

Salmonellosis in TAB Vaccinated Population Island of Oahu, Hawaii

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WATERBORNE INFECTIONS due to enteric bacteria are practically nonexistent in Hawaii today. No outbreak of typhoid fever, paratyphoid fever, or dysentery has been reported for more than 30 years. Hawaii is unique with respect to immunization against typhoid and paratyphoid fevers, since it is one of very few communities, and possibly the only U.S. civilian community, where vaccination against these enteric pathogens is compulsory. In 1942, the entire population was inoculated against typhoid, paratyphoid A, and paratyphoid B under Army auspices, and such vaccination was thereafter made mandatory at 3 years of age. TAB (typhoid, paratyphoid A, paratyphoid B) vaccination has since continued under Territorial and State law and regulations of the Hawaii State Health Department. Salmonellosis was made reportable in 1951, and in 1953 TAB vaccination was urged at the age of about 1 year, though not made mandatory. Consequently, today, the entire population over 4 years of age and many children 1-4 years of age are presumably protected against these long-recognized *Salmonella* types.

The effect of this immunization program on the incidence of typhoid cases and deaths has been very striking and gratifying. For example, in the 10 years prior to TAB vaccination, 678 typhoid fever cases and 97 deaths were reported compared with only 31 cases and 5 deaths during the decade following institution

of vaccination, reductions of 95 percent in cases and 83 percent in deaths. The effect of TAB vaccination on the incidence of infections due to other salmonellae, especially the various types of *Salmonella* groups B and D, cannot be evaluated because the multiplicity of *Salmonella* types was not recognized before 1942. In 1948, facilities for *Salmonella* typing were established in the bureau of laboratories of the Hawaii State Department of Health, and an intensive program of epidemiologic followup of all *Salmonella* cases and detected carriers was instituted on the island of Oahu.

Salmonella Cases and Carriers

In the 12-year period 1948-59, salmonellae were isolated from stool specimens of 3,055 persons (table 1), of whom 1,421 (46.5 percent) were considered "recognized cases" because they were symptomatic patients who had been hospitalized or had been treated at home. Epidemiologic followup detected 1,418 (46.4 percent) additional persons harboring salmonellae, 552 "missed cases" and 866 "carriers." Salmonellae were also isolated from specimens submitted by 216 dairy workers and persons requesting permits to go on the watershed. The term "missed case" designates individuals who were contacts of patients or others from whom salmonellae were isolated, who had diarrhea at the time of, or shortly before, collection or submission of stool specimens, and who were not under the care of a physician. Those disclaiming any knowledge of intestinal disturbances were placed in the category of carriers. The fact that as many individuals harboring sal-

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monellae were detected by epidemiologic follow-up as were found among symptomatic patients clearly indicates the importance and value of epidemiologic procedures as possible control measures.

Until 1953, few specimens were submitted directly by physicians treating nonhospitalized patients. Since then, after physicians, particularly pediatricians, were apprised of the possible role of salmonellae as incitors of enteric infections other than the classic typhoid and paratyphoid fevers A and B, 478 (40.8 percent) of 1,168 recognized *Salmonella* cases were detected in specimens from patients treated at home. However, the incidence of detected salmonellosis cases and carriers has not decreased in the last decade (table 1), a phenomenon which might well be associated with the greater awareness of the problem and consequent increasing numbers of specimens submitted.

Distribution Among Salmonella Groups

The distribution of cases and carriers of salmonellae with respect to the various *Salmonella* groups and source of specimens is shown in table 2. The data for the long-recognized types,

S. paratyphi (paratyphoid A), *S. schottmuel-leri* (paratyphoid B), *S. enteritidis*, and *S. typhi*, are specifically indicated in their respective groups for more ready comparison. The scarcity of these types is striking: *S. paratyphi* was isolated from only 1 patient; *S. schottmuel-leri* was found only 7 times (3 recognized cases, 2 missed cases, and 2 carriers); *S. enteritidis*, the most commonly encountered of the classic types, accounted for 47 isolations (29 recognized cases, 5 missed cases, and 13 carriers); and *S. typhi* was detected in only 19 people (9 recognized cases, 1 missed case, and 9 carriers). In contrast to the small numbers of these long-recognized enteric pathogens, other *Salmonella* types were obtained from 2,981 persons; 1,758 types (59 percent) were among groups B and D which have common O antigens with *S. schottmuelleri* and *S. typhi*, respectively, of the TAB vaccine. Table 2 also shows that 913 (64.4 percent) of 1,421 recognized cases, 318 (57.5 percent) of 552 missed cases and 488 (56.5 percent) of the 866 carriers detected by epidemiologic followup were associated with salmonellae of groups B and D. Of the isolations from specimens submitted by applicants for watershed permits and dairy workers, 95 percent of whom were carriers, 112

