

A Long-term Carrier of *Shigella sonnei*

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Abstract

It has been known that patients with the bacillary dysentery may continue to excrete the bacilli in convalescence and there are not a few healthy carriers without any manifestation of clinical sign. The duration of excretion of bacilli in both convalescent and healthy carriers is generally within a few weeks. A very small proportion of carriers continues to excrete the bacilli for long time. However, even in cases of which stool cultures have been repeatedly positive for the same type of *Shigella*, it would be difficult to decide a long-term carrier or reinfection.

The case reported here was designated as carrier of *Shigella sonnei* six times for about three years and half since he recovered from the bacillary dysentery. The strains isolated from the case belonged to *Shigella sonnei* I of which Colicin type was 6, and they were sensitive to antibiotics as Chloramphenicol, Tetracycline and Streptomycin. Regarding the present situation that all strains of *Shigella* isolated in Nagasaki prefecture are highly resistant to these antibiotics, the sensitivity pattern of these strains could be considered as a characteristic marker, so that it could be able to exclude a possibility to have been reinfected.

Some particular investigations as the roentgenographic examinations of the digestive tractus and gallbladder, sigmoidoscopy, rectal biopsy, bile extraction by duodenal intubation etc. were carried out in order to clarify the state of carrier in this case. However, the results were negative so that it could be unable to realize how do the bacilli harbour in the body of the carrier.

Introduction

Patients with the bacillary dysentery may continue to excrete the bacilli after recovery from an acute attack, although this excretion lasts generally for only a week or so. On

the other hand, there are healthy carriers which have not presented any clinical symptom. In the recent, it has been noticed that extremely mild cases have increased which are difficult to be differentiated to the healthy carrier, particularly in cases infected with *Shigella sonnei*¹⁾. The period of the excretion of the bacilli in the healthy carriers also is usually limited within two weeks. However, a very small proportion of convalescent and healthy carriers become exceptionally persistent carriers in which the excretion of the bacilli lasts for more than three months, although it may be unable to exclude perfectly a possibility of a reinfection in any case.

A long-term carrier of *Shigella sonnei* is presented in this paper in which the stool culture was positive for the bacilli during the period of three years and half whenever the rectal swab was examined.

Case

J. T. male, born August 1944, is an employee of the milk manufactory. His residence is in Aino Town near the Nagasaki City. He was infected with *Shigella sonnei* in the month of March 1965 and hospitalized at the Omura National Hospital as a patient with the bacillary dysentery. He was recovered from an acute and mild illness and discharged after three consecutive negative stool cultures for *Shigella sonnei*.

In the periodical examination of stool for the food handlers June 1965 he was checked with the positive stool culture for *Shigella sonnei* and isolated at the same hospital as a carrier of *Shigella*. He became free from the bacilli after the antibiotic therapy and was discharged.

The periodical stool culture for the food

handlers kept him again as the *Shigella* carrier on 8th June 1966. He was isolated at the Isahaya Health Insurance Hospital and treated with nalidixic acid 150mg three times daily for 6 days. Five days after the treatment, however, the positive stool culture was seen. Then, more three days treatment with 200mg of nalidixic acid three times daily was repeated and discharged after three consecutive negative cultures.

The next episode began on 19th November 1967. The third hospitalization as the *Shigella* carrier was done after the periodical examination at the same hospital and he was kept for 12 days until the stool cultures became negative consecutively three times. At that time, Colimycin 1,200mg daily was used for 5 days.

In 1968 he was again hospitalized on 28th February at the Isahaya Health Insurance Hospital as the *Shigella* carrier because of the positive result of the regular stool examination for the food handlers.

Colimycin 1,200mg was given for 10 days. Although the stool culture became negative tentatively, the positive results were obtained in May and November of the same year by the culture of rectal swabs.

He was hospitalized at the Hospital of the Institute for Tropical Medicine of Nagasaki University for the precise examination and perfect treatment of the carrier state.

Strains of Shigella isolated from the case

The biochemical and serological behaviour and sensitivity to various antimicrobial agents were examined on the strains which were isolated from the case November 1967, February and November 1968 (S1, S2, S3).

The strains were serologically identified as *Shigella sonnei* I.

According to the colicine typing, they belonged to type 6.

