Experimental Enteritis in Cynomolgus Monkeys Produced by Intragastric Administration of *Salmonella typhimurium*

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Abstract. To learn the minimum size of *Salmonella* organism required to develop gastroenteritis in humans, healthy cynomolgus monkeys were given intragastrically with various doses of a fimbriate (a wild-type) or a non-fimbriate of *Salmonella typhimurium*. Fourteen of 15 monkeys given $10^7$, $10^8$, or $10^9$ cells of a wild-type were infected. Among the monkeys infected, all 3 with $10^7$ cells, 4 of 5 with $10^8$ cells, and 2 of 6 with $10^9$ cells manifested enteritis. On the contrary, only 2 of 6 monkeys given $10^7$ or $10^8$ cells of a non-fimbriate were infected manifesting enteritis. Major symptom was watery diarrhea, but some cases excreted bloody mucous or loose stool. Abnormal stool was begun to excrete within the first a few days post administration in most of the cases. The watery diarrhea lasted for 2 to 3 weeks. The bloody mucous stool was excreted from the 2nd day to the 3rd day or from the 4th day to the 8th day. The loose stool was found on the 1st and 2nd days or the 2nd and 3rd days. At the onset of illness, abnormal stool contained $10^6$ to $10^8$ cells of the organism/g, and the number was increased during the course. At the autopsy conducted on the 2 monkeys excreted bloody mucous stool, gross change were found in the ileum and/or colon. The difference in the infectivity between the wild-type and non-fimbriate *S. typhimurium* is ascribed to the dierence in the ability of colonization in the intestine. It is suggested that an acute *Salmonella* gastroenteritis in human is possibly caused by a smaller size of the organism than that proved by the experiment with volunteers and isolated strains.

*Salmonella typhimurium* is the most common serovar causing *Salmonella* gastroenteritis or food poisoning in humans. Little is known, however, about the size of *Salmonella* organism needed to produce the disease occurring naturally. Based on the results obtained from the experiments with volunteers and isolated *Salmonella* strains [6–9, 11], it is suggested that ingestion of $10^8$–$10^7$ cells or more of the organism is required to produce an acute *Salmonella* gastroenteritis in adult humans [5, 13], though the size is rather variable depending upon the serovar used. However, such a large amount of *Salmonella* organism is not always contaminated in the food or other materials incriminated for human infection. In certain cases, food, dye or water contaminated with a small number of *Salmonella* organism was found to be responsible for the gastroenteritis in humans [1, 5, 11, 12, 14].

In the previous experiments, it was proved that strains of *S. typhimurium* harbored in the feces of carrier dogs, so-called wild-type strains, or the fimbriate descendants derived from one of the strains through mouse passage showed high infectivity against dogs [16] and mice [17, 18]. Kent et al. [4] reported that an acute gastro-

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enteritis developed in rhesus monkeys, when
$10^{10}$ cells of *S. typhimurium* was given
intragastrically, and there were much simi-
larities and few differences between the
disease produced in the monkeys and that
in man. Sugiyama et al. [15] also pro-
duced an acute gastroenteritis in Vietnam
monkeys, when a large amount ($10^7$–$10^8$
cells/kg of body weight) of *S. typhimurium*
or *S. dublin* isolated from bloody mucous
stools of patients was administered intra-
gastrically.

In order to learn the size of wild-type
*Salmonella* capable of producing an acute
gastroenteritis in humans, a non-fimbriate
descendant as well as a fimbriate descendant
of a wild-type strain of *S. typhimurium* were
administered intragastrically to cynomolgus
monkeys.

**Materials and Methods**

Animals: From 139 apparently healthy cynomol-
gus monkeys derived from Southeast Asia, 23 ani-
mals regardless of sex were selected. These animals
excreted no *Salmonella* and *Shigella* organisms in
their feces prior to administration, and showed no
or low degree of fimbrial agglutinin titer. Almost
all animals had O agglutinin titer varying from
1:10 to 1:40, and a half showed H agglutinin titer
from 1:10 to 1:20. The age varied from 2 to 5 or
more years and the body weight from 2 to 3.6 kg.
The animals fed with pelleted food and lemon.

