

## Epidemiology in History

### Measles Epidemics of Variable Lethality in the Early 20th Century

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Until the mid-20th century, mortality rates were often very high during measles epidemics, particularly among previously isolated populations (e.g., islanders), refugees/internees who were forcibly crowded into camps, and military recruits. Searching for insights regarding measles mortality rates, we reviewed historical records of measles epidemics on the Polynesian island of Rotuma (in 1911), in Boer War concentration camps (in 1900–1902), and in US Army mobilization camps during the First World War (in 1917–1918). Records classified measles deaths by date and clinical causes; by demographic characteristics, family relationships (for Rotuma islanders and Boer camp internees), and prior residences; and by camp (for Boer internees and US Army recruits). During the Rotuman and Boer War epidemics, measles-related mortality rates were high (up to 40%); however, mortality rates differed more than 10-fold across camps/districts, even though conditions were similar. During measles epidemics, most deaths among camp internees/military recruits were due to secondary bacterial pneumonias; in contrast, most deaths among Rotuman islanders were due to gastrointestinal complications. The clinical expressions, courses, and outcomes of measles during first-contact epidemics differ from those during camp epidemics. The degree of isolation from respiratory pathogens other than measles may significantly determine measles-related mortality risk.

Boer War; epidemiology; measles; mortality; Rotuma; US Army

Until the mid-20th century, measles was a leading killer of children and a recurrent cause of lethal outbreaks in epidemiologically isolated populations (e.g., islanders, residents of the Arctic and Amazonia) and newly congregated populations (e.g., military conscripts, refugee/concentration camp internees) (1–3). For example, in the wake of European exploration of the Americas during the 16th century, there were devastating outbreaks of measles after first contact in previously epidemiologically isolated indigenous populations (3). Some first-contact measles epidemics resulted in more than 20% acute mortality rates and widespread chronic illnesses (4). In the 20th century, most measles-related deaths were due to secondary bacterial pneumonias; however, prior to the 20th century, measles often caused lethal gastrointestinal illnesses and sometimes a fatal hemorrhagic illness known as black measles (5).

During the late 19th and early 20th centuries, before measles vaccine and antibiotics were available, measles-related

mortality rates markedly declined in both civilian and military populations. During the American Civil War, there were widespread deadly outbreaks of measles among newly conscripted soldiers who were crowded into mobilization camps; and during World War I, measles was still a major camp disease (3.2 cases and 0.2 deaths/100 man-years; case fatality, 6%). In contrast, during World War II, measles-related mortality rates (<0.0005 deaths/100 man-years) and case fatality rates (<0.1%) were extremely low, even among newly conscripted soldiers in recruit camps (5, 6). The declines in measles-related mortality rates in military populations reflected the experiences in civilian populations; the declines preceded the availability of measles vaccine and antibiotics and were not attributable to any specific medical interventions (7, 8).

We sought insights into the causes of the widespread declines in measles-related deaths during the late 19th and early 20th centuries by reviewing reports associated with

large, lethal measles epidemics in the early 20th century (9, 10). Our objectives were to assess the natures and relative frequencies of various clinical expressions of measles infection and to identify host-mediated determinants of lethal outcomes during measles epidemics in the following 3 epidemiologically isolated populations: residents of the Polynesian island of Rotuma in 1911 (11–13), detainees in concentration camps during the Boer War in 1900–1902 (6, 14–16), and newly conscripted soldiers in US Army mobilization camps in 1917–1918 (17–19). From our analyses, we hoped to gain insights into the historical causes of the declines of measles-related mortality rates, especially in isolated populations.

## METHODS

### Rotuma, South Pacific, 1911

Rotuma is an isolated Polynesian island 500 km from Fiji (12). Because the sailing time to Rotuma exceeded the incubation period of measles, Rotumans had been protected from exposure to measles until the virus arrived from Samoa in 1911. When a passenger with measles arrived at Rotuma on a sailing ship, the medical/port authority responsible for stopping the landing of sick passengers was absent (12). During the ensuing epidemic, 13% of the approximately 2,600 residents of Rotuma died of measles, and within 1 year of the epidemic, the population of the island was reduced by nearly one-fifth (11, 13). In the early 1960s, all entries in the island's birth and death registers for the years 1903–1960 were transcribed to be eventually contained in an electronic database at the University of Hawai'i at Mānoa. Records in the database document family relationships, dates and places of births and deaths, and causes of death of all Rotumans (12).