Table 1. Distribution of salmonellae among cases and carriers, by sources of specimens, island of Oahu, Hawaii, 1948-59

Year	Recognized cases		Epidemiologic followup		Others ²	Total
	Hospital	Home	Missed cases ¹	Carriers		
1948.....	84	(³)	54	120	12	270
1949.....	21	(³)	25	35	8	89
1950.....	32	(³)	79	90	4	205
1951.....	23	(³)	18	12	18	71
1952.....	93	(³)	62	70	17	242
1953.....	91	40	86	77	36	330
1954.....	85	50	75	65	24	299
1955.....	83	60	36	39	10	228
1956.....	83	52	38	60	15	248
1957.....	131	98	29	108	20	386
1958.....	82	75	20	73	12	262
1959.....	135	103	30	117	40	425
Total.....	943	478	552	866	216	3,055
Percent.....	30.9	15.6	18.1	28.3	7.1	100

¹ On basis of history.

² Includes 12 missed cases and 204 carriers among dairy workers and individuals requesting watershed permits.

³ Very few specimens submitted by physicians from patients treated at home before 1953.

Table 2. Distribution of persons harboring salmonellae, by *Salmonella* group and type and sources of specimens, island of Oahu, Hawaii, 1948-59

<i>Salmonella</i>	Sources of specimens					Total	
	Recognized cases		Epidemiologic followup		Others ²		
	Hospital	Home	Missed cases ¹	Carriers		Number	Percent
Group A: <i>S. paratyphi</i> ³	1					1	0. 03
Group B: <i>S. schottmuelleri</i> ⁴	1	2	2	2		7	. 2
Others.....	355	230	232	316	67	1, 200	39. 4
Group C.....	239	96	162	253	54	804	26. 3
Group D: <i>S. enteritidis</i>	23	6	5	13		47	1. 5
<i>S. typhi</i>	9		1	9		19	. 6
Others.....	198	89	78	148	45	558	18. 3
Group E.....	109	54	65	116	45	389	12. 7
Group G.....	8	1	7	9	5	30	1. 0
Total.....	943	478	552	866	216	3, 055	100. 0

¹ On basis of history.

² Includes 204 carriers and 12 missed cases among dairy workers and persons requesting watershed permits.

³ Paratyphoid A.

⁴ Paratyphoid B.

(51.8 percent) were of groups B and D. That TAB vaccination might be conducive to an increased incidence of carriers of *Salmonella* types in groups B and D is perhaps not surprising, if the population is overly exposed to such bacterial types. In view of the demonstration of Longfellow and Luippold (1) that the blood of TAB vaccinated army recruits protected mice against *S. typhimurium* (group B) and *S. enteritidis* (group D), the high incidence of recognized cases associated with *Salmonella* types of groups B and D was rather unexpected. Possibly consideration of age distribution and association with vaccination might yield a partial explanation.

Age Distribution

The age distribution of individuals from whom salmonellae were isolated is shown in table 3, where the data are presented in two categories—those harboring strains of *Salmonella* groups A, B, and D, against which a large part of the population had been vaccinated, and groups C, E, and G, for which vaccines had not been employed. Children under 4 years of age accounted for 40.9 percent of those persons harboring salmonellae of groups A, B,

and D, but only 21.6 percent of those from whom salmonellae of groups C, E, and G had been isolated; in those aged 4-19 years, approximately the same percentages of isolates were obtained for each of the two *Salmonella* categories (18.1 percent and 16.3 percent respectively). The population 20 years old and over accounted for 41.0 percent of the isolates of salmonellae of groups A, B, and D, but 62.5 percent of those in groups C, E, and G. Salmonellae of groups A, B, and D were detected in 751 children under 4 years old, in 331 among those 4-19 years of age, and 750 of the population 20 years and over, whereas those of groups C, E, and G, accounted for 264, 200, and 759 for the respective age groups. Thus, salmonellae of groups A, B, and D, were 2.8 times as frequent among children under 4 years of age and about 1.7 times as high for those aged 4-19 years than were salmonellae of groups C, E, and G, whereas in the population aged 20 years and over the incidence of these two categories of salmonellae was about equal. Whether this trend toward the reversal of the relative incidence of the two categories of *Salmonella* groups is related to the practice of TAB vaccination is an intriguing question.

