

WHO Collaborative Study on the Sero-epidemiology of Rubella in Caribbean and Middle and South American Populations in 1968*

W. R. DOWDLE,¹ W. FERREIRA,² L. F. DE SALLES GOMES,³
D. KING,⁴ M. KOURANY,⁵ J. MADALENGOITIA,⁶ E. PEARSON,⁷
W. H. SWANSTON,⁸ H. C. TOSI⁹ & A. M. VILCHES¹⁰

Knowledge of the rubella antibody profiles of female populations of various ages and in various geographical areas is essential for an intelligent and effective administration of rubella vaccine. The investigation reported was undertaken to extend a previous WHO collaborative study to include additional areas of the Americas. As in the other mainland areas included in the earlier study, the presence of rubella haemagglutination-inhibiting antibody was found to be a likely event in over 80% of the females of child-bearing age in Argentina, Brazil, Chile, urban Peru (Lima) and Uruguay. Antibody rates were significantly lower in Jamaica, Panama, rural Peru and Trinidad. These data confirm and extend earlier findings of low levels of rubella immunity in certain island or isolated populations.

Knowledge of the rubella antibody profiles of female populations of various ages and in various geographical areas is essential for intelligent and effective administration of rubella vaccine. In a previous WHO collaborative study on the sero-epidemiology of rubella (Rawls et al., 1967) it was found that a high percentage of the female populations in most areas of the world possessed antibody

to rubella at child-bearing age. However, some rural and island populations sampled had significantly lower immunity, suggesting a correlation between rate of acquisition of antibody and population density.

This present investigation was undertaken to confirm these earlier results and to extend the study to include other areas of the Americas. The authors' laboratories in Argentina, Brazil, Chile, Jamaica, Panama, Peru, Trinidad, and Uruguay collaborated with the World Health Organization in the survey.

* Requests for reprints should be addressed either to the senior author or to Virus Diseases, Division of Communicable Diseases, World Health Organization, 1211 Geneva, Switzerland.

¹ WHO Regional Reference Center for Respiratory Virus Diseases, National Communicable Disease Center, Health Services and Mental Health Administration, Public Health Service, US Department of Health, Education, and Welfare, Atlanta, Georgia 30333, USA.

² Health Laboratory Services, Division of Public Health Services, World Health Organization, Geneva, Switzerland. Formerly, Virus Diseases, Division of Communicable Diseases, World Health Organization.

³ Instituto Adolfo Lutz, São Paulo, Brazil.

⁴ University of the West Indies, Mona, Kingston, Jamaica.

⁵ Gorgas Memorial Laboratory and Servicio Nacional de Laboratorios, Panama, Republic of Panama.

⁶ Instituto Nacional de Salud, Lima, Peru.

⁷ Instituto Bacteriológico de Chile, Santiago, Chile.

⁸ Diagnostic Virus Laboratory, Port-of-Spain, Trinidad.

⁹ Instituto de Higiene, Montevideo, Uruguay.

¹⁰ Instituto Nacional de Microbiología, Buenos Aires, Argentina.

MATERIALS AND METHODS

Prior to undertaking the study, all collaborators met at the WHO Regional Reference Center for Respiratory Virus Diseases, National Communicable Disease Center (NCDC), Atlanta, Ga., and participated in a workshop organized by the Center and WHO on the standardization of rubella haemagglutination-inhibition (HI) techniques. This HI test was later applied in each laboratory under the same conditions, using standard reference sera.

Rubella haemagglutinin (HA) antigen from a single lot was distributed to each participating laboratory by the National Communicable Disease Center. The antigen was prepared according to the

method of Halonen et al. (1967) from BHK-21 tissue culture infected with rubella strain RA 27/3.

HI tests were performed using microtitre equipment and U-plates with 0.25% day-old chick erythrocytes and 4 units of antigen as described by Halonen et al. (1967). Immune sera and normal sera were included in each run as controls.

Survey sera were collected in 1967-68 by each laboratory from females in the age-groups 5-9, 10-14, 15-19, 20-24, and 25-34 years, representing, so far as was practical, urban and rural areas of their countries. Forty or more sera were collected from each age-group where possible. Sera were stored at -20°C. Immediately prior to testing, sera were extracted with kaolin to remove non-specific inhibitors and adsorbed with 50% chicken erythro-

cytes to remove chick cell haemagglutinins (Halonen et al., 1967).

