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Original Contribution

Extreme Mortality After First Introduction of Measles Virus to the Polynesian Island of Rotuma, 1911

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Rotuma is an isolated Polynesian island. In January 1911, most residents of Rotuma (population approximately 2,600) were exposed to measles virus for the first time. The official mortality register documented 491 deaths due to all causes among Rotumans during 1911 (cumulative measles-related mortality: 12.8%); most deaths occurred in April–May and were attributed to measles and its sequelae. Measles-related mortality rates were higher among young children (23.4 per 100 person-years) and young adults (17.1 per 100 person-years) than among adolescents (11.0 per 100 person-years) and older adults (5.6 per 100 person-years); females (16.2 per 100 person-years) died at a higher rate than males (13.2 per 100 person-years). Gastrointestinal complications (75%), not respiratory complications, were the predominant clinical manifestations of fatal measles cases; tuberculosis mortality was unusually high during the year of the epidemic. In 1911, measles-related mortality varied by nearly 3-fold across geographic districts (range, 7.4%–21.6%). The extreme mortality due to measles on Rotuma typifies the experiences of isolated populations after first encounters with measles; it suggests that prior exposures to a narrow range of microbes and genetic homogeneity predispose isolated populations to lethal outcomes when they are first exposed to highly contagious and pathogenic viruses (e.g., measles, influenza).

epidemics; measles; mortality; Pacific Islands

Abbreviations: CI, confidence interval; HLA, human leukocyte antigen; RR, rate ratio.

At the beginning of the 20th century, the island of Rotuma, on the western fringe of Polynesia (12°30′42″ S, 177°51′9″ E), was one of the most isolated places on earth. The first known recorded contact with Western explorers occurred in 1791, when the *HMS Pandora* arrived in search of the *Bounty* mutineers. Rotuma was inhabited by a Polynesian people whose subsistence economy was based on root crops and coconuts, while protein was supplied by pigs and fish. In the latter half of the 19th century, French priests and English Wesleyan ministers arrived and competed for converts. Antagonisms between the newly converted Wesleyans and Catholics mounted until 1878, when they culminated in a skirmish in which the Catholics were defeated by the numerically superior Wesleyans. The unrest that followed this conflict led the chiefs of Rotuma to cede the island to Great Britain to preclude French intervention. Cession was formalized in 1881, after which Rotuma was governed by the British as part of the Colony of Fiji, despite being nearly 500 km distant (1). The colonial administration closed Rotuma as a port of entry, thus requiring all visitors to the island to come from or go through Fiji. A Resident Commissioner was assigned to govern Rotuma, with a Council of Chiefs to advise him. Because of the island's extreme isolation, the assigned Resident Commissioner was usually also a medical officer. The Rotuman population was predominately of Polynesian ancestry, although interbreeding with other Pacific Islanders and a limited number of Caucasian seamen who had abandoned their voyaging life to live on Rotuma added to the composition of the gene pool (1).

In discussions with J. Stanley Gardiner in 1896, Chief Marafu described a highly lethal infectious epidemic that had occurred on Rotuma when he was a child (i.e., during the first half of the 19th century) (2). The description was inexact as to the nature of the disease, and there are no corroborating accounts by visitors to the island. As in Fiji, there was great official concern regarding the decreasing

native population, which when enumerated appeared to be related more to high infant and childhood mortality rates than to a falling birth rate (3, 4).

When measles is introduced into an isolated population, it often causes high mortality in all age groups. For example, during a measles epidemic in Fiji in 1875, approximately 20% of all island residents died (3–5). The extreme mortality from epidemic measles on Pacific islands is not easily explained, since there is no direct evidence of hypervirulent strains of measles virus or genetic predispositions to fatal outcomes after measles infection. In the late 19th century, transoceanic steamship travel brought measles virus to most Pacific islands. Because population censuses and mortality registrations were not yet institutionalized on many islands, the numbers, natures, and timing of deaths occurring during measles epidemics were generally not systematically documented (6). The measles epidemic on the island of Rotuma in 1911 is a notable exception.

A strict quarantine was established on Rotuma in response to the disastrous measles epidemic that occurred on Fiji in 1875. The quarantine and the geographic remoteness of Rotuma protected it from measles until late January 1911, when a ship bearing 2 sick women landed on the island; the island's medical officer was absent at the time (7, 8). During the ensuing measles epidemic, nearly all island residents were exposed to measles, and nearly 13% died. While the Faroe Islands epidemic of 1846 is often considered the classic ''virgin soil'' measles epidemic, mortality was nearly 10 times higher during the 1911 epidemic on Rotuma than during the Faroe Islands epidemic (9).

For other purposes, one of the authors recovered the detailed population and mortality registers kept by Hugh McDonald, the medical officer of Rotuma in 1911, as well as records of all births, marriages, and deaths of Rotumans that took place through 1961. These records enabled a detailed examination of mortality after a point-source introduction of measles virus into an immunologically naive population with a very narrow genetic base (due to geographic isolation and founder effect) (7, 8, 10). The findings suggest that prior exposure to a narrow range of microbes and the genetic homogeneity of the closed Rotuman population contributed to the extreme measles-related mortality in 1911.

MATERIALS AND METHODS

The primary data used for analyses were obtained from original documents located on Rotuma in the 1960s and from archives (located in Suva, Fiji) of birth, marriage, and death records pertaining to Rotumans. Mortality registers documented the following information regarding each death that occurred on Rotuma from 1911 to 1961: date of death, place of death, name, age, sex, cause(s) of death (1 or 2 diagnoses), names of parents, burial place and date, birthplace, and name of informant (10). Formal censuses were taken in 1891, 1911, and 1921; in addition, the Rotuman population was enumerated at least annually for medical officers' reports because of official concerns regarding depopulation (8, 10, 11).