Inocula: A fimbriate (F₁) and a non-fimbriate
(NF₁) descendants of a wild-type strain of *S. typhi-
murium* obtained from a dog-carrier through mouse
passage and culture on a blood agar plate were
submitted to present experiment [18]. The F₁
descendant was cultured in Duguid-Gillies’ broth [2]
for 48 hr at 37°C. The culture was repeated 3
times. In order to let the descendant have the
infectivity comparable to the parent wild-type *S.
typhimurium*, the 3rd broth culture was adminis-
tered intragastrically to a group of mice, NIH
strain, 4–5 week old. Each mouse was given 1 ml
of the culture having $10^6$ cells of the organism.
When the mouse died of sepsis 7 to 10 days later,
the small and large intestines were taken, and the
intestines were open with a pair of surgical scissors
in the longitudinal direction. After washing slight-
ly with physiological saline, one volume of the
intestinal wall was emulsified with 9 volume of the
Duguid-Gillies’ broth, and then serial 10-fold dilu-
tion was made on the emulsion containing $10^8$
cells of the inoculated organism/ml with a horse meat
infusion broth. In case of NF₁, 48 hr culture in the
Duguid-Gillies’ broth was used as inocula after
diluting with the horse meat infusion broth, since
the organism lacked an ability to colonize in the
mouse intestine.

Administration to monkeys: Prior to adminis-
tration of the inocula, 0.6 ml of ketamine hydro-
chloride (Sankyo Pharmaceutical Co., Tokyo) was
inoculated intramuscularly to each monkey. During
deep anesthesia, an indwelling tube for infant feed-
ing (Atom Co., Tokyo) was inserted into the stomach
through nasal cavity. Ten ml of an appropriate
dilution of inoculum containing $10^6$, $10^5$ or $10^4$
cells/ml in case of the F₁, and $10^6$ or $10^5$ cells in
case of the NF₁, was administered by a disposable
sterilized syringe through the tube inserted. The
remaining *Salmonella* organism in the tube was
washed down into the stomach with 5 ml of the
horse meat infusion broth.

When monkeys excreted the organism for a cer-
tain period giving an evidence of colonization and
showed a rising titer of agglutinins, it was regarded
as that an intestinal infection was established in
the animals.

Clinical observation: Vigor, appetite and property
of stool were observed daily for 4 weeks.

Recovery of *S. typhimurium*: Fecal specimens
were collected every day for the first 2 weeks.
Between the 3rd and 4th weeks, the specimens were
collected usually on the 21st and 28th days posts
administration. When diarrhea still continued during
the latter half observation period, the fecal
specimens were collected every day as long as the
property of the stool return to normal. The feces
showing normal property was cultured qualitatively
and quantitatively by the method described previ-
ously [16]. In cases of diarrheal, bloody mucous or
loose stool, 10-fold serial dilution was made with
physiological saline up to $10^{-4}$ dilution. On the
desoxycholate-hydrogen sulfide-lactose (DHL, Eiken
Co., Tokyo) and mannite lysin crystalviolet (MLCB,
Nissui Co., Tokyo) agar plates, 0.1 ml of each dilu-
tion/plate was spread and incubated for 24 hr at
37°C.

Blood collected every 7 day post administration
and that obtained at the onset of diarrhea were
cultured for *Salmonella*. Approximately 0.5 ml of
the blood was cultured in 3 ml of the horse meat
infusion broth for 24 hr at 37°C. One loopful of
the broth culture was streaked on the DHL and
MLCB agar plates and incubated for 24 hr at 37°C.
Table 1. Number of cynomolgus monkeys infected by intragastric administration of Salmonella typhimurium

<table>
<thead>
<tr>
<th>Inoculum</th>
<th>Number inoculated</th>
<th>Establishment of intestinal infection</th>
<th>Animal No.</th>
<th>Colonization in the intestine</th>
<th>Antibody***</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prior to administration</td>
<td>At the 28th day post administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>O</td>
<td>H</td>
</tr>
<tr>
<td>$10^7$ 3</td>
<td>+3</td>
<td></td>
<td>1*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$10^5$ 6</td>
<td>+5</td>
<td></td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$F_1$</td>
<td></td>
<td></td>
<td>$-1$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$10^5$ 6</td>
<td>+6</td>
<td></td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$NF_1$</td>
<td></td>
<td></td>
<td>$+1$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$10^7$ 3</td>
<td>-2</td>
<td></td>
<td>17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$10^5$ 3</td>
<td>-2</td>
<td></td>
<td>19**</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* No. 1 animal was sacrificed on the 4th day post administration.
** No. 19 animal was sacrificed on the 10th day post administration.

