected using methods traditionally used for isolating and identifying common bacterial enteric pathogens (on lactose-containing media they are indistinguishable from other nonpathogenic *E. coli* strains). Diagnosis in the clinical laboratory setting requires specific culture of stool specimens for the organism on special agar containing sorbitol (known as sorbitol-MacConkey agar); on this medium colonies of O157:H7 strains are colorless because they ferment sorbitol slowly or not at all, in contrast to most other *E. coli* strains which would appear pink to red.[10]

If this agar is not available, 5 to 10 lactose-positive colonies from MacConkey agar can be screened serologically or tested for sorbitol fermentation.

An Alphabet Soup of *E. coli*

- **EPEC**: Enteropathogenic *E. coli*. These strains cause diarrhea in children less than two years of age and are well known for causing outbreaks of diarrhea in hospital newborn nurseries.
- **ETEC**: Enterotoxigenic *E. coli*. A worldwide cause of diarrhea in children and adults. Responsible for 40% of diarrheal illness among United States travelers to developing countries. Produce either a heat-labile (LT) enterotoxin or a heat-stable (ST) enterotoxin, or both.
- **EIEC**: Enteroinvasive *E. coli*. Causes an uncommon but severe diarrheal illness that mimics bacillary dysentery produced by Shigella organisms.
- **EHEC**: Enterohemorrhagic *E. coli*. These strains have recently been shown to cause a distinctive hemorrhagic colitis characterized by bloody diarrhea with little or no fever. Hemolytic uremic syndrome may develop as a late complication. These strains belong primarily to serotypes O157:H7 and O26:H11.

Figure 2. Reported cases of hemorrhagic colitis with or without hemolytic uremic syndrome, by age group (where known, N=20), Virginia, 1992



Suspicious colonies tentatively identified using one of the above procedures are only confirmed to be O157:H7 strains if they agglutinate in commercially available O157 and H7 antisera.

Almost all *E. coli* O157:H7 have been shown to produce one or two Shiga-like toxins (SLT types 1 or 2) that are cytotoxic for Vero cells, but this is not the only strain associated with SLT production. Each SLT is encoded by a lysogenic toxin-converting bacteriophage (a bacterial virus carries the gene for the toxin). EHECs, including *E. coli* O157:H7, also carry a 60-megadalton virulence plasmid that codes for a novel type of fimbria that is involved in the attachment of the bacteria to the intestinal wall. Detection of toxin production can only be done in some reference laboratories and research facilities using enzyme-linked immunosorbent assays for the detection of toxin in stool extracts or DNA probes to detect genes responsible for toxin production in *E. coli* colonies on an isolation plate. DNA probes have also been developed to detect the EHEC plasmid.

An enzyme-linked immunosorbent assay for detecting serum antibody to *E. coli* O157 lipopolysaccharide appears to be both sensitive and specific in identifying persons with recent *E. coli* O157:H7 infection.[11] However, this is likely to be more useful as an epidemiologic tool than a clinical tool. It is also unclear if this test will serve as a good marker of natural immunity from infection in the distant past.

Treatment

Treatment for this self-limited illness is supportive, with replacement of fluids and electrolytes (oral or IV). It is presently unclear if antimicrobials have any role in lessening illness severity or preventing sequelae. Some studies suggest antimotility agents may increase the risk of HUS.

Prevention and Control

Measures to prevent transmission include thorough cooking of beef (in particular, ground beef should be cooked until it is no longer pink), pasteurization of milk, proper sewage and water treatment, and careful handwashing with soap and water after using the toilet and before preparation of food.

On January 28, 1993, the U.S. Food and Drug Administration (FDA) issued an interim guidance to federal, state, and local regulatory officials recommending that ground beef products be cooked to heat all parts of the food to at least 68.3°C (155°F), superceding their model food code which currently calls for ground beef to be cooked to an internal temperature of 140°F. This guidance has been incorporated into the Virginai Department of Health's inspection and educational programs.

The basis for FDA's recommendation is research showing that the cooking time required to achieve a 5 log kill (100,000-fold reduction in viable organisms) of *E. coli* O157:H7 in beef emulsions is 8.34 minutes at 60°C (140°F) and only 0.13 minutes at 68.3°C (155°F).[12] Coliform counts in retail raw ground beef may be 1,000 per gram or higher.[13]

Freezing at -80°C and storage at -20°C for up to 9 months do not significantly reduce the population levels of the organism in contaminated meat.

Studies are needed to determine how to reduce fecal contamination of meat during slaughter and processing.

Submitted by Carl W. Armstrong, MD, Office of Epidemiology, VDH.