RESULTS

The association of rubella HI antibody titre with prior rubella infection has been amply documented (Halonen et al., 1969) and, within the limits of laboratory test error, the percentage of sera with HI antibody present may be assumed to reflect the rubella experience of the population. Rubella HI antibodies at titres of 1:10 or greater were present in over 50% of the females in the youngest age-group tested (5-9 years) in all the populations except those in rural Jamaica (42%), rural Peru (25%), rural and urban Trinidad (10% and 18%), and rural and urban Panama (11% and 32%) (see the table). In the

AGE DISTRIBUTION OF RUBELLA ANTIBODIES IN CARIBBEAN AND MIDDLE AND SOUTH AMERICAN POPULATIONS IN 1968^a

Age-group (years)	Argentina				Brazil				Chile				Jamaica			
	Buenos Aires ^b		Rural		São Paulo		Rural		Santiago		Rural		Kingston		Rural	
	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%
5-9	35/55	64	7/11	64	22/39	56	37/46	80	37/38	97	29/33	88	27/40	68	17/40	42
10-14	42/50	84	13/14	83	39/43	91	41/43	95	24/24	100	29/29	100	30/40	75	11/40	28
15-19	112/141	79	24/33	73	49/54	91	35/39	90	42/47	89	50/50	100	21/40	52	17/40	42
20-24	102/127	80	29/34	85	45/54	83	36/40	90	81/83	98	26/26	100	21/40	52	21/40	52
25-34	101/118	86	34/37	92	48/54	89	35/40	88	86/89	97	25/25	100	26/40	65	21/40	52
≥35					47/51	92										
Age-group (years)	Panama				Peru				Trinidad				Uruguay			
	Panama City		Rural		Lima		Rural ^c		Port-of-Spain		Rural		Montevideo		Rural	
	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%	N+/NT	%
5-9	12/38	32	6/56	11	30/44	68	2/8	25	7/40	18	4/40	10	34/47	72		
10-14	19/33	58	12/48	25	43/46	93	17/51	33	11/40	28	11/40	28	39/42	93		
15-19	19/29	66	12/40	30	49/55	89	17/45	39	11/40	28	11/40	28	42/57	74	27/33	82
20-24	32/53	60	15/36	42	33/49	67	30/49	61	14/40	35	8/40	20	34/40	85	37/41	90
25-34	30/49	61	17/48	35	37/49	76	39/50	78	16/40	40	16/40	40	39/42	93	33/38	87
≥35	30/38	79	28/40	70									36/42	86	37/43	86

^a N+/NT = No. positive/No. tested for rubella antibody by HI test. Inhibition of haemagglutinin at serum dilution of 1:10 or greater was considered positive.

^b Also includes sera from Mendoza and Jujuy.

^c From isolated jungle population of Indians and mestizos.

10-14-year groups in the same populations, over 80% were seropositive, again with the exception of Jamaica, Panama, rural Peru and Trinidad. Only 28% of the females of this age in both rural and urban Trinidad and only 28% in rural Jamaica and 33% in rural Peru were seropositive. The proportions for urban and rural Panama were 58% and 25%, respectively. In all other areas except the islands, Panama and rural Peru, maximum antibody rates occurred in the 10-14-year age-groups and either remained the same or decreased slowly thereafter. Maximum antibody rates were not reached in the populations of the islands, or Panama or rural Peru until after the age of 25 years.

Except in Panama and Peru, there were no appreciable differences between the urban and rural populations in the age distribution of rubella antibody. The acquisition of antibody in persons in the rural areas of both Peru and Panama seemed to lag behind that of their urban counterparts. The rural Peruvian sera, however, were collected from Indians and mestizos living in isolated jungle areas under entirely different climatic conditions from those of the urban Peruvian population. The percentage of seropositives in rural Jamaica was also lower than in urban Jamaica in the 5-9-year and 10-14-year age-groups. However, a portion of the urban sera had been collected from a boarding-school which had reported a rubella outbreak the year before and this may have exaggerated the urban rubella experience.

DISCUSSION

This present study confirms the findings of the previous WHO collaborative study (Rawls et al., 1967) on the distribution of rubella antibody. Rubella antibody was present in over 80% of the females at the age of puberty in mainland populations. The finding of low antibody rates in Jamaica, Panama, Peru and Trinidad supports the correlation between population density and/or geographical location and antibody levels reported by others (Pitts et al., 1969; Rawls et al., 1967; Sever, 1967).

Reasons for the low rates of rubella immunity in these areas are not clearly understood. Ethnic difference as a possible explanation for its limited

spread has been adequately discounted in earlier studies (Rawls et al., 1967; Sever, 1967). Black (1966) has proposed that a certain minimum population density is necessary to maintain certain diseases in epidemic form. Theoretically, this minimal level is not reached on the islands and the disease must be periodically reintroduced from mainland areas. Panama is also geographically isolated and in this respect is similar to the islands. However, worldwide travel to and from Jamaica, Panama and Trinidad is a daily occurrence in all seasons, providing ample opportunity for frequent reintroduction of rubella from other areas. Furthermore, rubella was known to have been present in both Jamaica and Trinidad 1-3 years prior to the collection of study sera (Bisno et al., 1969; Miller & Thorburn, 1966). In spite of low antibody rates no major epidemics were recorded. This observation, coupled with the finding that antibody rates at any age are consistently lower than those on the mainland, suggest that "isolation" and the requirement of reintroduction are not the sole factors in limiting the spread of rubella.