For this analysis, the names of Rotumans who were alive anytime in 1911 were identified by aggregating and reviewing birth and death records from years prior to and during 1911. Because some Rotumans lived on Fiji or worked at sea, the locations of all Rotumans during the 1911 measles epidemic could not be determined with certainty; however, the presence of approximately 2,200 persons on the island during the epidemic is well documented.

One of the authors reviewed the unedited mortality register entries. Based on his review, 21 mortality categories were defined; these were further aggregated into 6 major mortality categories which were used for most analyses. The major mortality categories were measles-related, tuberculosis, gastrointestinal (diarrhea, dysentery, gastroenteritis), pneumonia and influenza, other infectious, and noninfectious. The ''measles-related'' category included all death records that listed ''measles'' as the first cause or an associated cause. All other death records were categorized on the basis of the first listed cause. No morbidity records other than annual Fijian medical reports were available for review (8). Relevant data were transcribed into Microsoft Excel (Microsoft Corporation, Seattle, Washington) spreadsheets and analyzed using SAS, version 9.1.3 (SAS Institute Inc., Cary, North Carolina).

The endpoints of the analyses were deaths (overall and in major mortality categories) occurring among members of a cohort that included all persons who had resided on Rotuma anytime during 1911. Cumulative mortality incidence (%) was calculated as the proportion of study cohort members who died during specified follow-up periods. For mortality rate calculations, person-time at risk for each cohort member was calculated as the number of days from the beginning of the follow-up period (January 1, 1911) or the date of birth (if after January 1, 1911) to the death of the cohort member or the end of the follow-up period (December 31, 1911). Survival experiences in relation to age group, geographic district, and birth cohort were summarized using the Kaplan-Meier and classical life-table (2-year intervals) methods.

RESULTS

Rotuma is a small (14 km $\times$ 6 km) and remote South Pacific island. In 1911, although the only contact between Rotuma and the rest of the world was by sea, there were no dedicated port facilities (i.e., inbound passengers landed on beaches) (Figure 1). Of the 2,616 Rotumans who were alive in 1911, there were similar numbers of males and females; approximately 40% were younger than age 15 years, and another one-third (34%) were between 16 and 35 years of age; and there was little racial/ethnic diversity (Table 1). During 1911, 491 Rotumans died from all causes; the cumulative mortality incidence during the year was 18.8%. More than two-thirds ($n = 334$) of all deaths occurring during the year were measles-related; the cumulative mortality incidence due to measles was 12.8%. Measles-related deaths began in February, peaked in April, sharply decreased in May, and continued sporadically through the rest of 1911 (Figure 2).

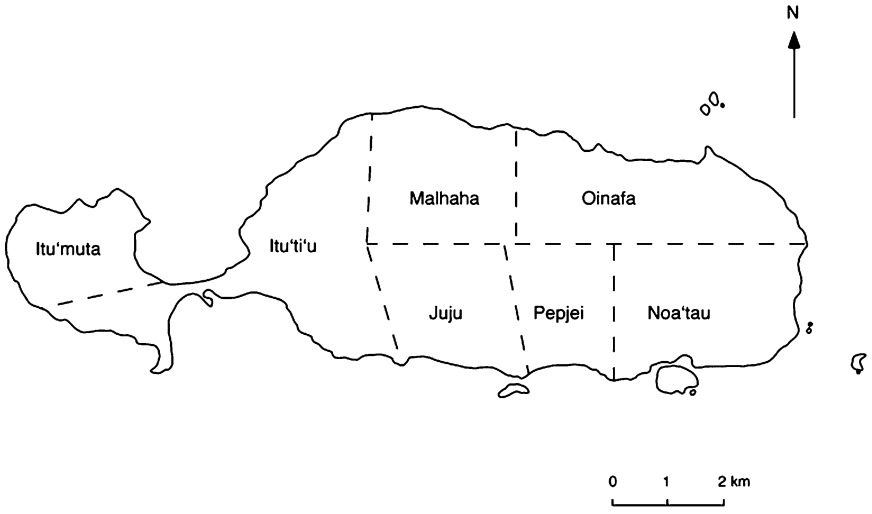

Figure 1. Map of the South Pacific island of Rotuma (12°30′42″ S, 177°51′9″ E) showing its 7 geographic districts (1).

During 1911, among Rotumans of both sexes and all age groups (except those older than 55 years), measles accounted for more deaths by far than any other category of mortality causes (Table 2). Notably, measles-related mortality rates were more than 2 times higher among infants and young children (age <6 years) (23.4 per 100 person-years) (rate ratio (RR) = 2.13, 95% confidence interval (CI): 1.52, 2.98) and more than 1.5 times higher among young adults (ages 16–35 years) (17.1 per 100 person-years) (RR = 1.55, 95% CI: 1.14, 2.12) than among school-aged children (ages 6–15 years) (11.0 per 100 person-years) (Table 2, Figure 3). During 1911, the incidence rate of measles-related mortality (unadjusted) was more than 20% higher among females (16.2 per 100 person-years) than among males (13.2 per 100 person-years) (RR = 1.22, 95% CI: 0.99, 1.52) and more than 3 times higher among Rotumans whose parents were both Rotumans (16.0 per 100 person-years) than among those of mixed-race Pacific Island parentage (5.0 per 100 person-years) (RR = 3.19, 95% CI: 1.19, 8.53) (Table 2).