Antibody: Somatic (O), flagellar (H) and fimbrial (F) agglutinin titers were examined every 7 day post administration followed by the method described previously [16].

Pathological observation: Two animals manifested severe symptoms excreting bloody mucous stool were sacrificed on the 4th or 10th day post administration by intramuscular inoculation of ketamine hydrochloride and bleeding. Immediately after death, macroscopic examination was performed, and the various organs and blood were collected for bacteriological examination. These specimens were examined by the method reported previously [16] or that mentioned above.

Results

All monkeys given $F_1$ descendant became infected except one with $10^5$ cells (Table 1). In the monkeys infected with the $F_1$ descendant, colonization of the organism in the intestine and production of O, H and F agglutinins were demonstrated. The antibody began to appear around the 7th day post administration and reached to the peak at the 21st or 28th day. Of the monkeys infected, all animals with $10^7$ cells, 4 with $10^5$ cells and 2 with $10^8$ cells manifested symptoms. In cases with $NF_1$, only 2 animals given either $10^5$ or $10^8$ cells were infected manifesting symptoms. In these 2 animals, production of O and H agglutinins was proved, but not F agglutinin. Two
control monkeys given 10 ml of the intestinal emulsion of a clean mouse prepared by the same method as that for the F₁ showed no symptoms at all.

Table 2. Symptoms observed in monkeys developed enteritis

<table>
<thead>
<tr>
<th>Inoculum</th>
<th>Animal No.</th>
<th>Incubation period</th>
<th>Constipation</th>
<th>Loose stool</th>
<th>Diarrheal stool</th>
<th>Vomit**</th>
<th>Bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>10⁷</td>
<td>1</td>
<td>1-2</td>
<td>±</td>
<td>+1*</td>
<td>+2</td>
<td>+1</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1-2</td>
<td>—</td>
<td>+1</td>
<td>+2</td>
<td>—</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2</td>
<td>+1</td>
<td>+2</td>
<td>—</td>
<td>—</td>
<td>+2</td>
</tr>
<tr>
<td>F₁</td>
<td>10⁵</td>
<td>4</td>
<td>+2</td>
<td>—</td>
<td>+4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>+1</td>
<td>+1</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>+2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>7</td>
<td>—</td>
<td>—</td>
<td>+7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>10³</td>
<td>10</td>
<td>3-4</td>
<td>—</td>
<td>—</td>
<td>+3</td>
<td>+4</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>7</td>
<td>—</td>
<td>—</td>
<td>+7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>NF₁</td>
<td>10⁷</td>
<td>16</td>
<td>—</td>
<td>+1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>10⁵</td>
<td>19</td>
<td>3</td>
<td>—</td>
<td>+3</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Figures indicate the first day began to manifest symptom.
** The vomits of No. 1 and No. 5 animals contained 10² and 10³ organism/g, respectively, but no organism was recovered from the vomit of No. 10.

Table 3. Days excreted abnormal stool and number of Salmonella organism recovered in monkeys developed enteritis

<table>
<thead>
<tr>
<th>Inoculum</th>
<th>Animal No.</th>
<th>Property of stool</th>
<th>Days* excreted abnormal stool</th>
<th>Number of Salmonella organism in diarrheal or loose stool</th>
</tr>
</thead>
<tbody>
<tr>
<td>10⁷</td>
<td>1</td>
<td>Loose</td>
<td>1</td>
<td>10³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bloody mucous</td>
<td>2-3 (Sacrificed on the 4th day)</td>
<td>10³ 10⁰-10⁶</td>
</tr>
<tr>
<td>F₁</td>
<td>10⁵</td>
<td>Loos</td>
<td>1</td>
<td>10³</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Watery</td>
<td>2, 4-8, 20</td>
<td>10⁵ 10⁰-10⁶</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Watery</td>
<td>7-9, 15-17</td>
<td>10⁴ 10⁵-10⁷</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Watery</td>
<td>2, 11-12</td>
<td>10⁴ 10⁰-10⁶</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>Watery</td>
<td>7-9, 15-17</td>
<td>10⁴ 10⁵-10⁷</td>
</tr>
<tr>
<td>10³</td>
<td>10</td>
<td>Watery</td>
<td>3, 6-11, 13-16</td>
<td>10⁵ 10³-10⁷</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Watery</td>
<td>7-9, 11</td>
<td>10⁴ 10⁴-10⁶</td>
</tr>
<tr>
<td>NF₁</td>
<td>10⁷</td>
<td>Loose</td>
<td>1-2</td>
<td>10⁴ 10⁵</td>
</tr>
<tr>
<td></td>
<td>10⁵</td>
<td>Watery</td>
<td>3</td>
<td>10⁵</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood mucous</td>
<td>4-8 (Sacrificed on the 10th day)</td>
<td>10⁴ 10³-10⁴</td>
</tr>
</tbody>
</table>