### Boer War concentration camps, South Africa, 1900–1902

During the Boer War in South Africa in 1900–1902, the British Army forcibly relocated rural farming families—mostly of Dutch heritage (Boers)—into concentration camps; 21 camps had more than 1,000 internees each with an estimated total population of 150,000 (15, 16). The camps were intended to serve a military purpose but became a humanitarian disaster. Lethal epidemics of infectious diseases spread throughout the camps, and nearly half of all children in the camps died of infectious diseases. For the analyses reported, data were derived from primary records maintained by the Boer Concentration Camp Database Project (<http://www.lib.uct.ac.za/mss/bccd/index.php>) at the University of Cape Town (16). The database is a continuously updated archive of records which, in 2012, consisted of data on 102,257 individuals (including 29,491 deaths, of which 5,854 were from unknown causes) who were detained in concentration camps from 1900 to 1902. Causes of death were reported by camp medical authorities or by family members. Diagnoses were not confirmed pathologically; however, medically trained observers were at the camps most of the time. Causes of death as reported on primary records were classified by a single investigator into disease categories. Deaths reportedly due to measles or pneumonias were combined because they

were not precisely differentiated by the medical staffs of the camps. Internees arriving at the same camp at the same time who either had the same surname or came from the same farmstead were classified as being in the same family or farm unit, respectively.

### US Army mobilization camps, 1917–1918

After the United States declared war in April 1917, there was a massive mobilization of men through enlistments and conscriptions. The training of military units occurred at more than 40 mobilization camps located throughout the United States and Puerto Rico (17, 19, 20). During the severe winter of 1917–1918, many troops were housed in crowded and poorly heated wooden barracks or tents. Many recruits had experienced measles as children and were thus immune; however, many others, particularly those from the rural South, had not been infected and were immunologically susceptible. During the winter of 1917–1918, there were large outbreaks of measles and nearly 2,000 measles-related deaths, mostly in mobilization camps and aboard troopships bound for Europe (6, 17, 19, 21). Most measles-related deaths among soldiers were caused by secondary bacterial pneumonias.

During the years 1917 and 1918, the Office of the US Army Surgeon General published annual summary reports; after the war, the medical experiences of the US Army during the war were reviewed in detail in a multivolume history (21). These reports summarized frequencies and rates of measles by month, mobilization camp, and the US state of origin of affected individuals (17, 21).

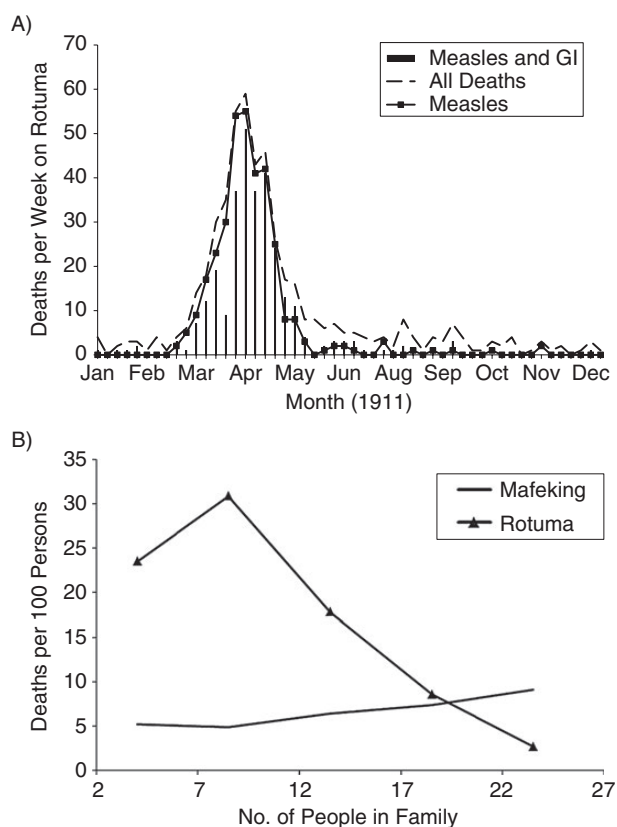
## RESULTS

### Rotuma

During the first-contact measles epidemic on Rotuma in 1911, island residents of all ages died. The highest age group-specific mortality rates during the epidemic were among young children (23% for those <5 years of age) and young adults (17% for those 16–24 years of age). The mortality rate was slightly higher among females (16%) than males (13%) (11, 13). During the epidemic period, measles-specific and overall mortality rates peaked at approximately the same times (April/May 1911) (Figure 1A).

Although the island is very small (43 km<sup>2</sup> in area), measles-specific mortality rates varied widely across its 7 geopolitical districts (range across districts, 7%–22%) and its 188 family groups (mean persons per family = 12; median mortality rate per family, 8%; range, 0%–100%) (Table 1). During the epidemic period, mortality rates were relatively low among families with any non-Rotuman ancestry (e.g., other Pacific islanders), even among family members who had never left the island (12, 13).