A large majority (75%) of all registered measles-related deaths included gastrointestinal illnesses (e.g., ileocolitis, diarrhea, dysentery) as associated causes. In contrast, only 1 measles-related death was associated with pneumonia, influenza, or other respiratory infection (data not shown). Deaths that were attributed to tuberculosis or gastrointestinal causes (without mention of measles) occurred sporadically through 1911 (Figure 2). Notably, there were more tuberculosis-related deaths among study cohort members in 1911 than in any other year through 1960 (Figure 4). Because tuberculosis and gastrointestinal pathogens were endemic on Rotuma in 1911, they probably co-circulated with measles throughout the epidemic period; if so, some deaths attributed to tuberculosis or gastrointestinal illnesses alone in 1911 may have been precipitated or complicated by measles.

The timing and intensity of measles-related mortality sharply varied across age groups. For example, measles-related deaths occurred sooner and the proportion affected overall was much greater among infants and young children (age <6 years) than among older Rotumans (Figure 5A). Measles-related deaths affected adults aged 16–35 years and aged 36–55 years concurrently; however, a much higher proportion of adults aged 16–35 years than Rotumans of any other age (except children under 6 years) were affected overall (Figure 5A). Similar proportions of Rotumans aged 6–15 years and aged 36–55 years, but relatively few older than age 55 years, died of measles during the epidemic period (Figure 5A). During the epidemic period, Rotumans as old as 80 years died of measles; the finding supports the historical evidence that the 1911 epidemic involved the first exposure of Rotumans, regardless of age, to the measles virus.

The timing, intensity, and overall mortality effects of measles also markedly varied across the 7 geographic districts of Rotuma (Table 3, Figure 5B). The first measles-related deaths in the various districts were recorded as follows (by week of calendar year 1911): Itu'ti'u (week 8); Oinafa (week 9); Pepjei, Juju, and Itu'muta (week 10); Noa'tau (week 12); and Malhaha (week 13). The dynamics of measles-related mortality did not precisely reflect—but probably indicate—the spread of measles virus throughout the island. The dates of index measles-related deaths across districts suggest that the virus spread throughout the island in approximately 5 weeks: from the likely point of introduction in the south, along the southern coast, and eventually to the northern coastal districts.

Although residents of each district were probably affected by the same strain of measles virus, there was more than a 3-fold difference in measles-related mortality across the districts (cumulative incidence of measles-related mortality by district was 7.4%–21.6%). The districts with the lowest and highest measles-related mortality rates, respectively, were Juju (7.4%) and Pepjei (9.7%)—both located on the southern coast and affected early in the epidemic period—and Malhaha (21.6%), which is on the northern coast

Table 1. Demographic and Disease Characteristics of the Population of Rotuma in 1911

Characteristic	No. of Persons	%
Total	2,616	100.0
Sex		
Female	1,321	50.5
Male	1,292	49.4
Unknown	3	0.1
Age group, years[a]		
<6	476	18.2
6–15	573	21.9
16–35	903	34.5
36–55	488	18.6
>55	176	6.7
Ethnicity		
Rotuman	2,350	89.8
Mixed-race Pacific Islander	89	3.4
Mixed-race European	79	3.0
Non-Rotuman Pacific Islander	74	2.8
European	16	0.6
Other	8	0.3
Location		
Rotuma	2,399	91.7
Fiji	210	8.0
Abroad	7	0.3
No. of deaths (1911–1961), by cause		
Infectious causes	1,474	56.3
Tuberculosis	354	24.0
Measles	334	22.7
Pneumonia	177	12.0
Influenza	174	11.8
Diarrhea, dysentery, or gastroenteritis	121	8.2
Other diseases of the respiratory system	102	6.9
Other infectious diseases	63	4.3
Filariasis	59	4.0
Meningitis	44	3.0
Diseases of the urinary system	27	1.8
Leprosy	17	1.2
Pertussis or whooping cough	2	0.1
Noninfectious causes	730	27.9
Debility, senility, etc.	215	29.5
All other causes	141	19.3
Diseases of the circulatory system	135	18.5
Uncertified deaths	84	11.5
Diseases of the nervous system	64	8.8
Malignant disease	32	4.4
Accidents and combat injuries	30	4.1
Malnutrition and scurvy	16	2.2
Neonatal and childbirth	13	1.8

[a] Age on December 15, 1911.

and was affected late in the epidemic. In general, however, there were not clear associations between measles-related mortality in various districts and either their geographic locations on the island or the time at which they were affected during the epidemic period (Figure 5B, Table 3).

There were remarkable differences in the all-cause mortality experiences of Rotumans in various birth-year cohorts (Figure 6). Most notably, more than 50% of Rotumans born in 1910 or 1911 died within 2 years of the 1911 measles epidemic. In general, mortality from all causes during and within the first few years after 1911 generally decreased with progressively older birth-year cohorts (birth years: 1902–1909) (Figure 6). In contrast to the experience in 1911, during a measles epidemic on Rotuma in 1927–1928, there were only 9 deaths among children under 16 years of age (data not shown).

DISCUSSION

This analysis documents that within several months after a point-source introduction of measles virus to a remote Pacific island, nearly 13% of the residents died from measles-related illnesses. During the 17th–19th centuries, various infectious diseases, including measles, were introduced by Western sailors and explorers into immunologically susceptible island populations, with devastating effects. For example, measles contributed to 80%–90% collapses of some Pacific Island populations within 1–2 generations following first contacts (12–14). The extraordinary lethality of measles in these isolated Pacific populations is well documented; however, because most such epidemics predated knowledge of virology and systematic enumerations of births, deaths, and resident populations, the epidemiologic and clinical characteristics of ''first contact'' measles epidemics remain unclear (3, 15). By 1911, there had been careful enumerations of all residents of Rotuma for many years; in addition, a medically trained observer had been routinely documenting deaths and describing their causes, although the possibility of misclassification and observer bias exists (8, 10). As a result, the Rotuman epidemic may be the most comprehensively documented of all ''first contact'' measles epidemics in isolated populations. With the possible exception of measles virus introductions among extremely remote tribal peoples, such epidemics are unlikely to recur in our highly interconnected modern world (16, 17).