References

1. Centers for Disease Control and Prevention. Preliminary report: foodborne outbreak of *Escherichia coli* O157:H7 infections from hamburgers — western United States, 1993. MMWR 1993;42:85-86.

2. Riley LW, Remis RS, Helgerson SD, et al. Hemorrhagic colitis associated with a rare *Escherichia coli* serotype. N Engl J Med 1983;308:681-685.

3. Griffin PM, Tauxe RV. The epidemiology of infections caused by *Escherichia coli* O157:H7, other enterohemorrhagic *E. coli*, and the associated hemolytic uremic syndrome. Epidemiol Rev 1991;13:60-98.

4. Ostroff SM, Hopkins DP, Tauxe RV, Sowers EG, Strockbine NK. Surveillance of *Escherichia coli* O157:H7, isolation and confirmation, United States, 1988. In: *CDC Surveillance Summaries*, April 1991. MMWR 1991;40(No. SS-1):1-6.

5. Ostroff SM, Griffin PM, Tauxe RV, et al. A statewide outbreak of *Escherichia coli* O157:H7 infections in Washington State. Am J Epidemiol 1990;132:239-247.

6. Pai CH, Gordon R, Sims HV, Bryan LE. Sporadic cases of hemorrhagic colitis associated with *Escherichia coli* O157:H7. Clinical, epidemiologic, and bacteriologic features. Ann Intern Med 1984;101:738-742.

7. Griffin PM, Ostroff SM, Tauxe RV, et al. Illnesses associated with *Escherichia coli* O157:H7

infections: a broad clinical spectrum. Ann Intern Med 1988;109:705-712.

8. Martin DL, MacDonald KL, White KE, Soler JT, Osterholm MT. The epidemiology and clinical aspects of the hemolytic uremic syndrome in Minnesota. N Engl J Med 1990;323:1161-1167.

9. Karmali MA, Petrie M, Lim C, et al. The association between idiopathic hemolytic uremic syndrome and infection by verotoxin-producing *Escherichia coli*. J Infect Dis 1985;151:775-782.

10. Karmali MA. Laboratory diagnosis of verotoxin-producing *Escherichia coli* infections. Clin Microbiol Newsletter 1987;9:65-70.

11. Barrett TJ, Green JH, Griffin PM, Pavia AT, Ostroff SM, Wachsmuth IK. Enzyme-linked immunosorbent assays for detecting antibodies to Shiga-like toxin I, Shiga-like toxin II, and *Escherichia coli* O157:H7 lipopolysaccharide in human serum. Curr Microbiol 1991;23:189-195.

12. Line JE, Fain A Jr, Moran AB, et al. Lethality of heat to *Escherichia coli* O157:H7. D-value and Z-value determinations in ground beef. J Food Protect 1991;54:762-766.

13. Restaino L, Lyon RH. Efficacy of Petrifilm VRB for enumerating coliforms and *Escherichia coli* from frozen raw beef. J Food Protect 1987;50:1017-1022.

Surveillance Report Available

The Office of Epidemiology has available copies of the most recent annual summary of reportable disease statistics, entitled *Reportable Disease Surveillance in Virginia, 1991*. Edited by C. Diane Woolard, MPH and Leslie M. Branch in the Bureau of Disease Surveillance and Epidemiologic Studies, this is a comprehensive, 142-page book with sections on the descriptive epidemiology of each reportable disease, numbers of cases reported and rates for each locality, beautiful State maps showing disease incidence by locality, and cancer registry statistics for Virginia. If you are interested in a copy of this report, please call the Office at (804) 786-6261. This publication is distributed free of charge.

Human Rabies Postexposure Prophylaxis: Common Questions from Physicians

Q. Should every person who has a rabies exposure get both Rabies Immune Globulin (RIG) and Vaccine (Human Diploid Cell [HDCV] or Rabies Vaccine Adsorbed [RVA])?

A. Yes, unless they have previously received complete vaccination regimens (preexposure or postexposure) with a cell culture vaccine or if another type of vaccine was used, a rabies antibody titer was documented (see accompanying postexposure prophylaxis schedule).

- Treatment failures have occurred when RIG was indicated and was not administered.
- The administration of RIG to someone who has previously been vaccinated may interfere with active antibody response.

Q. Is it ever too late to administer postexposure prophylaxis?

A. It is not too late if the patient does not have active rabies. However, the usual recommendation is that treatment begin within 24 hours of the exposure; the earlier treatment is given the more likely it is that onset of disease will be prevented.

- If the incubation period is long, a delay in initiating treatment is less likely to matter.
- Incubation periods in humans have been reported as short as 5 days to as long as 6 years, but usually falls in the 2 to 8 week range.
- There have been instances when the decision to begin treatment was not made until many months after the exposure.