Considering that salmonellosis is so fre-

quently thought of as primarily associated with bacterial food poisoning outbreaks, the fact that children under 1 year of age, who constituted about 3.0 percent of the population, comprised over 20 percent of all persons harboring salmonellae and 25 percent of those from whom

salmonellae of groups A, B, and D were isolated, is especially interesting and significant. In contrast to the foregoing, those aged 10-19 years (about 16.3 percent of the population) accounted for only 4.9 percent of positive *Salmonella* findings. In the other age groups the

Table 3. Age distribution of individuals harboring salmonellae, island of Oahu, Hawaii, 1948-59

Age (years)	<i>Salmonella</i> groups A, B, and D ¹		<i>Salmonella</i> groups C, E, and G		Total		Percent of population
	Number	Percent	Number	Percent	Number	Percent	
Less than 1.....	460	25.0	170	13.9	630	20.5	3.0
1-3.....	291	15.9	94	7.7	385	12.6	10.3
4-9.....	240	13.2	143	11.6	383	12.6	10.8
10-19.....	91	4.9	57	4.7	148	4.9	16.3
20 and over.....	750	41.0	759	62.1	1,509	49.4	59.6
Total.....	1,832	100.0	1,223	100.0	3,055	100.0	100.0

¹ Population over 4 years of age and some of those aged 1-4 had been vaccinated against paratyphoid A, paratyphoid B, and typhoid bacilli, which represent types in *Salmonella* groups A, B, and D, respectively.

Table 4. Number of cases and average annual age-specific case rates for predominant *Salmonella* types, island of Oahu, Hawaii, 1948-59

<i>Salmonella</i> group and type	Number of cases			Average annual case rates ⁴			Ratio of rates	
	Less than 1 year ¹	1-3 years ²	4 years and over ³	Less than 1 year	1-3 years	4 years and over	Less than 1 year 4 years and over	1-3 years 4 years and over
Group B:								
<i>S. typhimurium</i>	180	103	203	1,530	252	62	24.7	4.1
<i>S. derby</i>	66	26	74	558	64	22	25.4	2.9
Group D:								
<i>S. panama</i>	138	73	143	1,170	177	42	27.9	4.2
Total B+D.....	384	202	420	3,258	493	126	25.9	3.9
Group C:								
<i>S. montevideo</i>	17	7	101	145	17	30	4.8	.6
<i>S. oranienburg</i>	12	9	125	101	22	36	2.8	.6
Group E:								
<i>S. anatum</i>	36	17	124	304	42	30	8.4	1.2
Total C+E.....	65	33	350	550	81	96	5.7	.8
Total.....	449	235	770	3,808	574	222	17.2	2.5
Ratio $\frac{B+D}{C+E}$	5.9	6.1	1.2	5.9	6.1	1.3	-----	-----

¹ Very few TAB vaccinated.

² Partially (probably less than 25 percent) TAB vaccinated.

³ All, presumably, TAB vaccinated.

⁴ Per million of age group.

incidence of salmonellae was roughly proportional to their respective populations.

Salmonella carriers, as might have been expected, were rarely encountered among children under 1 year old. Only 18 (2.9 percent) of 630 infants from whom salmonellae were isolated were considered carriers; of 385 children 1-3 years of age harboring salmonellae, some of whom had been vaccinated, about 20 percent were carriers, whereas, of 2,040 individuals 4 years old and over, all of whom were presumably TAB vaccinated and from whom salmonellae were isolated, 47.9 percent were carriers. Thus, the incidence of carriers increased with age. The question therefore arises as to whether TAB vaccination is related to the relative incidence of carriers of salmonellae of groups B and D.

Age and TAB Vaccination

Of the 3,055 persons from whom salmonellae were isolated, about 4 percent were simultaneously harboring two or three *Salmonella* types. Designation as to which types were the inciting agents and which were merely incidental to a carrier state was not feasible. Therefore, the following discussion on the incidence of cases with respect to age, coupled with TAB vaccination, is restricted to those from whom a single *Salmonella* type was obtained. Thirty-nine *Salmonella* types were detected, six of which accounted for more than 75 percent of these cases. As three of the six types, *S. typhimurium*, *S. derby*, and *S. panama*, are in *Salmonella* groups B and D (which include the paratyphoid B and typhoid organisms against which the population 4 years of age and over and some of those 1-3 years old have been vaccinated), and the other three types, *S. montevideo*, *S. oranienburg*, and *S. anatum*, are in groups C and E (which are not represented in the TAB vaccine), a comparison of the age-specific case rates associated with these six types for the three population groups might be especially interesting and, possibly, significant.