Three findings emerge from this analysis of the Rotuman measles epidemic: First, the most frequent complications of ultimately fatal measles infections affected the gastrointestinal system rather than the respiratory system; second, among Rotumans who were alive in 1911, the tuberculosis mortality rate was higher during the year of the measles epidemic than in any other year through 1961; and third, during the measles epidemic period, there was a peak of measles-related mortality among young adults (''W-shaped'' mortality by age), who are typically the healthiest members of communities.

Measles virus infects the gut; gastrointestinal complications of fatal measles infections have been documented

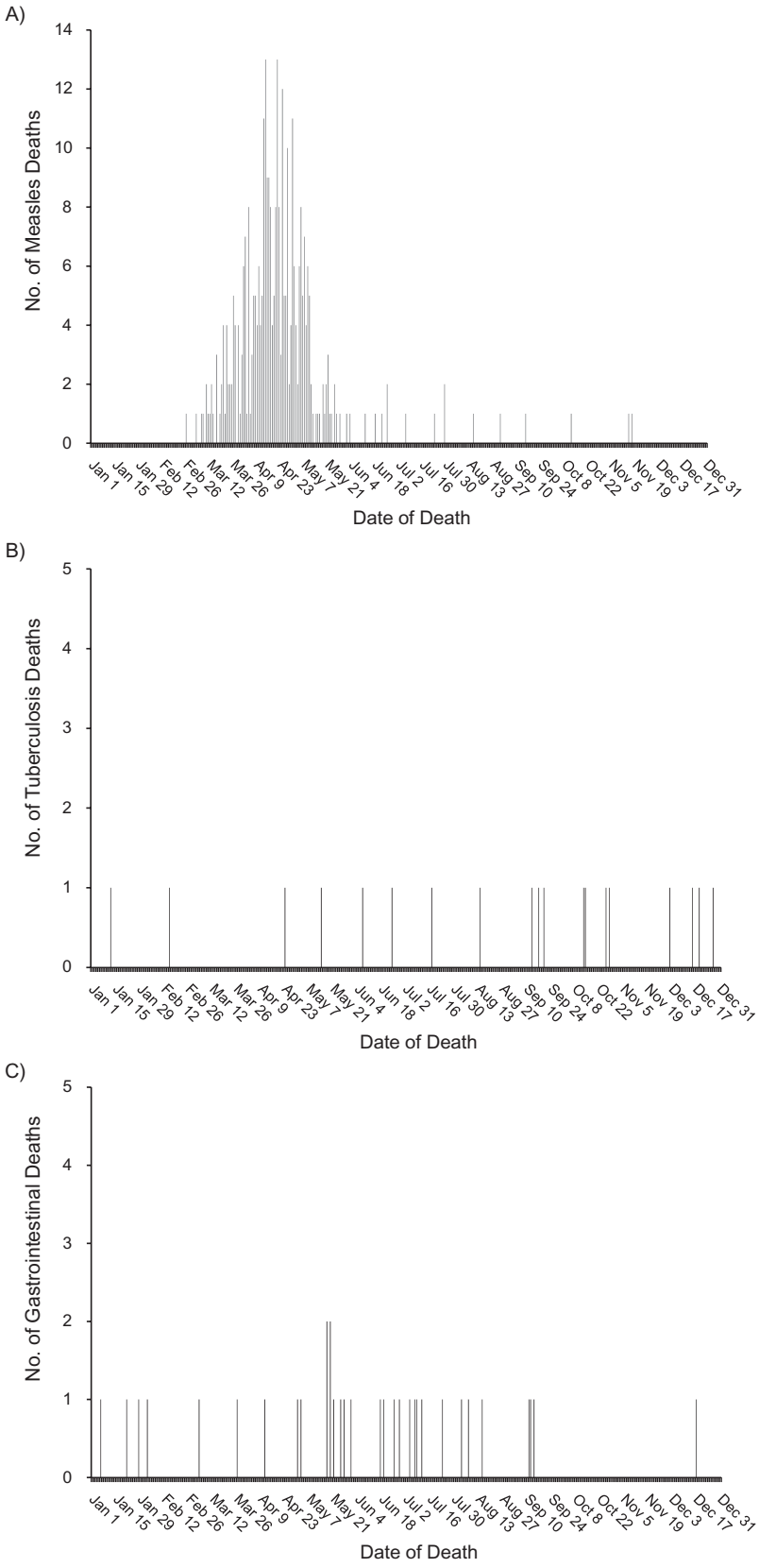

Figure 2. Measles mortality on Rotuma in 1911 following the introduction of the measles virus in late January (A) and all tuberculosis (B) and gastrointestinal (C) deaths occurring during the same time period.