The islands and Panama have a second major feature in common—all have tropical climates. Rural Peru, which also demonstrated low antibody rates, is also a tropical area. However, the data of Rawls et al. (1967) do not support a consistent correlation between antibody rates and climatic conditions. Some tropical mainland areas had high antibody rates. The low incidence of rubella antibody observed here may well be the result of a combination of factors.

The critical question is whether the low rubella antibody rates signify an increased risk to females of child-bearing age in these areas. Although Pitts et al. (1969) reported an increase in congenital anomalies in Trinidad after the 1960-61 outbreak and Miller & Thorburn (1966) reported congenital rubella in Jamaica after the 1964-65 outbreak, the theoretical danger of low antibody rates among females of child-bearing age may be offset by the low attack rates. However, increasing travel to the islands and Panama as well as increasing travel by the local population to mainland areas make it impossible to predict the extent of rubella spread in these areas in the future.

RÉSUMÉ

ÉTUDE COLLECTIVE DE LA SÉRO-ÉPIDÉMIOLOGIE DE LA RUBÉOLE EFFECTUÉE EN 1968
SOUS LES AUSPICES DE L'OMS DANS DES POPULATIONS DES CARAÏBES,
DE L'AMÉRIQUE MOYENNE ET DE L'AMÉRIQUE DU SUD

La présente enquête collective sur la séro-épidémiologie de la rubéole a été entreprise afin de confirmer et de compléter les données recueillies au cours de précédentes investigations. Des laboratoires d'Argentine, du Brésil, du Chili, de la Jamaïque, du Panama, du Pérou, de la Trinité et de l'Uruguay y ont participé. Dans chacun de ces pays, on a prélevé du sérum chez des sujets de sexe féminin appartenant aux groupes d'âge 5-9, 10-14, 15-19, 20-24 et 25-34 ans et recherché la présence d'anticorps anti-rubéole par l'épreuve d'inhibition de l'hémagglutination.

Des titres d'anticorps de 1 : 10 ou davantage ont été trouvés chez plus de 50% des fillettes de 5 à 9 ans, sauf dans les régions rurales de la Jamaïque et du Pérou ainsi

qu'à la Trinité et au Panama. Dans le groupe d'âge 10-14 ans, plus de 80% des sérums étaient positifs à l'exception des sérums collectés dans les pays qui viennent d'être cités où la proportion des échantillons positifs variait de 28 à 58%. Dans tous les pays, hormis les îles, le Panama et les régions rurales du Pérou, les taux de positivité maximaux ont été relevés dans le groupe d'âge 10-14 ans. Les taux restaient inchangés, ou diminuaient lentement, dans les groupes d'âge supérieur.

Ces données corroborent les observations faites précédemment et font ressortir le faible degré d'immunité envers la rubéole des populations de certaines îles ou de régions isolées.

REFERENCES

- Bisno, A. L., Spence, L. P., Stewart, J. A. & Casey, H. L. (1969) *Amer. J. Epidem.*, **89**, 74-81
- Black, F. L. (1966) *J. theor. Biol.*, **11**, 207-211
- Halonen, P. E., Ryan, J. M. & Stewart, J. A. (1967) *Proc. Soc. exp. Biol. (N.Y.)*, **125**, 162-167
- Halonen, P. E., Stewart, J. A., Herrmann, K. L., Casey, H. L., Ryan, J. M., Hall, A. D. & Caswell, K. E. (1969) *Amer. J. publ. Hlth*, **59**, 296-304
- Miller, C. G. & Thorburn, M. J. (1966) *W. Indian med. J.*, **15**, 177-188
- Pitts, O. M., Ravenel, J. M. & Finklea, J. F. (1969) *Amer. J. Epidem.*, **89**, 271-276
- Rawls, W. E., Melnick, J. L., Bradstreet, C. M. P., Bailey, M., Ferris, A. F., Lehmann, N. I., Nagler, F. P., Furesz, J., Kono, R., Ohtawara, M., Halonen, P., Stewart, J., Ryan, J. M., Strauss, J., Zdravilek, J., Leerhoy, J., Magnus, H. von, Sohler, R. & Ferreira, W. (1967) *Bull. Wld Hlth Org.*, **37**, 79-88
- Sever, J. L. (1967) *Epidemiology of rubella*. In: *First International Conference on Vaccines against Viral and Rickettsial Diseases of Man*, Washington, D.C., Pan American Health Organization, pp. 366-370