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Field Evaluations of Pre-exposure Use

Human Diploid Cell Rabies Vaccine

Following a case of human rabies in a Peace Corps volunteer (PCV) in Kenya in August 1983,[1] the Centers for Disease Control (CDC), in cooperation with the Office of Medical Services, U.S. Peace Corps, conducted serosurveys of 333 PCVs in eight countries to assess the adequacy of rabies pre-exposure prophylaxis. Initial results indicate a lower-than-expected antibody response at several time periods following primary immunization.

All PCVs had been immunized outside the United States between 1979 and 1983 using a three-dose regimen (days 0, 7, and 28) of 0.1 ml intradermal (ID) doses of human diploid cell rabies vaccine (HDCV) produced by the Merieux Institute.[2] Serum specimens were collected by either CDC or the Peace Corps medical staff, and the rapid fluorescent focus inhibition test (RFFIT) for rabies-neutralizing antibody was performed at CDC on all specimens. Time from the initial immunization to sera collection ranged from 42 days to 2 years.

PCVs serving in Kenya were most extensively studied. From September 1983 to October 1983, complete immunization histories and serum samples for rabies antibody determination were obtained from 90 of the approximately 250 PCVs in Kenya. Three cohorts were identified based on the time between primary immunization and collection of sera: (1) those immunized 45 days before phlebotomy; (2) those immunized 10-16 months before phlebotomy; (3) those immunized 2 years before phlebotomy. Serologic results for these groups were compared with results from previously published data at similar time periods after primary immunization (Table 1). Of the 25 specimens obtained 45 days after the beginning of primary immunization, only 17 (68%) were 0.50 or more international units (IU)/ml, and five (20%) were lower than 1:16.** One of this group of 25 had no detectable antibody (< 1:5 or < 0.05 IU/ml serum). An investigation in Kenya found no breaks in the vaccine cold chain; observations of vaccine admin-

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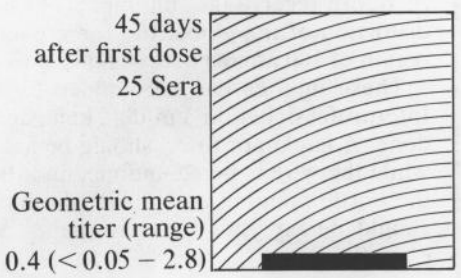
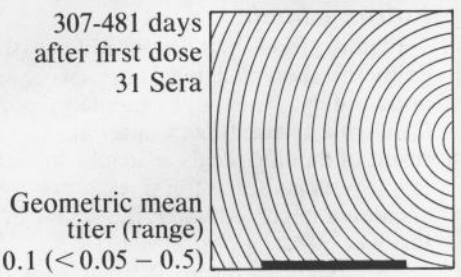
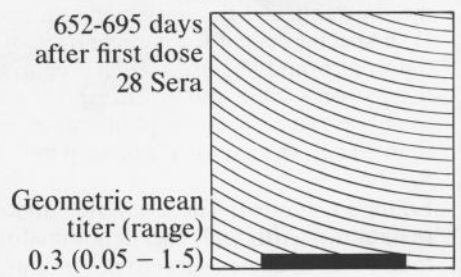
Table 1. Rabies antibody titers* at indicated times after primary intradermal immunization with human diploid cell rabies vaccine†

	Kenya Peace Corps Volunteers	*Oklahoma Veterinary Students*[5]
		
	45 days after first dose 25 Sera	49 days after first dose 26 Sera
	Geometric mean titer (range) 0.4 (< 0.05 – 2.8)	Geometric mean titer (range) 7.4 (1.5 – 25.7)
		
	307-481 days after first dose 31 Sera	365 days after first dose 26 Sera
	Geometric mean titer (range) 0.1 (< 0.05 – 0.5)	Geometric mean titer (range) 1.6 (0.3 – 10.0)
		
	652-695 days after first dose 28 Sera	730 days after first dose 11 Sera
	Geometric mean titer (range) 0.3 (0.05 – 1.5)	Geometric mean titer (range) 1.7 (0.4 – 5.6)

**Expressed as IU/ml serum.*
†Specimens from six PCVs did not fit into any of these cohorts and are therefore not shown in the table.

Continued

istration revealed satisfactory ID technique.

In addition to the PCVs serving in Kenya, 83 PCVs from Malawi, Morocco, Nepal, Central African Republic, Senegal, and Sierra Leone were studied within 4 months of primary immunization; 36 (43%) had titers less than 0.5 IU/ml or lower than 1:50; one (1%) of these had no detectable antibody.