Q. What if RIG was not administered on the same day as the first dose of vaccine?

A. RIG can be administered up to the 7th day after the initiation of vaccine. However, the earlier it is administered the more likely it is to offer passive protection when it is needed.

Rabies Immunizing Products

Human Rabies Vaccine

- Rabies Vaccine, Human Diploid Cell (HDCV)
  Immovax Rabies
  Connaught Laboratories, Inc.
  1-800-822-2463
- Rabies Vaccine Adsorbed (RVA)
  Michigan Department of Public Health
  1-517-335-8050

Rabies Immune Globulin (RIG)

- Hyperab
  Cutter Biologicals
  1-800-288-8370
- Imogam
  Connaught Laboratories
  1-800-822-2463

Q. Can I give HDCV or RVA at some other site than the deltoid area?

A. For adults, the vaccine should always be administered IM in the deltoid area. For children, the anterolateral aspect of the thigh is also acceptable.

- Treatment failures have occurred when HDCV was administered in the gluteal area.
- If HDCV or RVA is administered in the same site as RIG, the vaccine may be inactivated.

Q. Do titers need to be measured at the completion of postexposure prophylaxis?

A. Only for persons who are immunocompromised.

Q. Can I send my patients to the health department for treatment?

A. Some health departments do provide this service. However, because both RIG, HDCV, and RVA are commercially available, private medical providers are expected to treat their own patients.

Q. Where can I get RIG and HDCV or RVA?

A. Rabies immunizing products can be ordered through your regular pharmaceutical supplier or directly from the manufacturers (see boxed text). Your local health department can help you locate rabies biologics in an emergency.

Q. Who pays for rabies postexposure prophylaxis?

A. Most third party payers (including medicaid and medicare, if all requirements are met) will cover the cost of rabies prophylaxis if it was for a bona fide exposure and is described as treatment, not vaccination. Persons who have limited resources can apply to their local health department for medical assistance; payment will be on a sliding scale.

If you have other questions, please call your local health department or Dr. Suzanne Jenkins at 804-786-6261.

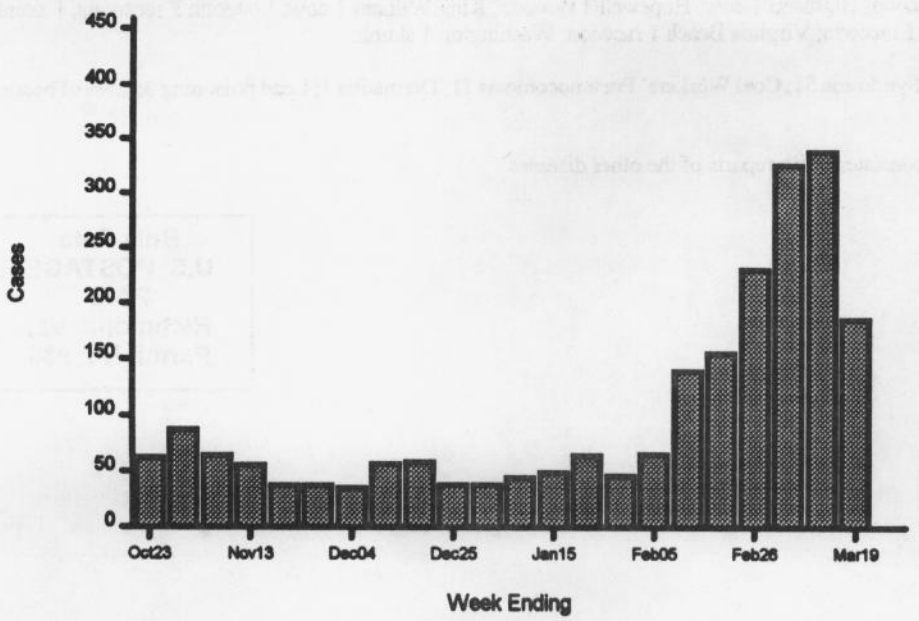
Submitted by Suzanne R. Jenkins, VMD, MPH, Office of Epidemiology, VDH.

Rabies postexposure prophylaxis schedule, United States, 1991

Vaccination status	Treatment	Regimen*
Not previously vaccinated	Local wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.
	HRIG	20 IU/kg body weight. If anatomically feasible, up to one-half the dose should be infiltrated around the wound(s) and the rest should be administered IM in the gluteal area. HRIG should not be administered in the same syringe or into the same anatomical site as vaccine. Because HRIG may partially suppress active production of antibody, no more than the recommended dose should be given.
	Vaccine	HDCV or RVA, 1.0 ml, IM (deltoid area†), one each on days 0, 3, 7, 14 and 28.
Previously vaccinated§	Local wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or RVA, 1.0 ml, IM (deltoid area†), one each on days 0 and 3.