During the Rotuman measles epidemic, gastrointestinal disorders (usually described as ileocolitis or dysentery/diarrhea) that followed measles infections were the most frequently reported causes of death (75%) (22) (Figure 1A). Mortality rates varied greatly on the basis of household size (Figure 1B). This is in direct contrast to mortality rates in the Mafeking Boer War concentration camp, which is the only



**Figure 1.** A) Epidemic curve of total and measles mortality rates on the Polynesian island of Rotuma in 1911 by week, also showing the number of deaths attributed to gastrointestinal (GI) complications (e.g., ileocolitis) following measles. B) Measles mortality rates by size of family unit in both Rotuma in 1911 and the South African Boer War Mafeking concentration camp in 1901–1902.

camp for which comparable data were available. In contrast to deaths in most epidemics of the 20th century, deaths from secondary pneumonias/other respiratory illnesses during the Rotuma epidemic were relatively uncommon. Mortality rates were not high during the next measles epidemic on the island in 1928 (7).

### Boer War concentration camps

During the Boer War, 102,257 individuals were forcibly confined to internment camps. Camp internees were predominately young (i.e., infants, children, and young adults) and from the Transvaal (56%) or Orange Free State (40%) regions of South Africa, and there were more female (56%) than male internees (Table 1). During the period of forced internment, nearly one-third (28.8%,  $n = 29,491$ ) of all internees died. Overall mortality rates were similar among males (28%) and females (29%), slightly higher among internees from the Transvaal (33.4%) than the Cape Colony (28.5%), and very high among internees who were born in a camp (47.1%) (Table 1).

Of all internee deaths of known causes ( $n = 20,359$ ), nearly two-thirds (64.8%) were reportedly due to measles ( $n = 6,747$ ) or pneumonias/other acute respiratory infectious diseases ( $n = 6,444$ ). Measles-specific mortality rates declined sharply with increasing age, from 17% among the youngest (aged  $\leq 5$  years) to 0.3% among the oldest (aged  $> 60$  years) (Table 2).

There were few deaths in the internment camps during calendar year 1900. However, internee deaths markedly increased beginning in January 1901, and the peak of weekly deaths was in October 1901 (maximum of 940 deaths/week). A second peak of weekly deaths occurred in January 1902 (maximum of 438 deaths/week). During 1900, 1901, and 1902, the mean numbers of deaths per week were 4.7, 411.0, and 80.7, respectively (Figure 2).

There were 45 named farmsteads, from which at least 200 residents/workers each were forced into camps. Among internees from this sample, mortality rates across farmsteads ranged from 4.4% to 42.3%; the median farm-specific mortality rate was 25.2% (data not shown). The overall mortality rate (23.0%) among internees from relatively small farms ( $< 200$  internees each) was slightly lower than the median mortality rate across the larger farms (data not shown).

The median camp-specific mortality rate across the “large camps” ( $> 1,000$  internees each) was 15.8% (range, 7.4%–96.1%). The overall mortality rate (60.4%) among internees confined in smaller camps ( $< 1,000$  internees each) was nearly 4 times higher than the median mortality rate across the larger camps (data not shown).

Across all farmsteads of origin and internment camps, there was marked variability in overall mortality percentages but relative consistency in the nature of the deaths. Across both farms of origin and destination camps, the relative contributions of measles and pneumonia to overall mortality rates were very similar (median, 45.0% of all deaths due to measles/pneumonia across farmsteads of origin; median, 44.4% across internment camps) (Figures 2 and 3). There were few deaths among adult internees, indicating that most adults had been infected with measles in the past.

The camp epidemics were not first-contact epidemics at the population level. Still, mortality rates were extreme because large numbers of immunologically susceptible individuals who had been relatively isolated on remote farmsteads were suddenly congregated in crowded camps. The circumstances enabled measles and other respiratory pathogens to efficiently cocirculate among nonimmune members of the confined populations.

Most deaths of camp internees were due to bacterial pneumonias that complicated measles infections. During camp epidemics, measles infections severely compromised the lower respiratory tracts of those infected. In turn, respiratory bacterial strains that were cocirculating with measles were able to invade the lower respiratory tracts of measles-infected hosts if the hosts had no preexisting immunity against the respective bacterial strains.