Table 2. Numbers of Deaths, Mortality Rates, and Rate Ratios for Measles in Rotuma, by Cause of Death, January 1–December 31, 1911

Characteristic	Cause of Death															
	All Causes				Measles				Tuberculosis				Diarrhea, Dysentery, or Gastroenteritis			
	No.[a]	Rate[b]	RR[c]	95% CI	No.	Rate	RR	95% CI	No.	Rate	RR	95% CI	No.	Rate	RR	95% CI
Total	491	21.6			334	14.7			19	0.8			33	1.5		
Sex[d]																
Female	280	24.8	1.34	1.12, 1.60	183	16.2	1.22	0.99, 1.52	14	1.2	2.82	1.02, 7.85	22	2.0	2.0	0.98, 4.16
Male	211	18.5	1	Referent	151	13.2	1	Referent	5	0.4	1	Referent	11	1.0	1	Referent
Age group, years																
<6	167	46.6	3.33	2.53, 4.40	84	23.4	2.13	1.52, 2.98	5	1.4	6.95	0.83, 60.69	13	3.6	3.1	1.17, 8.08
6–15	71	14.0	1	Referent	56	11.0	1	Referent	1	0.2	1	Referent	6	1.2	1	Referent
16–35	163	20.5	1.47	1.11, 1.94	136	17.1	1.55	1.14, 2.12	10	1.3	6.30	0.82, 49.89	6	0.8	0.6	0.20, 1.98
36–55	64	14.3	1.02	0.73, 1.44	49	11.0	0.99	0.68, 1.46	3	0.7	3.35	0.35, 32.79	6	1.3	1.1	0.37, 3.52
>55	26	16.1	1.15	0.73, 1.81	9	5.6	0.51	0.25, 1.02	0	0.0	0.00		2	1.2	1.1	0.21, 5.20
Ethnicity																
Rotuman	468	23.1	1.67	0.92, 3.04	324	16.0	3.19	1.19, 8.53	18	0.9			30	1.5	1.2	0.16, 8.64
Mixed-race Pacific Islander	11	13.8	1	Referent	4	5.0	1	Referent	0	0.0			1	1.3	1	Referent
Mixed-race European	10	14.4	1.04	0.44, 2.45	5	7.2	1.43	0.38, 5.34	0	0.0			2	2.9	2.3	0.21, 25.29
Non-Rotuman Pacific Islander	2	2.7	0.20	0.04, 0.89	1	1.4	0.27	0.03, 2.43	1	1.4			0	0.0	0.0	
European	0	0.0	0.00		0	0.0	0.00		0	0.0			0	0.0	0.0	
Other	0	0.0	0.00		0	0.0	0.00		0	0.0			0	0.0	0.0	
Location																
Rotuma	487	23.7	12.29	4.59, 32.87	332	16.1	16.80	4.17, 67.27	19	0.9			32	1.6	3.2	0.44, 23.64
Fiji	4	1.9	1	Referent	2	1.0	1	Referent	0	0.0			1	0.5	1	Referent
Abroad	0	0.0	0.00		0	0.0	0.00		0	0.0			0	0.0	0.0	

Table continues

Table 2. Continued

Characteristic	Cause of Death											
	Pneumonia and Influenza				Other Infectious Diseases				Noninfectious Diseases			
	No.	Rate	RR	95% CI	No.	Rate	RR	95% CI	No.	Rate	RR	95% CI
Total	31	1.4			20	0.9			54	2.4		
Sex[d]												
Female	16	1.4	1.08	0.53, 2.18	16	1.4	4.00	1.35, 12.08	29	2.6	1.17	0.69, 1.20
Male	15	1.3	1	Referent	4	0.4	1	Referent	25	2.2	1	Referent
Age group, years												
<6	21	5.9	7.41	2.56, 21.69	13	3.6	6.13	1.75, 21.56	31	8.6	43.20	6.00, 322.02
6–15	4	0.8	1	Referent	3	0.6	1	Referent	1	0.2	1	Referent
16–35	2	0.3	0.32	0.06, 1.74	1	0.1	0.22	0.02, 2.05	8	1.0	5.00	0.64, 40.85
36–55	1	0.2	0.28	0.03, 2.54	1	0.2	0.37	0.04, 3.64	4	0.9	4.45	0.51, 40.69
>55	3	1.9	2.35	0.53, 10.55	2	1.2	2.10	0.35, 12.56	10	6.2	30.95	4.03, 245.87
Ethnicity												
Rotuman	26	1.3	0.20	0.08, 0.53	20	1.0			50	2.5	1.96	0.27, 14.22
Mixed-race Pacific Islander	5	6.3	1	Referent	0	0.0			1	1.3	1	Referent
Mixed-race European	0	0.0	0.00		0	0.0			3	4.3	3.43	0.36, 33.07
Non-Rotuman Pacific Islander	0	0.0	0.00		0	0.0			0	0.0	0.00	
European	0	0.0	0.00		0	0.0			0	0.0	0.00	
Other	0	0.0	0.00		0	0.0			0	0.0	0.00	
Location												
Rotuma	31	1.5			20	9.6			53	2.6	5.38	0.74, 38.68
Fiji	0	0.0			0	0.0			1	0.5	1	Referent
Abroad	0	0.0			0	0.0			0	0.0	0.00	

Abbreviations: CI, confidence interval; RR, rate ratio.
[a] Number of deaths.
[b] Number of deaths per 100 person-years.
[c] Crude rate ratio.
[d] Sex was unknown for some persons (mortality rate for persons of unknown sex: 3.00 per 100 person-years).