* Days post administration.
** The first day began to excrete loose, watery or bloody mucous stool.
*** From the 2nd day to the last day excreted abnormal stool.
Fig. 1. Number of Salmonella organism recovered from stool. Nos. 4 and 10 animals were given $10^5$ and $10^6$ cells of fimbriate S. typhimurium (F1), respectively.

* N: Normal stool, D: Watery diarrhoeal stool, L: Loose stool, $\Delta$: Stool was not available,
-: Not examined, but normal stool was excreted.
** +: The organism was recovered by qualitative culture only.

Symptoms manifested by the infected monkeys are shown in Table 2. Major symptom was watery diarrhea with or without mucus. Some animals excreted bloody mucous stool or loose stool. Most animals started to excrete diarrheal, bloody mucous or loose stool within the first a few days post administration, but in some animals (Nos. 7 and 11), incubation period was one week. Constipation was observed in 2 animals. Nos. 1, 5 and 10 monkeys vomited on the day 1st or 4th. The vomits of Nos. 1 and 5 contained $10^5$ and $10^6$ cells of the organism/g, respectively, but no organism was recovered from the vomit of No. 10.

Fig. 2. Number of Salmonella organism recovered from the intestine and others at post-mortem examination.

No. 1 animal was given $10^7$ cells of fimbriate S. typhimurium (F1) and sacrificed on the 4th day post administration. No. 19 animal was given $10^5$ cells of non-fimbriate S. typhimurium (NF1) and sacrificed on the 10th day post administration.

* N: Normal stool, D: Watery diarrhoeal stool, L: Loose stool, B: Bloody mucous stool, $\Delta$: Stool was not available.
+: The organism was recovered by qualitative culture only.
-: No organism was recovered.
-: Not examined.

Bacteremia occurred in only 2 animals given $10^7$ cells of the F1 (Nos. 2 and 3). No marked difference was observed between the symptoms shown by the monkeys with the F1 and those by the animals with NF1.
Excretion of watery diarrhea lasted for 2 to 3 weeks showing intermittent excretion of normal or loose stool, or constipation (Table 3, Fig. 1). In cases of the animals excreting loose stool only (Nos. 3 and 16), the abnormal stool was found on the 1st and 2nd days or the 2nd and 3rd days. The bloody mucous stool was excreted from the 2nd day to the 3rd day (No. 1) or from the 4th day to the 8th day (No. 19), though the animal was sacrificed on the 4th or 10th day. At the onset of the disease, $10^8$ to $10^9$ cells of the organism/g was recovered from the abnormal stool. During the course of illness, the number of the organism in feces was increased in most cases showing $10^4$ to $10^6$/g, or kept almost the same number of the organism as that of the onset for a while in some other cases, and then the number of the organism in feces decreased gradually and disappeared. In the cases infected without manifesting gastrointestinal symptoms, low number of Salmonella organisms, $10^3$/g or less, was recovered from their feces, but excretion period was variable.