### US Army recruit camps

The massive mobilization ( $> 4$  million men) of manpower for the US Army during the First World War precipitated

**Table 1.** Demographic Characteristics of Boer War Concentration Camp Population, South Africa, 1900–1902

Characteristic	All Persons		Deaths		
	No.	%	No.	%	Mortality Rate %
Total refugees	102,257	100.0	29,491	100.0	28.8
Sex					
Female	53,247	52.1	14,940	50.7	28.1
Male	42,036	41.1	12,379	42.0	29.4
Unknown	6,974	0.0	2,172	7.4	31.1
Age (from any source)					
Known	89,243	87.3	25,363	86.0	28.4
Unknown	13,014	12.7	4,128	14.0	31.7
Race					
White	94,812	92.7	28,697	97.3	30.3
Black	442	0.4	215	0.7	48.6
Other	214	0.2	26	0.1	12.1
Unknown	6,789	6.6	553	1.9	8.1
Nationality					
Transvaal	49,424	48.3	16,494	55.9	33.4
Free State	48,788	47.7	11,892	40.3	24.4
Cape Colony	1,363	1.3	389	1.3	28.5
Unknown	2,682	2.6	716	2.4	26.7
Marital status					
Single	69,248	67.7	23,106	78.3	33.4
Married	20,451	20.0	1,346	4.6	6.6
Widowed/divorced	1,777	1.7	141	0.5	7.9
Unknown	10,781	10.5	4,898	16.6	45.4
Head of family					
Yes	17,820	17.4	987	3.3	5.5
No	84,437	82.6	28,504	96.7	33.8

measles epidemics in mobilization camps. Most measles epidemics and associated deaths occurred during the winter of 1917–1918 (Figure 4A).

Across the 39 major mobilization camps in the continental United States, measles-related mortality rates varied from 0 to 60 (median, 6) per 10,000 soldiers, and case fatality percentages varied from 0% to 5% (median, 2%). Measles-related mortality rates varied in relationship to the home states of the mobilized soldiers (Figure 4C, Table 3) (21). In general, measles-related mortality rates were higher among soldiers from rural southern states (e.g., Mississippi) and other predominately rural states (e.g., Vermont).

In the early 20th century in the United States, lack of immunity to measles among adult men was a marker of lifelong social isolation. Such isolation was characteristic of life on rural farms that were detached from urban centers in which measles efficiently circulated. Large measles epidemics resulted when such isolated rural residents were conscripted into the US Army. In these US Army mobilization camps, most measles-related deaths were due to secondary bacterial pneumonias. During camp epidemics, gastrointestinal complications following measles infections were uncommon;

gastrointestinal complications were not listed among the 17 most common complications following measles (21).

During the epidemic periods of interest for this report, mortality rates from diseases overall were much lower among soldiers at affected US Army mobilization camps (median, 2.0%) than among Rotuman islanders or Boer concentration camp internees (Figure 4B, Table 3). Compared with their Rotuman and South African counterparts, US soldiers were generally young adult men who were certified to be healthy, physically fit, and well-nourished prior to entering service; also, as soldiers, they received professional medical and nursing care throughout the course of severe illnesses, such as measles.

## DISCUSSION

The 3 measles epidemics described in this report covered a spectrum of epidemiologic isolation (Rotuma was most isolated; US Army camps were least isolated) and caused a range of measles-attributed mortality rates (12% in Rotuma, 4.5% in Boer War camps, and 0.06% in US Army camps). However,



**Table 2.** Mortality Rates in Boer War Concentration Camps, South Africa, 1900–1902<sup>a</sup>

Cause of Death	No.	% of All Deaths
Respiratory		
Measles	6,747	28.5
Pneumonia	2,867	12.1
Other diseases of respiratory system	3,577	15.1
Pertussis or whooping cough	814	3.4
Tuberculosis	228	1.0
Influenza	167	0.7
Diphtheria	167	0.7
Total respiratory	14,567	61.6
Gastrointestinal		
Typhoid fever	2,327	9.8
Diarrhea, dysentery, or gastroenteritis	2,367	10.0
Total gastrointestinal	4,694	19.9
Other known causes		
Ill-defined fever	1,098	4.6
Malnutrition or scurvy	685	2.9
Diseases of the nervous system	672	2.8
Debility, senility	636	2.7
Diseases of the circulatory system	321	1.4
Accidents or combat injuries	146	0.6
Puerperal fever or accidents of birth	121	0.5
Diseases of the urinary system	104	0.4
Malignant disease	72	0.3
Total other known causes	3,855	16.3
Other/uncertified		
All other causes	345	1.5
Uncertified deaths	176	0.7
Total other/uncertified	521	2.2
Deaths with known/uncertified causes	23,637	
Deaths with unknown causes	5,854	
Total deaths	29,491	100.0

<sup>a</sup> Cause-of-death classifications made by current investigators on the basis of either medical officer reports or Afrikaans translations of general descriptions of death.

the epidemics had markedly different epidemiologic and clinical characteristics (Table 3).