Table 4 shows the number of cases, the average annual age-specific case rates per million for the three population groups, and the ratios of the case rates for children aged under 1 year and 1-3 years to those of the population 4 years

old and over for each of the six *Salmonella* types.

For *S. typhimurium* (group B) the case rate for infants under 1 year old was 1,530 per million, 24.7 times as high as that for the vaccinated population 4 years and older, which had an age-specific case rate of only 62 per million. Those aged 1-3 years, some of whom had been vaccinated, showed a case rate of 252 per million or 4.1 times that of the older vaccinated population.

Similarly, for *S. derby* (group B) the case rate for infants (558 per million) was 25.4 times, and that for the age group 1-3 years (64 per million) was 2.9 times that of the population over 4 years old (22 per million).

For *S. panama* (group D, containing *S. typhi* of the TAB vaccine), the case rate was 177 per million for the partially vaccinated group aged 1-3 years and 1,170 per million for the unvaccinated infants, or 4.2 and 27.9 times as high, respectively, as the rate of 42 per million for the vaccinated population over 4 years old.

Thus, age-specific case rates for the predominating *Salmonella* types of groups B and D were 3.9 and 25.9 times as high for the partially vaccinated children 1-3 years old and nonvaccinated infants, respectively, than that of the TAB vaccinated population 4 years old and older. In contrast to the foregoing, the combined case rates for *S. montevideo* (group C), *S. oranienburg* (group C), and *S. anatum* (group E), in *Salmonella* groups from which there is no representative in the TAB vaccine, was somewhat lower (0.8 times) for the partially vaccinated group aged 1-3 years and only 5.7 times as high for the unvaccinated infant group, as for the older vaccinated population of 4 years and older.

In the age groups under 1 and 1-3 years, there were about 6 times as many cases due to the foregoing *Salmonella* types of groups B and D as to those of groups C and E, whereas for the population 4 years and older the corresponding ratio was only 1:2. Obviously, in families where *Salmonella* cases occurred, all the children must have been exposed to the same organisms. It would seem, therefore, that the much higher relative incidence of cases associated with salmonellae of groups B and D (as compared with those of groups C and E) among the

nonvaccinated children may be attributed, in part at least, to the heterologous immunity against salmonellae of groups B and D conferred on the older population by TAB vaccination.

In our experience, *S. typhimurium* and *S. panama* have been isolated from the bloodstream on a number of occasions and occasionally from the spinal fluid, in cases of meningitis, especially from young children. Furthermore, infants (under 1 year), who constituted about 3 percent of the population, accounted for more than 30 percent of recognized *Salmonella* cases. Salmonellosis in Hawaii must not, therefore, be considered as a disease which is merely, or primarily, associated with food poisoning among adults. *Salmonella* infections constitute an important cause of severe systemic, as well as enteric, infections of young children.

Incidence of Salmonella Types

The number of individuals from whom various types of salmonellae were isolated is shown in table 5. The types are listed in the order of their frequency in the appropriate *Salmonella* groups.

The rarity of salmonellae of group A is strik-

ing, as *S. paratyphi* (paratyphoid A) was isolated from only one individual.

Salmonellae of group B were isolated from 1,217 persons. *S. typhimurium* and *S. derby* were by far the most common types detected, accounting for 699 and 363 individuals, respectively. *S. bredeney* was isolated from 78 and *S. sandiego* from 36 persons. The infrequency of *S. schottmuelleri* (paratyphoid B), detected in only seven individuals (five patients and two carriers), is especially interesting and possibly significant.

Salmonellae of group C, obtained from 827 individuals, were distributed among 17 different types; no types were detected for 4 of these persons. *S. montevideo* and *S. oranienburg*, the most frequently determined types and generally associated with food poisoning outbreaks, accounted for 259 and 216 findings, respectively. *S. birkenhead* was found in specimens from 84 persons, *S. infantis* in 65, and *S. bovis-morbificans* in 63, whereas the long-recognized *S. cholerae-suis* was isolated only 4 times.

