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Human Rabies, 1994

The April 14, 1995, issue of the Morbidity and Mortality Weekly Report (MMWR) described the investigations by state and local health departments and CDC into three deaths due to human rabies that occurred in October and November 1994. The following includes the editorial note associated with the MMWR report and a table describing all six cases of rabies-associated deaths that occurred in 1994.

In 1994, six rabies-associated deaths occurred in humans -- the highest annual number of rabies deaths in the United States since 1979. Clear evidence of an animal bite (as reported by the patient or a family member) was documented for nine (27%) of the 33 human rabies deaths during 1977-1994, compared with 24 (89%) of 27 deaths during 1960-1976. Of the nine bite exposures in cases that occurred during 1977-1994, eight were associated with dogs outside the United States or near the Mexico-U.S. border, compared with five of 24 bite exposures during 1960-1976.

Nucleotide sequence analysis enables the identification of rabies virus variants responsible for human infection and assists in elucidating the circumstances that may have led to virus exposure. This analysis has been conducted on specimens from all 18 cases since 1980 for which no animal bite was identified. Of these, 10 (56%) cases were associated with variants present in insectivorous bats; seven (39%) were associated with variants present in domesticated dogs outside the United States or at the U.S.-Mexico border; and one was associated with a variant present in skunks in the south-central United States.

Bat rabies is enzootic in the United States and has been documented in all 48 contiguous states. Because some bat bites may be less severe -- and therefore more difficult to recognize -- than bites inflicted by larger animals, rabies postexposure prophylaxis should be considered for any physical contact with bats when bite or mucous membrane contact cannot be excluded.

Despite the increase in human rabies in 1994, the overall occurrence of human rabies in the United States has declined since the mid-1950s. This trend reflects several factors, including improvements in human postexposure prophylaxis and dog rabies control. Most cases of human rabies in the United States now result from a lack of identification or recognition of risks (e.g., contact with bats) and the failure to administer treatment.

In 1993, the number of reported cases of animal rabies in the United States reached a record level (9495 cases), primarily reflecting the ongoing epizootic of raccoon rabies in the eastern United States and the emergence of coyote rabies in south Texas. The estimated cost of human postexposure prophylaxis as a result of potential exposure to these animals is $45 million annually (A total of 200 persons associated with the three cases described in this MMWR article received postexposure treatment). The cases described in this report and the substantial medical costs associated with prophylaxis emphasize the need for strengthening control and prevention measures, including appropriate vaccination of all dogs and cats, consideration of rabies in the differential diagnosis early in the course of neurologic disease of unknown origin, avoidance of stray and wild animals by humans and pets, and consideration of postexposure prophylaxis for persons potentially exposed to bats even where a history of physical contact cannot be elicited.

SOURCE: MMWR 44(14);269-272 DATE: Apr 14, 1995

In This Issue:

Human Rabies Cases, United States, 1994

State of Residence	Date of Onset	Date of Death	Age	Sex	Bite Reported	Virus Variant
California	12/29/93	01/18/94	44	M	No	Silver-haired bat
Florida	06/03/94	06/21/94	40	M	No	Haitian dog
Alabama	09/29/94	10/11/94	24	F	No	Mexican free-tailed bat
West Virginia	10/03/94	10/15/94	41	M	No	Silver-haired bat
Tennessee	11/08/94	11/23/94	42	F	No	Silver-haired bat
Texas	11/13/94	11/27/94	14	M	No	Texas fox/Mexican dog

Helicobacter pylori in Peptic Ulcer Disease*

VEB Editor's Note: The following is a summary of a conference on *Helicobacter pylori* sponsored by the National Institutes of Health in February 1994.

Abstract

The National Institutes of Health Consensus Development Conference on Helicobacter pylori *in Peptic Ulcer Disease brought together specialists in gastroenterology, surgery, infectious diseases, epidemiology and pathology, as well as the public, to address the following questions: (1) What is the causal relationship of* H. pylori *to upper gastrointestinal disease? (2) How does one diagnose and eradicate* H. pylori *infection? (3) Does eradication of* H. pylori *infection benefit the patient with peptic ulcer disease? (4) What is the relationship between* H. pylori *infection and gastric malignancy? (5) Which* H. pylori*-infected patients should be treated? (6) What are the most important questions that must be addressed by future research in* H. pylori *infections? Following 1½ days of presentations by experts and discussion by the audience, a consensus panel weighed the evidence and prepared their consensus statement.*

Among their findings, the consensus panel concluded that: (1) ulcer patients with H. pylori *infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation with the illness or on recurrence; (2) the value of treating nonulcer dyspepsia patients with* H. pylori *infection remains to be determined; and (3) the interesting relationship between* H. pylori *infection and gastric cancers requires further exploration.*

What is the Causal Relationship of *H. pylori* to Upper Gastrointestinal Disease?