Mortality percentages were high overall during the first-contact epidemic on Rotuma and the camp epidemics during the Boer War. However, most deaths on Rotuma were due to gastrointestinal disorders, whereas most deaths of Boer War internees were due to pneumonias. Most Rotumans had had very little contact with outside populations or with diverse respiratory infectious agents either before or during the measles epidemic. Thus, although their respiratory tract defenses were compromised by their primary measles infections, measles-

infected Rotumans, unlike camp detainees, were unlikely to contact potentially invasive respiratory bacteria to which they had no preexisting immunity.

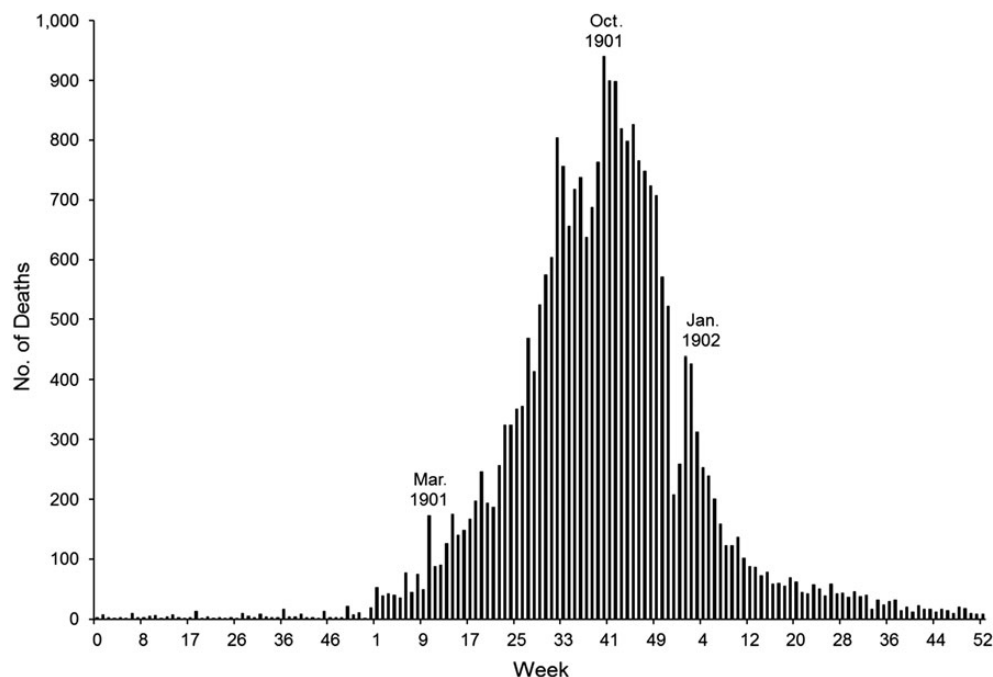
The Boer War camp epidemics affected a civilian population of mixed ages and both sexes that was forced off widely separated farms and into concentration camps during war time. During the courses of their measles illnesses, affected internees were likely exposed to numerous and diverse respiratory infectious agents. Most deaths during the measles epidemics at the camps were due to pneumonias/other respiratory complications, as is still true in modern African refugee camps (14–16, 24).

The US Army mobilization camp epidemics affected young adult men from diverse geographical and demographic backgrounds who were crowded together in military encampments. As were the Boer war internees, many US soldiers who were affected by measles were likely exposed to diverse respiratory bacterial strains throughout the courses of their measles illnesses. Most deaths during the military epidemics were due to secondary bacterial pneumonias (18, 19, 25).

The acute pathological effects of measles include the destruction of respiratory epithelium and depression of cellular immunity (7, 8). These effects interact to transiently increase measles-infected hosts' susceptibility to respiratory bacterial strains to which they are not immune. Measles-infected individuals who had been epidemiologically isolated throughout their lives and were exposed during their measles-related illnesses to novel (to their immune systems) bacterial respiratory pathogens were at particularly high risk of life-threatening bacterial pneumonias (18).

The Boer War and First World War camps were ideal epidemiologic settings for the rapid transmission of measles virus among nonimmune camp residents (15, 18). Such settings are also particularly dangerous environments for measles-infected individuals who are likely exposed to high concentrations of diverse respiratory bacterial pathogens to which they are not immune and may be transiently hypersusceptible (15). If measles patients could be protected from bacterial respiratory pathogens that are novel to their immune systems, the clinical courses of their infections would likely be less complicated and their chances of surviving much improved (18). A study of First World War-era soldiers with measles provided empirical support for this hypothesis. During the study, rates of secondary bacterial pneumonias and mortality were much lower among soldiers who recuperated from measles in their own barracks (bacterial pneumonia, 1.6%; mortality, 0.4% (1/256)) rather than in crowded hospital wards (bacterial pneumonia, 9.5%; mortality, 2.1% (11/532)) (21).