Only three *Salmonella* types, *S. panama*, *S. enteritidis*, and *S. typhi*, were represented in 649 individuals from whom *Salmonella* group D strains were isolated; no type was determined for 2 others in this group. *S. panama*

Table 5. Frequency of occurrence of Salmonella types, island of Oahu, Hawaii, 1948-59

<i>Salmonella</i> group and type	Number of persons	<i>Salmonella</i> group and type	Number of persons	<i>Salmonella</i> group and type	Number of persons
Group A		Group C—Continued		Group E	
<i>S. paratyphi</i> (paratyphoid A).....	1	<i>S. manhattan</i>	38	<i>S. anatum</i>	381
Group B		<i>S. oslo</i>	29	<i>S. weltevreden</i>	40
<i>S. typhimurium</i>	699	<i>S. newport</i>	18	<i>S. meleagridis</i>	17
<i>S. derby</i>	363	<i>S. kentucky</i>	13	<i>S. give</i>	16
<i>S. bredeney</i>	78	<i>S. tennessee</i>	10	<i>S. newington</i>	9
<i>S. sandiego</i>	36	<i>S. thompson</i>	9	<i>S. senftenberg</i>	2
<i>S. saint-paul</i>	16	<i>S. muenchen</i>	9	<i>S. taksony</i>	1
<i>S. heidelberg</i>	9	<i>S. cholerae-suis</i>	4	Total.....	466
<i>S. schottmuelleri</i> (paratyphoid B).....	7	<i>S. bareilly</i>	2	Group G	
<i>S. californica</i>	1	<i>S. decatur</i>	2	<i>S. grumpensis</i>	38
Undetermined.....	8	<i>S. blockley</i>	1	<i>S. poona</i>	1
Total.....	1,217	<i>S. denver</i>	1	<i>S. worthington</i>	1
Group C		Undetermined.....	4	Total.....	40
<i>S. montevideo</i>	259	Total.....	827		
<i>S. oranienburg</i>	216	Group D			
<i>S. birkenhead</i>	84	<i>S. panama</i>	583		
<i>S. infantis</i>	65	<i>S. enteritidis</i>	47		
<i>S. bovis-morbificans</i>	63	<i>S. typhi</i>	19		
		Undetermined.....	2		
		Total.....	651		

was by far the most commonly encountered type, accounting for 583 of the isolations; *S. enteritidis* was obtained from 47, and *S. typhi* from only 19 individuals. The infrequency of paratyphoid B and *S. typhi* may well be an index of the specific protective efficacy of TAB vaccination.

Salmonellae of group E, isolated from 466 individuals, were distributed among seven types of which *S. anatum* was by far the most dominant, having been obtained from 381 individuals; *S. weltevreden* was detected in specimens from 40, *S. meleagridis* from 17, *S. give* from 16.

Group G was represented by three types, *S. grumpensis*, *S. worthington*, and *S. poona*. The two latter types were each found in only 1 individual and in both instances together with another *Salmonella* (*S. derby* and *S. panama*, respectively), and *S. grumpensis* was found in 38 individuals, often together with other types.

Specimens from 117 persons yielded two *Salmonella* types, and three types were found in specimens from 15 persons. *S. typhimurium*, with *S. anatum*, the most frequent combination, was found in 25 persons; *S. derby* with *S. anatum* in 12; *S. derby* with *S. panama* in 10; *S. panama* with *S. anatum* in 8; *S. derby* with *S. grumpensis* in 7; and *S. typhimurium* with *S. derby* in specimens from 6 individuals. Other combinations were less frequently encountered. The most frequent combinations of three *Salmonella* types were *S. derby*, *S. panama*, and *S. anatum*, isolated from four individuals, and *S. typhimurium* with *S. derby* and *S. anatum*, found in three others. Salmonellae together with shigellae were found in specimens from 13 individuals (7 with *S. sonnei* I, 4 with *S. flexneri* III, and 2 with *S. flexneri* II). In four other instances, salmonellae were found together with enteropathogenic *Escherichia coli* (two, type O111B4; one, O55B5; and one, O127B8). The importance of fishing many suspicious colonies and typing a goodly number of them, if a true picture of the incidence of infecting *Salmonella* types is to be obtained, is manifest.

Interestingly, in the course of examining specimens submitted from inhabitants of Canton and Christmas Islands, four *Salmonella* types not found in Hawaii were detected, *S.*

carran and *S. cerro*, each from one individual, *S. gatuni* from three, and *S. adelaidae* from seven. These findings might be of special epidemiologic significance should an outbreak due to one of these types occur in Hawaii.