Initial surveys of groups immunized within the last 16 months with ID preexposure HDCV in the United States revealed different results. All 57 persons in a cohort from North Carolina had titers 1:50 or higher at 38 days after primary immunization. Forty-two days after primary immunization, all of 61 persons immunized ID and studied by the RFFIT in Wisconsin had antibody levels of 1:50 or higher. However, analysis of an adult cohort of 193 persons immunized in Maryland revealed 188 (97%) with titers of 1:50 or higher, four (2%) with titers 1:16-1:50, and one (1%) with no detectable antibody at 41-97 days after primary ID immunizations. Reported by K Pulley, PhD, R Gibbs, MD, K Miller, MD, Peace Corps, Washington, DC; S Waterman, M Mandara, Peace Corps, Nairobi, Kenya; B Ainsworth, Peace Corps, Lilongwe, Malawi; J Bond, MD, Washington County Health Dept, Hagerstown, Maryland; D Howard, DVM, North Carolina State University School of Veterinary Medicine, Raleigh; J Calkins, University Health Svc, University of Wisconsin—Madison, D Nelson, Wisconsin State Laboratory of Hygiene, Madison; Div of Viral Diseases, Center for Infectious Diseases, CDC.

***At present, CDC considers an antibody titer of 1:16 or higher an adequate response to vaccination in sera collected 14-21 days after the last injection.[3] The World Health Organization considers 0.5 IU/ml an adequate response.[4]*

Editorial note: The use of HDCV administered ID has become widespread throughout the world because of the cost savings when using small doses for rabies pre-exposure prophylaxis. However, the U.S. Food and Drug Administration's (FDA) National Center for Drugs and Biologics has not approved the ID use of rabies vaccine; and an application for licensure of ID rabies vaccine is presently being considered. In May 1982, the Immunization Practices Advisory Committee (ACIP) reviewed the data from 11 carefully conducted clinical studies in the United States and Europe, and at that time, found the ID route an acceptable alternative to the intramuscular (IM) route.[2] The rabies antibody titers following ID immunization were lower than those after IM immunization and persisted for a shorter period of time. The data presented here indicate that HDCV administered ID to PCVs in multiple

Safety Tips for Festive Occasions[1]

Champagne-Cork Injury to the Eye

Many eye injuries from flying champagne corks have occurred since the invention of the champagne cork at the end of the 17th century. A recent series described eye injuries in eight patients, four of whom were waiters or waitresses.[2] It is interesting that the inventor of the champagne cork, a Benedictine monk by the name of Dom Perignon, was himself blind, although the cause is not known.

A 1 ounce cork shooting from an upright bottle can reach a height of 40 feet. Quite often the cork is ejected spontaneously on removing the wire around the bottle neck. It has been recommended that champagne be served at a temperature of 8.3°C (47°F), and at this temperature the pressure in the bottle is about 90 lb. per square inch. At room temperature or higher the bottle pressure is even greater, and it may be further increased by shaking the bottle.

From this knowledge, it can be calculated that the cork strikes the eye at a velocity of about 45 feet per second. At this speed a cork could fly to the eye from the held bottle in less than 0.05 seconds, before the blink reflex (which takes about 0.1 second) can exert its protective effect. The cornea could therefore receive the full impact. Considering the small area of impact and the distortion of the globe, the force exerted on the eye is estimated to be in the region of 100 atmospheres—similar to that in a blast injury.

These injuries can be avoided by care in opening the bottle. The Comité Interprofessionel du Vin de Champagne has recommended how this should be done. A napkin or towel should be held over the cork and the neck of the bottle while the wire is being undone, and the cork is then to be gently eased off with the bottle pointing away from the face and other persons in the room. There should be no "pop", just a sigh. "White gloves may be worn but are not essential."

Patron Flambé

Flaming foods and drinks add a festive touch to a meal. Patrons of restaurants enjoy the showmanship of the server and fully expect that the flaming shows are done safely. This, unfortunately, is not always the case. The University of California Irvine Burn Center has reported treating eight patients for burns as a result of flaming meals or drinks in restaurants.[3] Many of the patients (half were employees) suffered full thickness burns and required skin grafting. Three of the accidents occurred when the liquor in the bottle caught fire, producing a flame thrower effect.