The biochemical behaviour was as follows :

	S1	S2	S3
Fermentation of			
Adonitol	-	-	-
Dulcitol	-	-	-
Sorbitol	-	-	-
Arabinose	+	+	+
Xylose	-	-	-
Rhamnose	+	+	+
Maltose	-	-	-
Salicin	-	-	-
Inositol	-	-	-
Lactose	-	-	-
Sucrose	-	-	-
Mannitol	+	+	+
Glucose	+	+	+
Indole production	-	-	-
H ₂ S production	-	-	-
Sodium citrate utilization	-	-	-
Gelatin liquefaction	-	-	-
KNO ₃ reduction	-	-	-
Voges-Proskauer	-	-	-
Methyl red	+	+	+
Urea decomposition	-	-	-

The sensitivity of the strains to various antimicrobial agents was investigated by the dilution method. The result was as follows :

Drug	Minimum Inhibitory Concentration (mcg/ml)		
	S1	S2	S3
Chloramphenicol	3.12	3.12	3.12
Tetracycline	1.56	1.56	1.56
Streptomycin	6.25	6.25	6.25
Kanamycin	6.25	6.25	6.25
Colimycin	12.5	12.5	25.0
Furadiomycin	6.25	6.25	6.25
Aminobenzyl-Penicillin	6.25	6.25	6.25
Nalidixic acid	3.12	3.12	3.12
Furazolidone	1.56	1.56	1.56
Furatrizine*	1.56	1.56	1.56

*WHO uses the term "Dihydroxymethyl-Furalazine"

The pathogenicity of the strains was investigated by Dr Ghoda and his colleagues, Kitasato Institute, by the ligated intestinal loop method in rabbits, which was originally developed by S. N. De and modified by Ghoda and Sasaki²⁾. The ligated intestinal loops in which approximately 10⁸ of the strains S1, S2 and S3 were injected, were found to be markedly swollen in autopsies which were done about 20 hours after challenge.

Their contents were serous with blood and pus, and a little less number of organisms than challenged was counted. Such finding used to be seen in the challenge experiment with *Shigella*, and in the experiments of challenge with strains of *E. coli* which were isolated from stool cultures of the case, almost no change in the loop was seen in autopsies.

As far as the finding in the ligated loop experiment in rabbits is concerned, the pathogenicity of these strains were proved to be comparable to other strains of *Shigella*.

Results of stool cultures after the hospitalization in the Nagasaki University Hospital

The carrier was admitted in the ward of the Institute of the Nagasaki University on 11 November 1968. During the period of the hospitalization from 11 November through 30 November 1968, rectal swab was taken every day to carry out the bacteriological examination on rectal content. As media for culture, SS agar, BTB agar and Mackonkey agar were used to isolate the dysentery bacilli.

It was only two times on SS agar that colonies of *Shigella* were recognized: only one colony was found with 7 colonies of *E. coli* on 11 November and 7 colonies of *Shigella* were presented on 12 November.

BTB agar and Mackonkey agar indicated no colony of *Shigella* but two kinds of colo-

nies of *E. coli*, lactose fermentizing and non-fermentizing, on the same days.

Afterwards, results of culture on the three kinds of medium remained negative for *Shigella* during the period of the hospitalization.

The combined treatment with one gram of Tetracycline and one gram of Dihydroxymethylfuratrizine, divided in four times daily, started on 22nd November and continued for one week. The number of colonies of *E. coli* on BTB agar and Mackonkey agar decreased markedly after the treatment, but did not disappear absolutely.

Since he was discharged on the end of November 1968, he has come to the Institute once a week for the continuation of bacteriological examination of rectal swabs. The isolation of *Shigella* from his rectal content has been tried 21 time from 4 December 1968 through 19 May 1969. However, every culture resulted in negative for *Shigella*.

In the third week of the hospitalization, Magnesium sulfate was repeatedly given as a purgative. The carrier had a few times loose bowel movement after the administration of the purgative, but a provocation for the excretion of *Shigella* did not succeed.

Results of other examinations

He was a thin but well nourished young man. Physically he had no complain. No peculiar finding was recognized by the ordinary physical examination. Suspected harbouring bacilli in the gallbladder, the extraction of bile was tried twice, on 16 May 1968 and 14 November 1968, by the duodenal tubing. The results of the bacteriological examination of bile were negative for the dysentery bacilli. A normal shadow of the gallbladder was obtained by the cholecystography taken on 13 November 1968.