A strong association between *H. pylori* and upper gastrointestinal disease has been reported. The causal relationship between *H. pylori* and chronic superficial gastritis is well established. A causal relationship between *H. pylori* and peptic ulcer disease is more difficult to establish from the available data in part because of the lack of an animal model and because only a small proportion of individuals harboring the organism develop ulceration. However, nearly all patients with duodenal ulcer have *H. pylori* gastritis.

The strongest evidence for the pathogenic role of *H. pylori* in peptic ulcer disease is the marked decrease in the recurrence rate of ulcers following the eradication of infection. To date there is no convincing evidence for an association of *H. pylori* infection with nonulcer dyspepsia. The prevalence of *H. pylori* infection is no higher in patients with nonulcer dyspepsia than in the general population. Studies are needed to determine whether *H. pylori*-infected patients with nonulcer dyspepsia would benefit from treatment of the infection.

All patients with gastric or duodenal ulcers who are infected with *H. pylori* should be treated with antimicrobials.....

How Does One Diagnose and Eradicate *H. pylori* Infection?

Methods to diagnose patients with *H. pylori* infection can be divided into invasive and noninvasive diagnostic tests (see Table on page 3). The invasive tests include endoscopy followed by gastric biopsy and histologic demonstration of organisms, biopsy with direct detection of urease activity in the tissue specimen, and biopsy with culture of the *H. pylori* organism. Although culturing the organism is traditionally considered the "gold standard" for diagnosis of many infectious agents, it is the least sensitive diagnostic test (approximately 70-80 % positivity). Both histologic demonstration of the organism by Giemsa or Warthin-Starry stains and urease testing have sensitivities and specificities above 90%.

Excellent diagnostic sensitivities and specificities (>95 %) are also obtained with noninvasive tests for the initial diagnosis of *H. pylori* infection. These include serology for immunoglobulin G antibodies to *H. pylori* antigens and breath tests of urease activity using orally administered ^{14}C- or ^{13}C-labeled urea. A number of highly accurate serologic kits for diagnosis of *H. pylori* infection are available. Labeled urea breath tests have had restricted availability as research tools in the past, but commercial assays will be available in the near future.

It is important to note that with the exception of the serologic assays all of the tests for diagnosis of *H. pylori* infection may be falsely negative in patients who have taken antibiotics, bismuth compounds, or omeprazole in the recent past.

Presently, there is no readily available, inexpensive, and accurate noninvasive method to monitor eradication of *H. pylori*. Without such an assay, routine monitoring for relapse, reinfection, or treatment failure cannot be recommended. Even if such a test were available, testing all patients treated for *H. pylori* infection probably would not be necessary in view of the high efficacy of treatment and low reinfection rate. Important exceptions would be patients with complicated, recurrent or refractory peptic ulcers who should be evaluated for successful eradication of infection before cessation of antiulcer therapy.

Consideration of the therapeutic options should take into account efficacy, compliance, side effects, and cost. A triple antimicrobial regimen consisting of bismuth subsalicylate, tetracycline, and metronidazole has been studied extensively and can yield eradication rates of approximately 90%. Substitution of amoxicillin for tetracycline or metronidazole lowers efficacy only slightly (greater than 80%). One promising study reported efficacy of approximately 90% with the combination of ra-

Diagnosis Modalities for *Helicobacter pylori* Infection†		
MODALITY	**ADVANTAGES**	**DISADVANTAGES**
Endoscopy with biopsy	Detection of ulcers, neoplasms	Invasive, expensive, time consuming
Culture	Antimicrobial susceptibilities possible	Not optimally sensitive, time consuming
Histology	More sensitive than culture, allows direct visualization	Insensitive with small numbers of organisms, time consuming
Urease detection	Rapid	Bacterial overgrowth can result in false positives
Serology	Noninvasive, rapid, quantitative, inexpensive	Can't determine pathology, doesn't change with therapy
Urea breath tests	Noninvasive, rapid, quantitative, changes with therapy	Can't determine pathology, expensive instrumentation

nitidine, metronidazole, and amoxicillin. Although variable, eradication rates of greater than 80% have also been reported with the combination of omeprazole (a proton-pump inhibitor) and amoxicillin. Omeprazole should be given at least twice daily, and the two agents begun at the same time because immediate pretreatment with omeprazole lowers efficacy of the omeprazole-amoxicillin combination. Two- or three-drug regimens should last two weeks. If therapy is begun at the time of active peptic disease, treatment with antisecretory agents in addition to antimicrobials is recommended. If symptoms persist or recur after initial treatment, diagnostic reevaluation should be undertaken and a second course of therapy considered. Side effects are more frequent with the three-drug regimen than with the two-drug regimen but have been mild in either case and infrequently have prevented completion of therapy. Safety and efficacy of antimicrobial therapy in *H. pylori*-infected children and adolescents have not been studied in detail.