As a result of these accidents, the Newport Beach (California) Fire Department established the following requirements for serving flaming food or drinks: (1) a special permit for flaming food or drinks; (2) a maximum of 30 ml (1 oz) of liquor or brandy be used when preparing the dish; (3) preparation of the dishes at the patron's table and no transport of the food or drink while ignited; (4) a wet towel be available in the preparation area in case of accident; (5) no flame higher than 20 cm. (8 in.); (6) a spill-stop pouring device to be put on all bottles used for flambe.

Editor's comment: These injuries undoubtedly occur in the home as well as the restaurant. Although the denominators (total champagne bottles opened and total flaming dishes served) are unknown they are undoubtedly large, signifying that the incidence of these injuries is probably very low. It is regrettable, however, that any occur at all.

References

1. Adapted from: State of California, Department of Health Services. Safety tips for festive occasions. California Morbidity. 1982 (48).
2. Archer D, Galloway N. Champagne-cork injury to the eye. Lancet 1967; 2: 487-9.
3. Achauer BM, Bartlett RH, Allyn PA. Face Flambé. JAMA 1982; 247: 2271.

countries has not resulted in antibody titers as high as those demonstrated in vaccine trials conducted in the United States and Europe between 1978 and 1982. [5,6] All the above studies are based on the use of Merieux Institute's HDCV; there are no available data on response to ID vaccination with Wyeth Laboratories' HDCV.

Several factors might hypothetically contribute to the less satisfactory antibody responses seen in PCVs, including immunosuppressive effects of multiple vaccinations, immune serum globulin, or malaria chemoprophylaxis administered concurrently with the vaccine; a greater likelihood of cold-chain infractions; and perhaps a greater likelihood of receiving vaccine subcutaneously rather than ID. However, none of these factors appears at this time sufficient to explain the magnitude of the discrepancies in antibody responses described in the published trials and those observed in these recent field experiences. CDC and FDA are investigating other factors, including variations in vaccine potency.

Because the nature and extent of the problem are not completely delineated, certain precautions appear to be indicated. If ID pre-exposure rabies prophylaxis is given, routine serologic testing should be done 2-3 weeks after immunization. Any individual with a postimmunization titer of lower than 1:16 (approximately 0.16 IU/ml) should receive an additional dose of vaccine and have serum retested 2-3 weeks later. Persons whose only experience with rabies vaccine has been ID pre-exposure prophylaxis and whose antibody response is unknown should, if immunized within the past 12 months, have serum tested for rabies antibody; if immunized more than 12 months previously, such persons should receive a single booster dose of vaccine and have serum retested 2-3 weeks later. Serologic testing does not appear to be necessary for persons receiving IM rabies pre-exposure prophylaxis.

For postexposure prophylaxis, persons (1) who have had three 1.0 ml IM doses of HDCV or (2) who have received ID vaccine and who have a documented rabies titer of 1:16 or higher should continue to receive two 1.0 ml IM doses of HDCV—one dose each on days 0 and 3, as currently recommended. Any person who has received ID vaccine and who has not had a documented rabies antibody titer of 1:16 or higher should be treated with a single, 20 IU/kg dose of human rabies immune globulin (HRIG) and five 1 ml IM doses of HDCV—one each on days 0, 3, 7, 14, and 28.

It should be reemphasized that all persons who have received adequate pre-exposure prophylaxis with HDCV should, following a rabies exposure, receive two 1.0 ml IM postexposure booster doses of vaccine to ensure protection.

Additional Guidelines Regarding Intradermal

Administration of Rabies Vaccine

In light of the findings reported above, the Division of Epidemiology, Virginia Department of Health has issued additional recommendations regarding the intradermal (ID) use of human diploid cell rabies vaccine (HDCV). If it is elected to administer ID pre-exposure rabies prophylaxis, these procedures should be followed:

1. At this time only Merieux vaccine is used in the 0.1 cc ID regimen. There is no available data on response to ID vaccination with Wyeth Laboratories' HDCV.
2. The schedule for administration of the 3 doses of vaccine should be adhered to as closely as possible i.e., Day 0, Day 7 and Day 21 or 28.
3. The site of administration is the lateral aspect of the upper arm over the deltoid.
4. Great care must be taken to be sure the vaccine is administered *intradermally;* some inadvertent subcutaneous administrations have occurred and may result in lower titers and shorter duration of immunity. A bleb should appear at the site of the injection if it is properly administered.
5. A *minimum of 0.1 cc* should be administered, intradermally. The potential for the administration of a less than adequate dose is amplified by using the 1 cc vial for multidoses of 0.1 cc. Rarely can more than six (6) 0.1 cc doses be extracted safely from a 1 cc vial.
6. Reconstitute and handle the vaccine correctly. Be sure the cold chain has not been broken. Be sure the vaccine is properly mixed with the diluent. Merieux Institute claims that once reconstituted HDCV will remain stable for up to eight hours if maintained under refrigeration. However, it seems prudent to use the reconstituted vaccine as soon as possible.
7. Please inform all patients that pre exposure immunization does not guarantee protection. If they become aware of bona fide exposures they must receive booster vaccinations as described in the final 2 paragraphs of the MMWR article.
8. A routine booster of 0.1 cc intradermally should be administered every 2 years as qualified in the MMWR article.
9. Please keep a record of names and addresses of all people who receive rabies pre exposure immunization. They may need to be contacted in the future if other changes should occur in the present immunization recommendations.