Barium study of the upper gastrointestinal tract was carried out on 12 November 1968. The roentgenographic finding of the stomach and upper intestine indicated no abnormality except ptosis of the stomach.

The roentgenographic examination of the colon using barium enema with air contrast was tried twice, on 4 April 1968 and 19 November 1968. No abnormal figure as stenosis, dilatation, tumor or ulcer, was found although the mucous membrane of the sigmoid and descendens seemed to be slightly oedematous and the motility was a little hyperkinetic.

The sigmoidoscopic examination and rectal biopsy was carried out on 12 March 1968 and 15 November 1968. Both examinations indicated that the mucous membrane of the rectum and colon was slightly oedematous and hyperemic, but neither ulcer nor tumor was recognized. The histological finding of the snippet of the mucous membrane of the rectum showed almost normal appearance of the intestinal wall except slight cell proliferation in the tunica propria.

The serum antibody against the stock culture of *Shigella sonnei* and the own bacilli was twice examined by the agglutination test, but no elevation of titer was found.

Discussion

The problem of the carrier in *Shigella* infection contains important unsolved questions; for instances, in what site of the body do the bacilli survive? is there any essential difference between patients and carriers? how is a role of the carrier for the transmission of the disease? how different is the pathogenicity of the bacilli isolated from the carrier to that of the patient? etc... So far, these questions have remained to be not clarified. Besides, the recent clinical

manifestation of Shigellosis in our country has become so mild that it may be unable to demarcate by a distinct line between patient and carrier.

The fact seems to make more difficult to decide even the definition of the carrier in *Shigella* infection.

However, if the duration of a carrier state lasts longer than three months, nobody would have an objection to designate the case as a carrier of *Shigella*.

Since old times it has been known that a small proportion of infected persons with *Shigella* has become a long-term carrier.

In our country, long-term carriers have recently been reported by some authors. 3)4)5)6) But, anywhere in the endemic area like our country it should be very difficult to exclude a possibility of a reinfection instead of a decision as a carrier state.

The case reported here was proved to have excreted *Shigella sonnei* I in stool during the period from June 1965 through November 1968, whenever the periodical stool examination was carried out once or twice yearly. In the recent, *Shigella sonnei* has taken the place of *Shigella flexneri* which had been predominating in Japan for more than fifty years. Since a few years ago about 90% of the isolated strains of *Shigella* in the Nagasaki prefecture belong to the group of *Sonnei*.

The Colicin type of the strains of this case is type 6. It cannot be a particular marker to characterize the strains, because Type 6 and 14 have been the most popular Colicin types in the Nagasaki prefecture.

As far as the drug-sensitivity of the strains of *Shigella* is concerned, a considerable increase of the highly resistant strains of *Shigella*, particularly *Sonnei*, to Chloramphenicol, Tetracycline and Streptomycin has

been recognized in the last five years in the Nagasaki prefecture as well as in the whole country. Figure 1 indicates the proportion of the resistant strains of *Shigella sonnei* among those isolated at the Nagasaki Municipal Hospital from 1958 up to 1967, and the percentage of the resistant strains of *Shigella sonnei* and *flexneri* isolated at the Kosei Hospital in Sasebo City during the same period is shown in Figure 2. According to these Figures, all strains of *Shigella sonnei* (Nagasaki City) and *Shigella sonnei* and *flexneri* (Sasebo City) are highly resistant to these three antibiotics. In fact, no sensitive strain of *Shigella sonnei* has been detected from dysentery cases which were admitted at the isolation hospitals in Nagasaki and Sasebo Cities since 1967.

Therefore, the fact that the strains which were isolated from this case November 1967, February and November 1968 are sensitive to the antibiotics should be worth of note.

At the moment when he was attacked with *Shigella sonnei*, March 1965, about half of the strains of *Shigella sonnei* in the Nagasaki prefecture were still sensitive to the antibiotics. It is presumed that he was infected with a sensitive strain of *Shigella sonnei* at that time, and the strain may have survived anywhere in his body without changing its sensitivity pattern to the antibiotics.