Summary and Conclusions

Of the population of the island of Oahu, Hawaii, during the 12-year period 1948-59, presumably all those 4 years of age and older, a small portion of the age group 1-3 years, but probably none of the infants, had been vaccinated against typhoid fever and the paratyphoid fevers A and B.

Salmonellae comprising the TAB vaccine were isolated from only 27 persons, 1 paratyphoid A, 7 paratyphoid B, and 19 typhoid, indicating specific effectiveness of the vaccine. However, 36 other *Salmonella* types were isolated from 3,028 different individuals. Six types, *S. typhimurium*, *S. derby*, *S. panama*, *S. montevideo*, *S. oranienburg*, and *S. anatum*, accounted for over 75 percent of the individuals found to be harboring salmonellae. Two or three different *Salmonella* types were present simultaneously in about 4 percent of the individuals from whom salmonellae were isolated.

Practically as many individuals (1,418) harboring salmonellae were found among missed cases and carriers as were detected by examination of specimens from suspected cases (1,421), a fact which is indicative of the value of epidemiologic followup as a control measure.

The relative incidence of carriers seemed to increase with age and presumed TAB vaccination. Of those harboring salmonellae, 2.9 percent of the infants, 20 percent of the age group 1-3 years, and 47.9 percent of the population 4 years old and older were carriers.

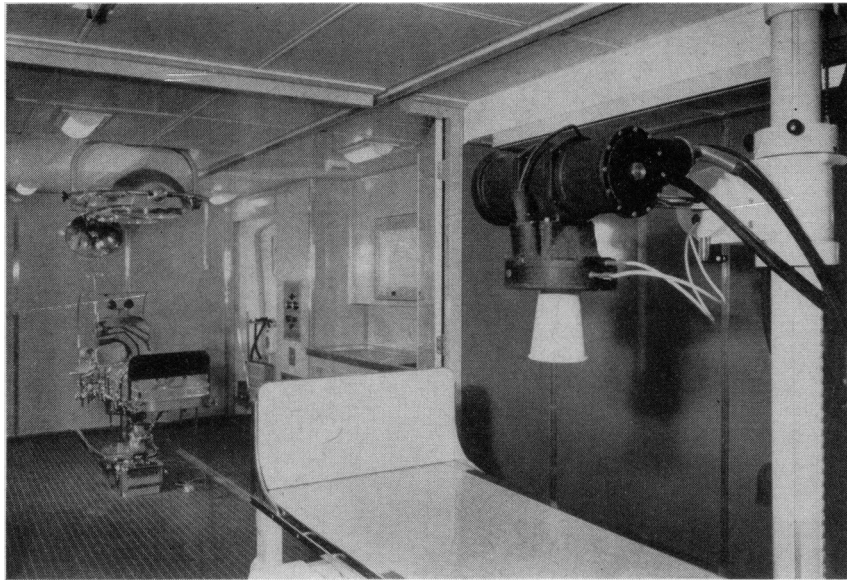
Cases due to salmonellae of groups B and D were 25.9 times as high among unvaccinated infants as among the vaccinated population 4 years old and older, whereas those due to types in groups C and E were only 5.7 times as frequent, a phenomenon which may possibly be attributed to the heterologous immunity against salmonellae of groups B and D conferred on the older population group by TAB vaccination.

Considering that children under 1 year old, who constituted about 3 percent of the population, accounted for 20.5 percent of those from whom salmonellae had been isolated and more than 30 percent of recognized cases, salmonellosis on Oahu during the 12-year period ap-

pears to have been primarily associated with infections of infants.

REFERENCE

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S.S. France

The new luxury liner *France* is the most recent of five foreign ships to carry a Certificate of Sanitary Construction from the Public Health Service.

To insure that the ship would get Public Health Service approval, the owners paid for translation of a PHS handbook for use by the shipbuilding firm, for a PHS sanitary engineer to travel to France twice for consultations during construction of the vessel, and for a final checkup by a PHS engineer and a PHS inspector at the shipyard after its shakedown cruise.

The other foreign vessels to receive the certificate are the *Gripsholm*, the *Bergensfjord*, the *Leonardo da Vinci*, and the *Cristoforo Colombo*, built to meet the requirements of the Public Health Service in respect to drinking water, plumbing, storage and handling of food, swimming pools, and ratproofing.

Modern medical facilities on the *France*, covering some 4,280 sq. ft., include doctors' offices and waiting rooms, X-ray and fluoroscope rooms, and a hospital containing operating, delivery, recovery, and five recuperating rooms. A portion of the hospital is shown above.