References

1. CDC. Human rabies—Kenya. MMWR 1983;32:494-5.
2. ACIP. Supplementary statement on pre-exposure rabies prophylaxis by the intradermal route. MMWR 1982;31:279-80, 285.
3. ACIP. Rabies prevention. MMWR 1980;29:265-80.
4. Sinnecker H, Atanasiu P, Bahmanyar M, et al. Vaccine potency requirements for reduced immunization schedules and pre-exposure treatment. Joint WHO/IABS Symposium Standardization of Rabies Vaccines for Human Use Produced in Tissue Cultures (Rabies III), Marburg/Lahn. Develop Biol Standard 1977;40:267-71.
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6. Nicholson KG, Turner GS, Aoki FY. Immunization with a human diploid cell strain of rabies virus vaccine: two-year results. J Infect Dis 1978;137:783-8.

Reprinted from the MMWR 1983; 32: 601-3

Erratum

Last month's Epidemiology Bulletin *(#8) contained an article on* Yersinia enterocolitica *infections in Virginia. Yersiniosis was incorrectly spelled as yersinosis in that article.*

Month: September, 1983

Disease	State					Regions				
	This Month	Last Month	Total to Date 1983	Total to Date 1982	Mean 5 Year To Date	This Month N.W.	This Month N.	This Month S.W.	This Month C.	This Month E.
Measles	0	0	23	14	686	0	0	0	0	0
Mumps	0	5	30	33	94	0	0	0	0	0
Pertussis	1	0	46	23	12	0	1	0	0	0
Rubella	0	1	2	12	101	0	0	0	0	0
Meningitis—Aseptic	71	42	199	152	157	14	22	9	8	18
Other Bacterial	15	4	183	153	135	2	0	3	3	7
Hepatitis A (Infectious)	13	12	101	137	189	3	5	0	2	3
B (Serum)	43	40	414	367	348	4	11	5	7	16
Non-A, Non-B	9	1	61	58	36	2	0	1	1	5
Salmonellosis	217	172	1,080	1,117	973	32	31	32	60	62
Shigellosis	27	24	137	117	318	8	3	1	1	14
Campylobacter Infections	64	58	403	266	*145	11	17	4	15	17
Tuberculosis	38	39	374	466	—	—	—	—	—	—
Syphilis (Primary & Secondary)	49	49	426	458	424	0	6	6	15	22
Gonorrhea	1,970	1,919	15,292	14,822	16,670	—	—	—	—	—
Rocky Mountain Spotted Fever	13	10	60	70	88	4	0	3	3	3
Rabies in Animals	30	51	520	441	115	7	23	0	0	0
Meningococcal Infections	3	3	62	54	61	1	0	0	0	2
Influenza	3	8	896	340	2,266	1	0	2	0	0
Toxic Shock Syndrome	0	1	6	6	*7	0	0	0	0	0
Reyes Syndrome	0	0	5	4	12	0	0	0	0	0
Legionellosis	1	2	19	16	14	0	0	1	0	0
Kawasaki's Disease	1	2	34	11	14	0	0	0	0	1
Other:	—	—	—	—	—	—	—	—	—	—

Counties Reporting Animal Rabies: Arlington 1 raccoon; Augusta 1 raccoon; Culpeper 1 skunk; Fauquier 1 raccoon; Orange 1 raccoon; Rockingham 1 gray fox; Spotsylvania 1 raccoon; Stafford 1 raccoon; Alexandria 4 raccoons; Fairfax 13 raccoons, 2 skunks, 1 bat; Loudoun 2 raccoons.

Occupational Illnesses: Occupational hearing loss 1; Occupational pneumoconiosis 52; Asbestosis 6; Hypersensitivity pneumonitis 3.

*3 year means

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Wishing Readers A Safe And Happy Holiday Season And New Year