The investigations using the roentgenographic examinations of the digestive tractus and gallbladder, sigmoidoscopy, rectal biopsy and duodenal intubation were carried out for the purpose to clarify the state of carrier in this case. However, any positive result was unable to be obtained.

This carrier was detected by the periodical stool examination which is compulsorily once or twice yearly carried out on hotel and restaurant employees and food handlers. Pro-

Fig 1. Proportion of Resistant Strains of *Shigella sonnei* to C. T. S. Nagasaki Municipal Hospital
by
Kunihiko Aikawa

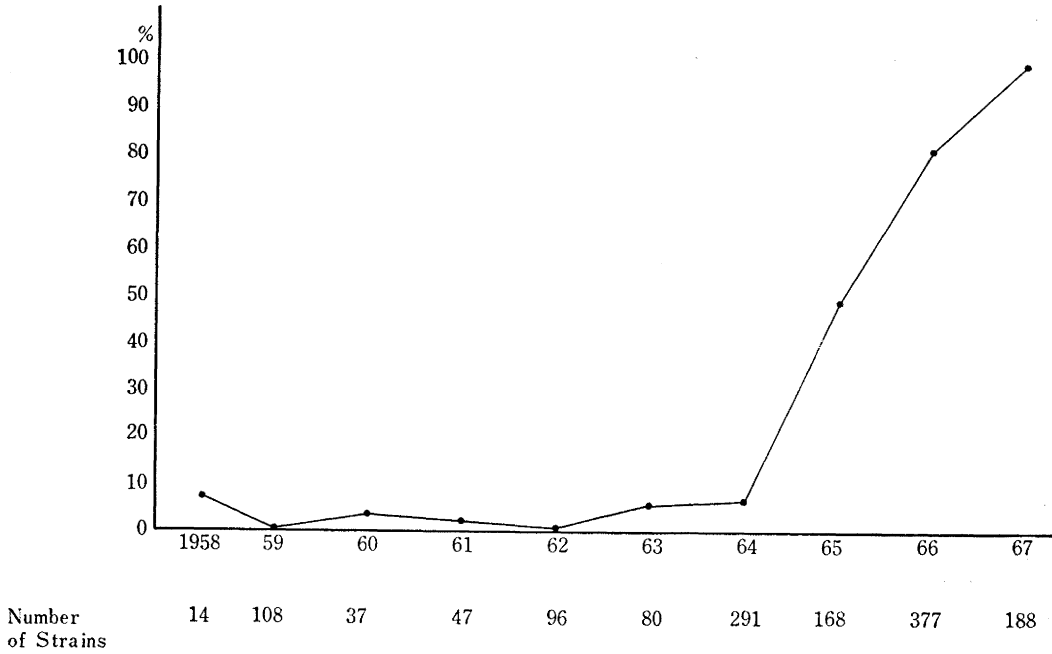
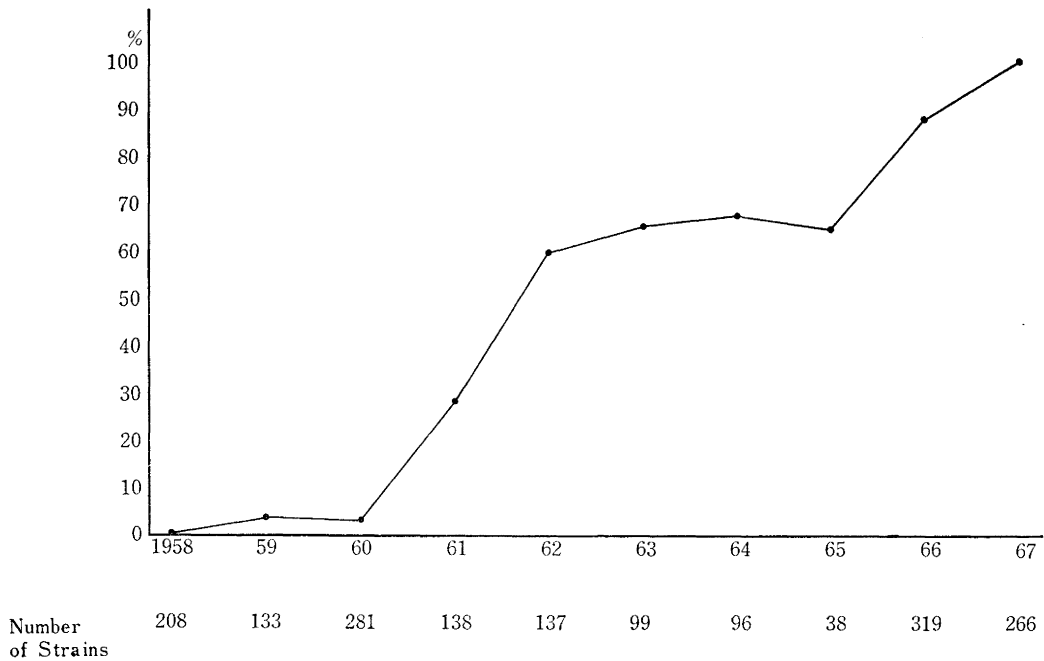