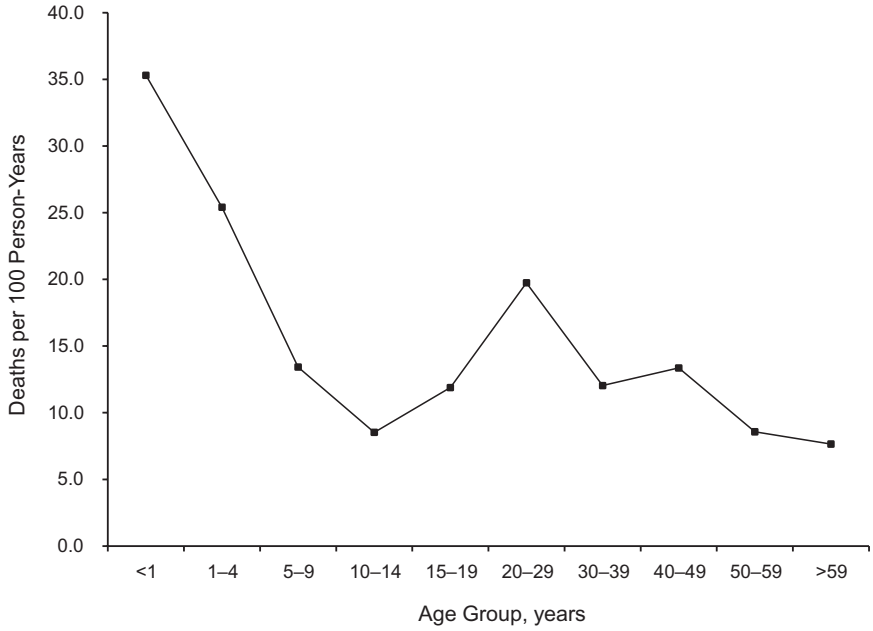

Figure 3. Measles-related mortality among residents of Rotuma during calendar year 1911, by age group.

during epidemics in the general population of the Faroe Islands and among malnourished children in Bangladesh and Guatemala (9, 18, 19). In general, however, respiratory infections (e.g., bacterial pneumonia) far exceed gastrointestinal complications as causes of postmeasles mortality; only 8% of all reported measles cases in the United States from 1987 to 2000 were complicated by diarrhea (20).

It is likely that malnutrition and/or dehydration contributed to the extreme measles-related mortality on Rotuma. As measles spread inexorably through each of the villages on the island, the adults and children of each

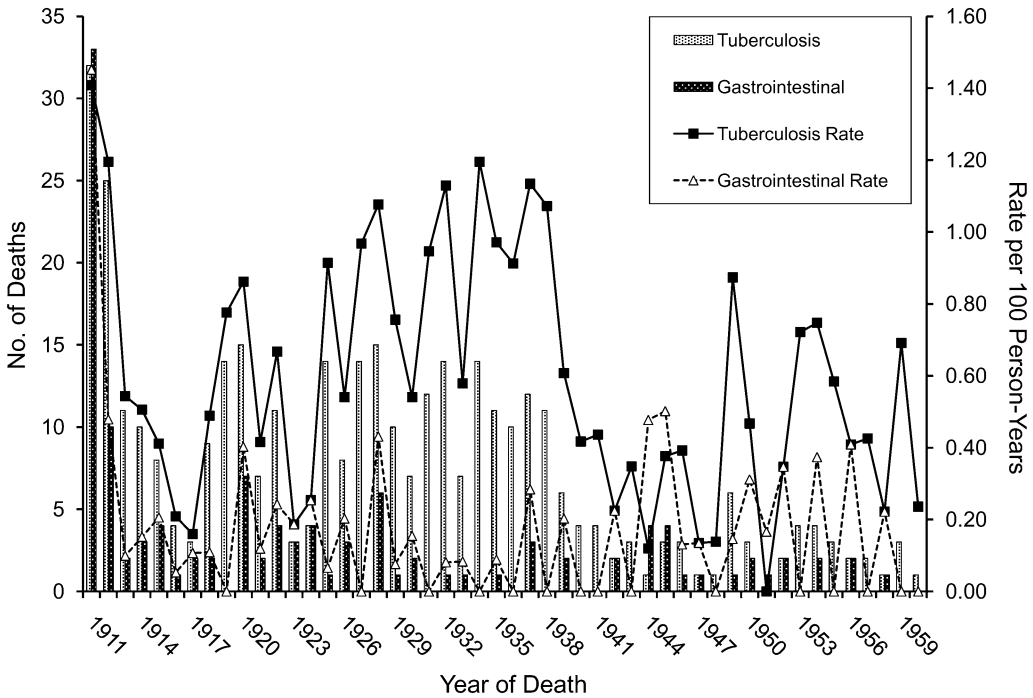

Figure 4. Annual numbers of deaths (left *y*-axis) and incidence rates of death (right *y*-axis) due to tuberculosis and gastrointestinal illnesses among persons who resided on Rotuma in 1911, by calendar year, 1911–1960.