During the epidemic on Rotuma, the clinical expressions and fatal end-stages of measles among island residents markedly varied from those during the other epidemics considered here. The clinical end-stages of most of the fatal measles infections of Rotumans were gastrointestinal—not respiratory—inflammatory conditions (13). These gastrointestinal conditions were generally described by the British medical officer on Rotuma as “ileocolitis” or “dysentery/diarrhea.” During first-contact measles epidemics on both Hawai'i (in 1846) and Fiji (in 1875), the few Westerners present emphasized the severe gastrointestinal effects of the disease (1, 2, 22, 23, 26). Because



**Figure 2.** Epidemic curve of weekly all-cause mortality rates in Boer War concentration camps in South Africa, 1900–1902.

the measles virus is highly conserved, the differences in the clinical manifestations of measles during the Pacific island epidemics are unlikely due to variations in measles virus strains.

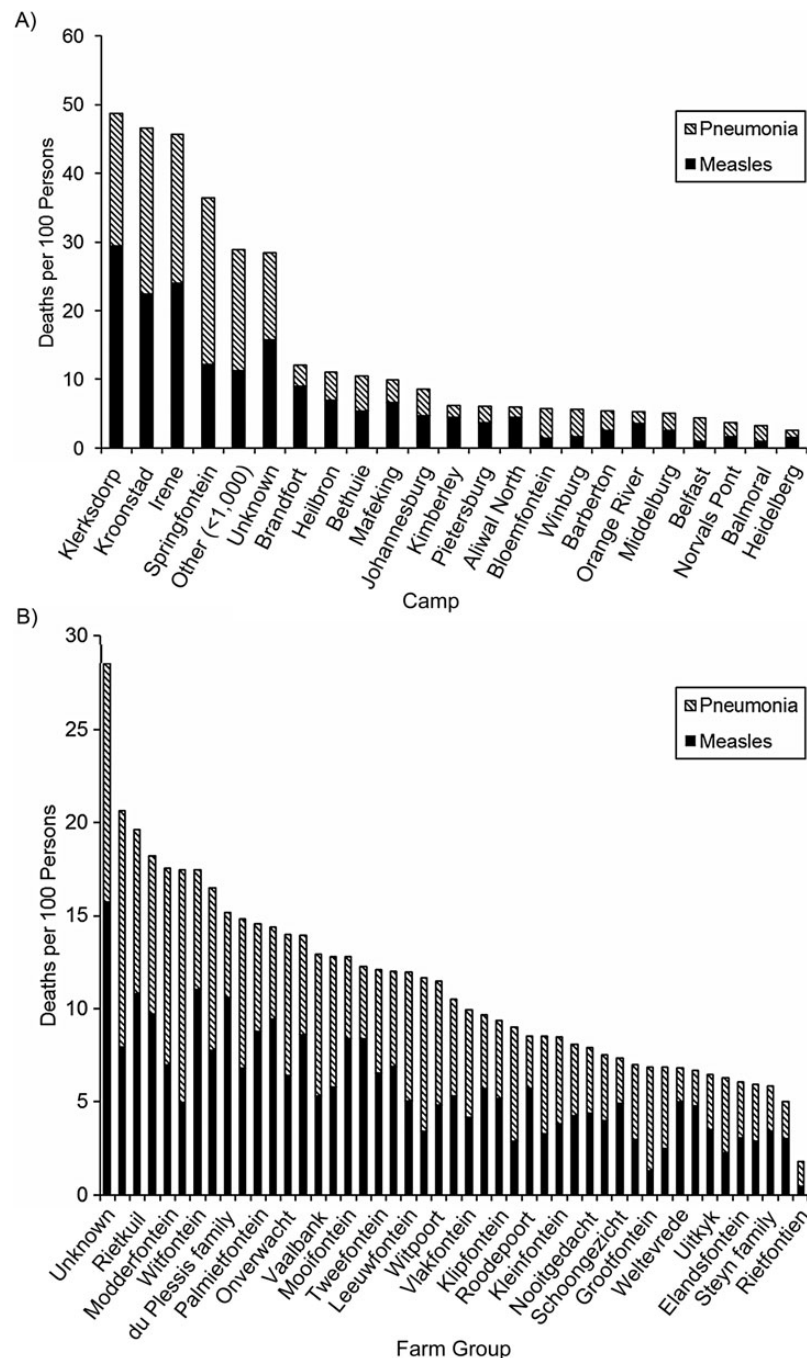
Some observers have analogized the epidemiologic isolation of Boer farm residents prior to their internments to the isolation of Fijian islanders prior to the introduction of measles (14, 15). The analogy has some utility in explaining the high measles-related mortality rates; however, the analogy does not account for the markedly different clinical manifestations of measles during the Boer War concentration camp and Fijian epidemics (14, 15).