*These regimens are applicable for all age groups, including children.
†The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.
§Any person with a history of preexposure vaccination with HDCV or RVA; prior postexposure prophylaxis with HDCV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

Influenza-like illness reported through March 19 of from sentinel physicians in Virginia (34 offices reporting). Activity in March has been characterized as 'widespread.' Nineteen influenza type B isolates have been reported from the northern region, and one each from the central and eastern regions. There have been 35 reported isolates of influenza type A from the northern region, some of which have been further characterized as A/Beijing/353/89 (H3N2). Two seroconversions to influenza type A and two seroconversions to influenza type B have been reported from the southwest region.



Virginia Reports Third Rabid Ferret

On January 26, 1993 an unvaccinated pet ferret that was usually kept indoors escaped from the house. The next day it was found with what appeared to be bite wounds. On February 25, while still under treatment for infected wounds, it began acting strangely and bit a member of the family. It was euthanized and tested for rabies; brain material was fluorescent antibody positive. Postexposure treatment was administered to five family members

and close friends.

This is the third rabid ferret reported in Virginia. All three rabid ferrets have had a history that indicated an opportunity to be exposed to a rabid animal. The first report, from Fairfax County in 1982, concerned a pet ferret that had a behavior change approximately a month after having been observed in a fight with a raccoon. The second animal, from Loudoun County in 1992, had escaped from the house and had been attacked by an unknown animal approximately one month before developing ascending paralysis.

These histories are similar to those for many of the rabid dogs and cats in Virginia and point out the importance of considering any bite wound that could have come from a wild animal as a potential rabies exposure. The safest recommendation for unvaccinated pets in these circumstances is euthanasia. An alternative would be at least six months of strict isolation. Vaccinated pets that have possible rabies exposures should receive an immediate booster. After boostering, dogs and cats should be confined and observed for three months. Because data on vaccinated ferrets that are exposed to wild rabies virus is so limited, these animals should be placed in strict isolation for a minimum of three months following their booster vaccination.

Cases of Selected Notifiable Diseases, Virginia, February 1 through February 28, 1993.*

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	112	11	31	16	39	15	175	89	84
Campylobacteriosis	26	6	6	4	8	2	42	69	63
Gonorrhea†	530	-	-	-	-	-	921	3786	2685
Hepatitis A	16	0	9	1	3	3	28	19	19
Hepatitis B	12	1	2	6	2	1	21	38	39
Hepatitis NANB	2	0	1	1	0	0	2	6	6
Influenza	18	10	0	4	1	3	217	108	875
Kawasaki Syndrome	2	0	2	0	0	0	2	5	3
Legionellosis	0	0	0	0	0	0	0	2	2
Lyme Disease	3	0	2	0	0	1	3	11	4
Measles	0	0	0	0	0	0	1	4	2
Meningitis, Aseptic	27	3	11	7	1	5	35	41	29
Meningitis, Bacterial‡	4	0	1	2	0	1	5	30	29
Meningococcal Infections	2	0	1	1	0	0	6	13	10
Mumps	5	0	3	1	0	1	9	14	11
Pertussis	1	0	0	0	1	0	1	2	2
Rabies in Animals	22	5	8	3	3	3	55	30	31
Reye Syndrome	0	0	0	0	0	0	0	0	0
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	0
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	69	7	21	10	16	15	129	109	140
Shigellosis	30	5	3	0	14	8	41	17	49
Syphilis (1° & 2°)†	43	0	1	0	3	39	87	102	106
Tuberculosis	0	0	0	0	0	0	0	38	37

Localities Reporting Animal Rabies: Alexandria 1 raccoon; Appomattox 1 skunk; Arlington 1 raccoon; Augusta 1 dog, 1 raccoon; Brunswick 1 fox; Charlotte 1 cow; Fairfax 3 raccoons; Frederick 1 raccoon; Highland 1 cow; Hopewell 1 raccoon; King William 1 cow; Loudoun 2 raccoons, 1 skunk; Montgomery 1 raccoon; Shenandoah 1 cow; Suffolk 1 raccoon; Virginia Beach 1 raccoon; Washington 1 skunk.

Occupational Illnesses: Asbestosis 8; Carpal Tunnel Syndrome 51; Coal Workers' Pneumoconiosis 11; Dermatitis 1; Lead poisoning 3; Loss of hearing 12; Repetitive Motion Disorder 2; Silicosis 1.

*Data for 1993 are provisional.

†Total now includes military cases to make the data consistent with reports of the other diseases.

‡Other than meningococcal.

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