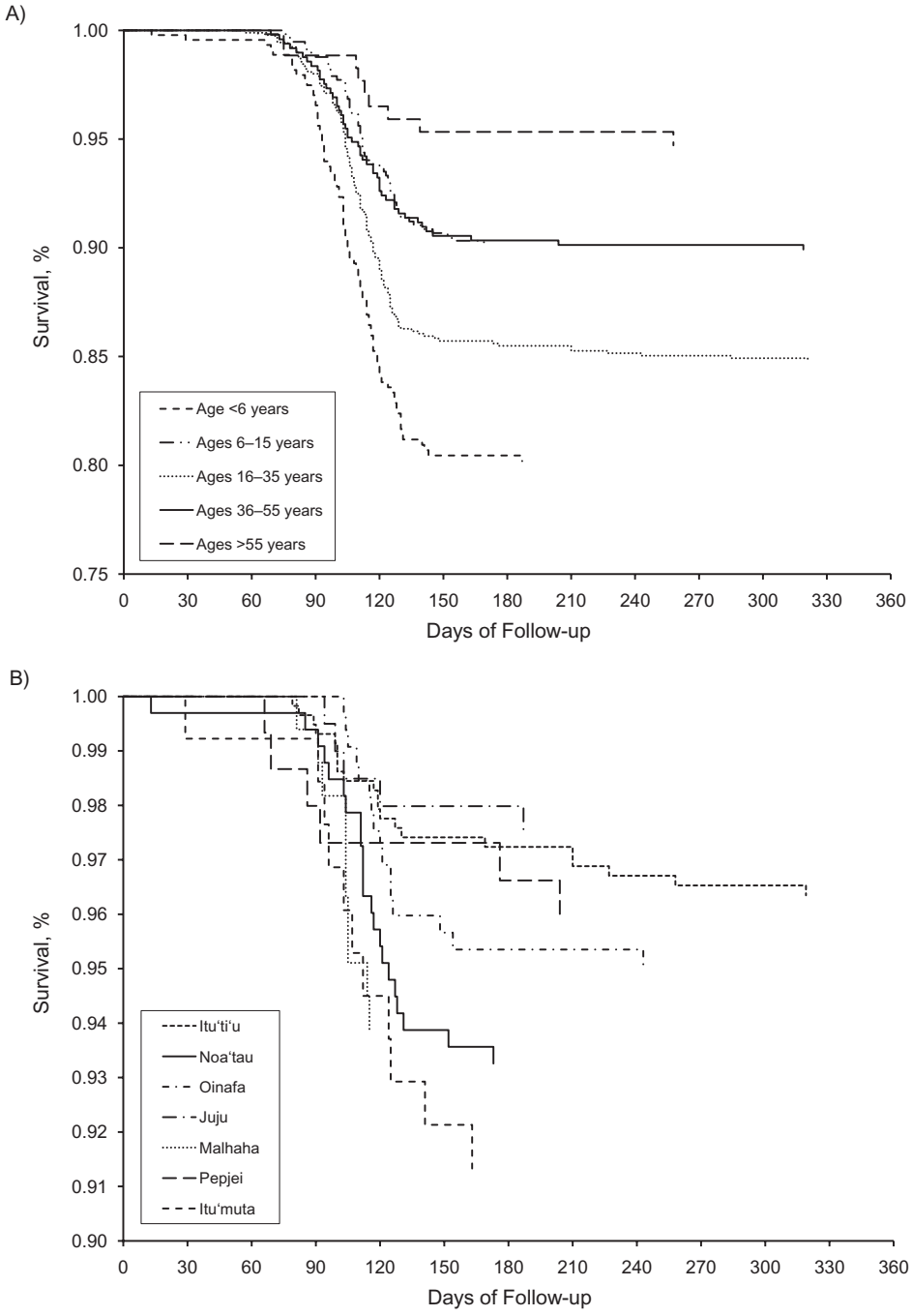

Figure 5. Kaplan-Meier curve for survival following the 1911 measles epidemic on Rotuma, by A) age group and B) geographic district. (For districts, refer to the map in Figure 1.)

affected village were probably sickened at the same time. As a result, care providers were probably unable to provide adequate food, water, and nursing care for themselves or others. In the wake of prolonged and widespread disability among the principal care providers, basic nursing care and nutrition were undoubtedly degraded. In such settings, diarrhea and measles can interact to push previously healthy infants and children into malnourished and/or dehydrated states; without treatment, such states significantly increase the risk of life-threatening secondary infections (18, 19).

More than one-half of the children in the 1910 and 1911 birth-year cohorts died during their first 2 years of life, and only 24% survived to middle age. This finding indicates that infants (the persons most dependent on others for their survival) were most severely affected—perhaps from starvation

Table 3. Distribution of Measles Deaths by Geographic District in Rotuma, 1911

Characteristic	Itu'ti'u		Noa'tau		Oinafa		Juju		Malhaha		Pepjei		Itu'muta	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total population	653		412		410		229		190		186		211	
Women	322	49.3	210	51.0	215	52.4	112	48.9	105	55.3	95	51.1	108	51.2
Men	331	50.7	202	49.0	195	47.6	117	51.1	85	44.7	91	48.9	103	48.8
Total mortality	143		106		66		39		52		28		43	
Sex														
Female	83	58.0	63	59.4	34	51.5	21	53.8	30	57.7	17	60.7	26	60.5
Male	60	42.0	43	40.6	32	48.5	18	46.1	22	42.3	11	39.3	17	39.5
Cause														
Measles	93	65.0	85	80.2	50	75.8	17	43.6	41	78.8	18	64.3	26	60.5
Nonmeasles	50	35.0	21	19.8	16	24.2	22	56.4	11	21.1	10	35.7	17	39.5

and dehydration—during and following the epidemic period. Because of the short- and long-term synergies between measles and other debilitating conditions, the mortal effects of widespread measles epidemics can persist for months after introductions into relatively fragile (in terms of nutrition, sanitation, and hygiene) communities. In 1911 on Rotuma, measles-related mortality was higher among women than among men, as has been previously reported in many populations, for unclear reasons (21).

The pathophysiologic manifestations of measles virus infection are primarily determined by the nature and magnitude of the cellular immune response; for example, children with agammaglobulinemia, but not lymphocyte disorders, generally tolerate measles virus infection well (22, 23). Reactivations of latent tuberculosis infections following measles are enabled by the temporary suppression by measles of the cellular immune system. In the pre-antibiotic era, reactivated tuberculosis cases were life-threatening. During the First World War, up to 3% of US Army soldiers with measles had subsequent reactivations of tuberculosis; this finding has not been noted in more recent studies (24, 25).