We surmise that the clinical manifestations and outcomes of most measles infections during epidemics reflect the immunological statuses of those affected and epidemiologic characteristics of the environments in which infected individuals interact among themselves and with others. Specifically, the diversity, intensity, and timing of exposures and immunological responses to respiratory tract bacteria over the lifetimes of individuals prior to their measles infections and during transient periods of increased respiratory tract susceptibility soon after their measles infections determined the clinical expressions and ultimate outcomes of their infections.

Antibiotics and measles vaccine were not available, and thus did not affect measles mortality rates, until at least the mid-20th century. Nursing care did affect survival during measles epidemics, especially when the primary providers and caregivers in families and other self-supporting groups were simultaneously affected. It is unlikely, however, that the Nightingale nursing revolution significantly decreased

measles-related mortality rates in general (6, 10, 26). There is no evidence of variability of the intrinsic pathogenicity of measles strains (7, 8). Human genetic factors may have played some role in determining the clinical severity and lethality of measles infections described in this report because both the Rotuman and South African populations had limited intermarriage with outside groups, likely resulting in largely homogenous human leukocyte antigen phenotypes (27). This would not have been true in the US epidemic because the soldiers came from all types of genetic backgrounds. None of the groups described (Polynesian, Boer, American) are at increased risk of dying from measles in modern times. Such decreases in lethality within 2 reproductive generations cannot be explained by Darwinian evolution alone.

In the absence of extant clinical material, we must speculate as to the mechanisms of extreme mortality rates during first-contact measles epidemics. These geographically isolated populations had not only avoided measles virus, they had also missed exposure to a wide variety of ordinary respiratory pathogens such as pneumococcus and rhinovirus (28–30). It is highly likely that their immune systems had relatively few T-cell clones from previous infections with a very limited number of human leukocyte antigen genotypes because of their very narrow genetic base. In isolated populations, the lack of immunological experience increased the chances of a pathogenic overreaction to any severe infection, as opposed to ordinary development of immunity. Even today, the balance between pathology and immunity during a systemic infection can be disrupted under circumstances not requiring geographical isolation (29, 30). During first-contact