Resistance to antimicrobials, in particular to nitroimidazoles such as metronidazole, is an important problem and a cause for treatment failure in some studies. Application of currently available one-drug regimens has led to enhanced antimicrobial resistance and thus is strongly discouraged.

Does Eradication of *H. pylori* Infection Benefit the Patient with Peptic Ulcer Disease?

Available studies have demonstrated clearly the principal benefit of eradication in patients with peptic ulcers is a substantial reduction in the risk of ulcer recurrence (to less than 10% in one year). The side effects of current regimens for eradication of *H. pylori* infection are generally minor and are outweighed by the benefit of reduced ulcer recurrence. When combined with standard antisecretory therapy, *H. pylori* eradication may contribute to a modest reduction in time to ulcer healing. Moreover, eradication of *H. pylori* infection may enhance healing of ulcers refractory to conventional therapy.

The potential cost savings associated with treating *H. pylori* infection have not been established but may be substantial.

Which *H. pylori*-Infected Patients Should be Treated?

All patients with gastric or duodenal ulcers who are infected with *H. pylori* should be treated with antimicrobials regardless of whether they are suffering from the initial presentation of the disease or from a recurrence. At the present time there is no reason to consider routine detection or treatment of *H. pylori* infection in the absence of ulcers.

Conclusion

The discovery of *H. pylori* as a gastrointestinal pathogen has had a profound effect on current concepts of peptic ulcer disease pathogenesis. Evidence presented at this Consensus Development Conference has led to the following conclusions:

- Ulcer patients with *H. pylori* infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation with the illness or on recurrence.
- The value of treatment of nonulcer dyspepsia patients with *H. pylori* infection remains to be determined.
- The interesting relationship between *H. pylori* infection and gastric cancers requires further exploration.

*Adapted from *Helicobacter pylori* in Peptic Ulcer Disease. NIH Consensus Statement 1994 Feb 7-9; 12(1):1-22.

† Adapted from Blaser, MJ. *Helicobacter pylori* and related organisms. 1995. In: Mandell, Douglas and Bennett, eds. Principles and Practice of Infectious Diseases, 4th ed. Churchill Livingstone Inc.

Cases of Selected Notifiable Diseases, Virginia, March 1 through March 31, 1995.*

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	79	3	10	9	31	26	235	349	276
Campylobacteriosis	19	4	2	5	6	2	78	107	90
Gonorrhea†	1013	63	90	147	229	484	2898	3195	3617
Hepatitis A	14	0	2	5	3	4	48	33	40
Hepatitis B	10	0	1	3	1	5	22	26	47
Hepatitis NANB	0	0	0	0	0	0	0	13	9
Influenza	36	7	0	23	1	5	564	802	654
Kawasaki Syndrome	3	0	1	2	0	0	3	4	6
Legionellosis	2	1	0	0	1	0	2	2	3
Lyme Disease	1	0	0	1	0	0	2	11	9
Measles	0	0	0	0	0	0	0	1	8
Meningitis, Aseptic	14	3	4	1	1	5	34	36	47
Meningitis, Bacterial‡	13	2	1	3	2	5	33	17	31
Meningococcal Infections	11	1	2	1	1	6	21	19	15
Mumps	3	0	0	0	1	2	7	11	15
Pertussis	0	0	0	0	0	0	0	13	6
Rabies in Animals	34	6	3	8	13	4	78	85	60
Reye Syndrome	0	0	0	0	0	0	0	1	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	41	6	7	8	6	14	162	161	187
Shigellosis	10	2	4	1	0	3	36	131	68
Syphilis (1° & 2°)†	155	3	1	15	21	115	342	349	362
Tuberculosis	22	0	5	0	5	12	29	76	84

Localities Reporting Animal Rabies: Accomack 1 raccoon; Arlington 1 raccoon; Augusta 1 raccoon; Bath 1 raccoon; Buckingham 1 raccoon; Charlotte 1 skunk; Cumberland 1 raccoon; Dinwiddie 2 raccoons; Essex 1 raccoon; Fairfax 1 raccoon; Fauquier 1 raccoon; Floyd 1 raccoon; Franklin County 1 skunk; Frederick 1 raccoon, 1 skunk; Grayson 1 raccoon; Halifax 2 raccoons; Hanover 2 skunks; Hopewell 1 raccoon; Louisa 1 raccoon; Middlesex 1 fox; Montgomery 2 skunks; Patrick 1 raccoon; Pittsylvania 1 skunk; Prince Edward 1 raccoon, 1 skunk; Prince William 1 raccoon; Pulaski 1 skunk; Richmond City 1 raccoon; Westmoreland 1 skunk.

Occupational Illnesses: Asbestosis 16; Carpal Tunnel Syndrome 50; Coal Workers' Pneumoconiosis 21; De Quervain's Syndrome 2; Lead Poisoning 1; Loss of Hearing 27.

*Data for 1995 are provisional.

†Other than meningococcal. ‡ Includes primary, secondary, and early latent.

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