It is a common belief that the clinical expressions of "childhood infections" such as measles are more severe when they affect adults than when they affect ordinary children; the factual basis of this assertion is unclear (26). During the 1918 influenza pandemic, there was a mortality peak among young adults; the "W-shaped" mortality by age distribution is a unique and unexplained characteristic of the 1918 influenza pandemic (27, 28). Notably, there was also a peak of measles-related mortality among young adults during the Rotuma epidemic. The finding of relatively high mortality among the healthiest members of affected populations (i.e., young adults) may reflect dysfunctional immune responses to, rather than inherent pathologic effects of, influenza and measles

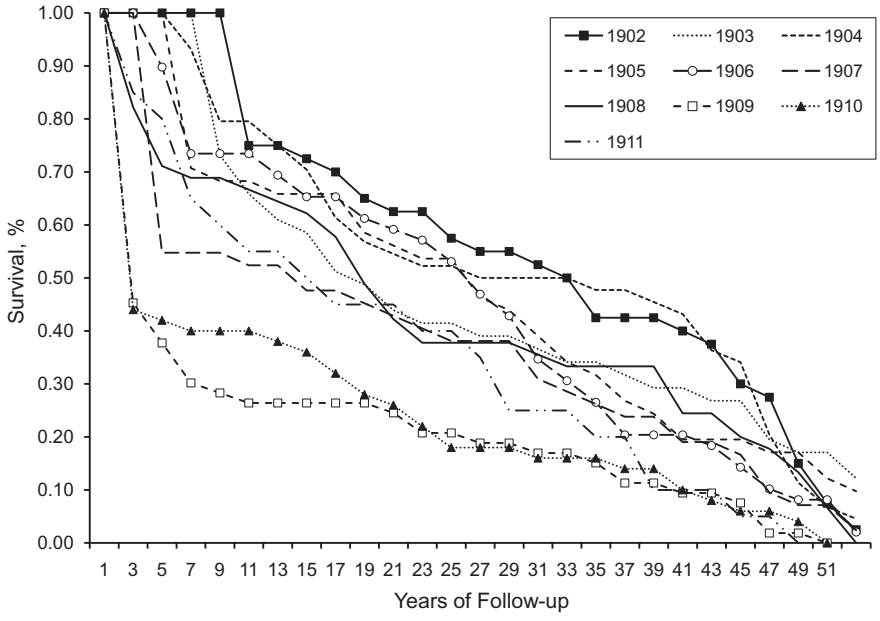

Figure 6. Cumulative probability of survival (all causes of mortality), by birth-year cohort (1902–1911), among residents of Rotuma in 1911.

viruses in immunologically naive populations. Definitive investigations of the natures and causes of W-shaped mortality curves during viral disease epidemics are inhibited by the lack of biologic specimens from relevant epidemics, the scarcity of other well-documented examples, and the end of epidemiologic isolation of populations due to globalization.

Despite the small size of Rotuma, measles mortality varied more than 2-fold across the 7 geographic districts of the island (Figure 5B). Such geographic variability was also seen during the 1875 Fijian epidemic (5). The variability in mortality is not readily correlated with sociologic or economic differences across the Rotuman districts. Other studies have suggested household crowding, family size, intensity of viral exposure, and increased adaptation of measles to the population as possible explanations for increased measles mortality during epidemics (29–33). During the Rotuma epidemic, measles-related mortality did not closely correlate with the timing of index measles-related deaths in the districts (Figure 5B). Because details regarding the spread of measles virus on Rotuma are unclear, it is not possible to determine any specific cause of mortality heterogeneity on such a small island (30).

It is informative to compare and contrast the epidemiologic and clinical characteristics of the measles epidemics that affected Rotuma in 1911 and the Faroe Islands in 1846. Both epidemics occurred during the pre-antibiotic and prevaccine eras; and after point-source introductions of the virus into the island populations, the resulting measles epidemics spread rapidly among the immunologically receptive hosts. However, mortality was approximately 10 times higher on Rotuma than in the Faroe Islands, and there was a mortality peak among young adults on Rotuma but not in the Faroe Islands. The sharp differences in the clinical expressions of measles in these isolated populations may reflect genetic differences between the populations. However, characteristics of later measles epidemics in populations close to the Faroe Islands suggest that genetics is not the predominate determinant of measles-related mortality. In 1915, 527 cases of measles affected Scottish military recruits; recruits from urban areas such as Glasgow were spared (probably because of naturally acquired immunity from earlier measles infections), but 12% of those from the rural highlands died (34). In 1951, a traveler from Denmark introduced measles virus into the very isolated Inuit population of southern Greenland; 1.8% of the population died during the ensuing epidemic. The measles-related mortality among the Inuit was similar to that on the Faroe Islands during the 1846 epidemic; however, the ethnic compositions of the 2 affected populations markedly differed (9, 35). There may be a genetic component to mortality risk during measles epidemics in island populations; however, in light of the experiences of non-Pacific Island populations that have been affected by measles, it seems unlikely that genetic factors are the predominant determinants of the clinical courses and outcomes of measles infections.

Measles virus infections cause immune dysfunction; however, measles-related immune dysfunction has not been directly linked to mortality among adults (36). Extreme measles-related mortality is generally associated with epidemics in isolated populations. The observation may correlate with the assumptions that many adults in isolated settings are exposed to few infectious agents and a narrow range of infectious agents during their lives. Cellular immune dysfunction, particularly of T cells in isolated adult populations, could explain extraordinary mortality events that occur upon first contact (37). If this hypothesis were valid, measles-related mortality would have human leukocyte antigen (HLA) type specificity, homozygous persons would be at highest risk, and large proportions of isolated populations with little HLA variability would potentially be at very high risk.

HLA types are known to influence the immune response to attenuated infections caused by measles vaccine (38–40). Although they are relatively sparse, the relevant data from Rotuma suggest that mixed parentage may have had a protective effect against measles-related mortality. Studies with genetic components of the current Rotuman population may be informative regarding the relation between HLA type and mortality risk after measles infection. As genomic tools and analytical methods improve and become more available, their application may further elucidate the dynamics of the last large measles epidemic with extreme mortality in the Pacific (41).

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