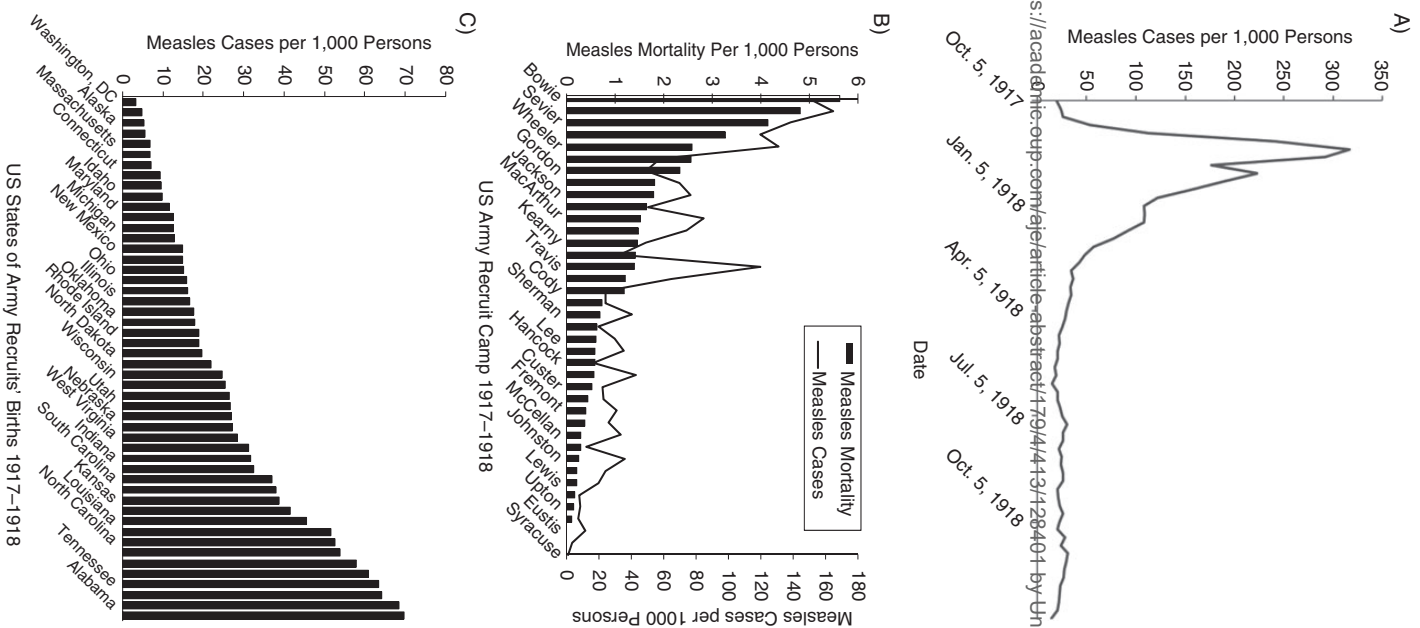


**Figure 3.** Measles and pneumonia mortality rate distributions A) by camp, and B) by individual family (same surname)/farm group (came to the camp together) in Boer War concentration camps, South Africa, 1901–1902.

epidemics, immunopathology was a more likely outcome than in measles-experienced populations.

Immunopathology may have been demonstrated by the unusual clinical presentations often seen during first-contact epidemics, such as hemorrhagic/black measles and severe gastroenteritis, which are suggestive of immune dysfunction. Severe gastrointestinal symptoms, such as subacute dysentery

following measles, were especially described during Pacific epidemics (2, 11, 26). Because measles virus particularly infects the mucus-secreting intestinal cells, the massive cellular immune stress of measles may disorder the host's tolerance of their own bacterial microflora; such disruptions may enable invasion of the gut wall by normally tolerated bacteria with subsequent inflammatory reactions and chronic malabsorption.



**Figure 4.** Measles mortality rates in US Army recruit camps in 1917–1918. A) Epidemic curve by week for the continental United States; B) morbidity and mortality rates by specific recruit camp in the United States; and C) by US state of origin of military conscript (home town, not where soldier died of measles).

**Table 3.** Comparison of Measles Epidemic Mortality Rate Patterns During the Early 20th Century

Unit by Epidemic Location	Population Information	Years	Measles Mortality Rate, %		Total Mortality Rate, %		Isolation Factor	Modern Equivalent
			Median	Range	Median	Range		
Island of Rotuma	2,600 Persons	1911					Polynesian island with few shipping contacts, 500 km from administrative center in Fiji	Isolated tribal group (few if any remain who have never been exposed to measles)
Family			Not reported	Not reported	8	0–100		
District			12.0	7.4–22	17	16–29		
Boer War camps in South Africa	>1,000 Persons each in 21 camps	1901–1902					Single farms scattered across the South African veldt, usually with large extended families	African refugee camp (23)
Family or farm			4.99	0.44–10.98	25	4.4–42		
Camp			4.45	1.00–29.51	16	7.4–96		
US Army recruit camps	>1 Million men in 40 camps	1917–1918					Male military conscripts largely from rural Southeastern United States where there were few transportation links in 1918	Adult measles vaccine failure
US state			2.1 <sup>a</sup>	0.33–7.0	1.1	0.38–2.4		
Camp			0.06 <sup>b</sup>	0.0–0.6	2.0	0.38–4.5		

<sup>a</sup> Measles cases, not deaths.  
<sup>b</sup> Deaths, not cases.



populations also accounts for the rarity of severe gastrointestinal effects of measles today (except in some malnourished populations who are already immunocompromised) (22, 32, 33). Of note, most measles-related deaths in modern developed countries are due to primary viral pneumonitis or encephalitis, although modern epidemics can occasionally involve high mortality rates (6, 7, 13, 21, 34).

We conclude that the key factor determining the extraordinary mortality rates during first-contact epidemics was extreme isolation. Extremely isolated populations are immunologically naïve to measles and other viruses with epidemic potential (e.g., influenza), have limited exposures to respiratory bacterial strains, and are prone to develop imbalanced, immunopathological reactions when exposed to novel infectious agents. Effects of extreme isolation may account for the devastation of many Pacific Island populations during the 1918–1920 influenza pandemic (35, 36). By the 20th century, only islands such as Rotuma were sufficiently isolated to create epidemiologic conditions comparable to those in earlier times (2, 3).

We further surmise that the most important determinant of the dramatic and widespread decline of measles mortality rates during the late 19th and early 20th centuries was globalization. With the development and expansion of land and sea transportation networks, previously isolated populations were interconnected with and integrated into the global community. Such globalization increased the intensity and diversity of exposures of previously isolated populations to respiratory, gastrointestinal, and other infectious and immunoreactive agents; enhanced balance within and between their humoral and cellular immune repertoires; and improved the effectiveness of immunological responses to novel infectious agents.

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