Fig. 2 Proportion of Resistant Strains of *Shigella sonnei* and *flexneri* to C. T. S. Kosei Hospital (Sasebo City)
by
Shukei Goto



bably he may not have been checked as a carrier unless he was working in the milk manufactory.

It can be supposed that there may be not a few long-term carriers which continue an intermittant excretion of the bacilli after recovery from the dysentery. Approximately 0.3% of stool samples which were collected

by the periodical examination on hotel and restaurant employees and food handlers were reported to be positive for Shigella. It can be presumed that among those positive cases there may be some long-term carriers.

The question, how do the bacilli survive in the body of the long-term carrier, should be an important task to be solved.

Summary

A long-term carrier of Shigella, male born August 1944, was reported.

He was infected with Shigella sonnei March 1965. Afterwards, from June 1965 until November 1968, he was confined six times at the isolation hospital. The strains isolated from the case are Shigella sonnei I, Colicin type 6 and sensitive to Chloramphenicol, Tetracycline and Streptomycin. Their sensitivity pattern was considered as an important marker to exclude a possibility of reinfection, regarding the fact that all strains of Shigella sonnei isolated in Nagasaki prefecture are highly resistant to these antibiotics.

Some particular examinations were carried out for the purpose to clarify the state of

harbouring the bacilli for long time, but failed to know, how do the bacilli survive in the body.

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ソ ン ネ 赤 痢 菌 長 期 保 菌 者 の 一 例

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摘 要

赤痢患者が症状消滅後もある期間排菌をつづける者のあること、なんらの臨床症状のみられない健康保菌者が近年特に増加していることは、一般に認められている。しかし、保菌期間が年余にわたる長期例の報告は少ないし、またそのような例について、再感染が否かを判断する資料が見当たらないのが常である。

ここに報告する例は、1944年8月生れの青年であって、1965年3月ソネ菌赤痢に罹患、隔離入院させられたが、抗生剤治療により順調に治癒退院した。本人は某乳業会社に勤務していたために、毎年食品ならびに接客業者のための定期検便をうけた。その結果、1965年6月から1968年11月までの約3年半の期間に、6回にわたって、ソネ菌が便中に証明された。

菌は *Shigella sonnei* I, コリシン型6, クロラムフェニコール・テトラサイクリン・ストレプトマイシン感受性であった。長崎地区における赤痢菌特にソネ菌の薬剤感受性は最近の5年間に著しく変化し、1962年以来分離されるソネ菌を主体とする赤痢菌は悉く C.T.S に高度の耐性を示すもののみとなった。この例は、当時約半数は感受性があったソネ菌に感染、その菌が3年有半にわたって体内に生残していたと推定される。

赤痢菌がこのように長期間保菌される場合、腸内のいづれかの個処に生残しているものか、あるいは胆嚢をチフス保菌者のように棲息場所に選んでいるのか、を知るために、各種X線検査、十二指腸ゾンデによる胆汁採取、直腸鏡検査、直腸生検などを行なったが、菌の存在場所を確認することはできなかった。

患者の自家菌ならびに保存ソネ菌に対する血中抗体の上昇は認められなかった。

この菌の病原性について、北里研究所合田朗博士が行なったウサギ小腸ループを用いる実験によれば、一般の赤痢菌と同様に、ループ内接種後膿血を混じた漿液の貯溜によりループの著明な腫脹がみられている。