Two animals manifested severe symptoms excreting bloody mucous stool were sacrificed on the 4th (No. 1) or 10th (No. 19) day post administration (Fig. 2). Since No. 1 animal was sacrificed at the critical condition, the administered Salmonella organism distributed widely its body. The gastrointestinal walls, caecal content, mesenteric lymph node, and liver harbored $10^5$ to $10^7$ cells of the organism/g, while no organism was recovered from the heart blood. The ileum showed diffuse hyperemia and edem, and Peyer’s patches became thick and apparent. Intussusception was found in two different parts of the ileum, the middle part and terminal part. The other animal showed only a slight and small erosion in the ileocecal valve, and slight, small and disseminated erosion in the colon. The walls of caecum and colon, and caecal content harbored a large amount of the organism (NF$_1$), $10^6$ to $10^7$ cells of the organism/g, but those of the stomach, duodenum and ileum, mesenteric lymph node and lung had $10^5$ cells of the organism/g or less. No organism was recovered from the jejunum, liver, spleen, kidney and heart blood.

**Discussion**

At the symposium on “Public Health Aspect of Salmonella”, the senior author suggested hypothetically that Salmonella harbored in the feces or organs, so-called wild-type strains, might have high infectivity in comparing with the strains isolated using selective media and subcultured on an artificial medium [3]. Later, the hypotheses was proved in dogs [16] and mice [17, 18]. In this experiment, a fimbriate descendant showed also high infectivity against cynomolgus monkeys. Since the inoculum of the fimbriate descendant was prepared from the intestine of a mouse died of sepsis by an intragastric administration of the descendant, it should have infectivity as high as that of the parent wild-type S. typhimurium harbored in dog feces. It seemed that the observed difference in the infectivity between the fimbriate and non-fimbriate descendants is largely dependent upon the difference in the ability of colonization in the intestine. The fimbriae may play some role in the initiation of colonization [18]. For developing enteritis, however, some bacterial factors other than the fimbriae and host factor might be concerned. In fact, there is no remarkable difference in the rate of manifesting enteritis between the monkeys infected with the fimbriate descendant and those with non-fimbriate descendant. In some animals, especially the ones with a small dosage of the fimbriate
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descendant, carrier state was established, but no symptom of gastrointestinal disorder was shown. Since no fimbrial agglutinin was produced in the monkeys infected with the NF4 descendant, it was unlikely that the animals became infected with symptom as a result of the descendant acquired an ability to produce fimbriae in the monkey intestine.

Sakazaki suggested that an oral invasion of 10^7 cells or more of Salmonella organism is one of the essential factors to produce an acute gastroenteritis in adult humans [13]. When monkeys were given 10^10 cells of S. typhimurium [3], or 10^7–10^8 cells of S. typhimurium or S. dublin/kg [15], an acute gastroenteritis resembling that in humans was produced. The authors paid special precaution to perform the present experiment under the natural condition as could as possible. Therefore, a small dosage of a fimbriate descendant having infectivity comparable to the parent wild-type S. typhimurium was administered intragastrically to the monkeys given no pre-treatment such as starvation, antibiotic administration and others. As a result, it was demonstrated that the monkeys given a small dosage such as 10^6 or 10^8 cells of the organism developed enteritis.

Whether or not the result mentioned above can be extrapolated to human cases occurring naturally, it largely depends upon the evaluation about the similarity between the disease produced in the monkeys and that occurred in humans. Okudaira [10] carried out pathological examination on 8 fatal food poisoning cases in humans due to S. typhimurium (3 cases), S. enteritidis (3 cases), S. schottmuelleri (1 case) and S. krefeld (1 case). All the cases except one who died with influenza-like symptoms showed abdominal ache and diarrhea with or without vomit and others. Major gross change existed between the ileum and caecum showing edem and hyperemia. A half of them showed edem or slight inflammatory change in the stomach, and granuloma cells were found in the mesenteric lymph node of a case only. Kent et al. [4] stated that striking clinical abnormalities found in the monkeys were only the character of stools. The animals developed diarrhea within 1 to 3 days post administration, but no cases showed vomit, bacteremia and systemic granuloma. At the post-mortem examination on the animals killed at various times, colitis was present by 24 hrs after and severe inflammatory response in the ileum was found at 4 days after. Focal lesions were found in the stomach and jejunum. Sugiyama et al. [15] reported that the monkeys showed vomit and diarrhea within 2 to 4 days after administration. Bacteremia was found on the 4th day, but did not on the 10th day. Major change was found in the ileum at the onset of the disease. Hyperemia, edem and petechial hemorrhage were found in the ileum. It seemed that the symptoms observed in cynomolagus monkeys in this experiment have much similarities to those in an acute gastroenteritis in humans and monkeys in the above described reports. Although involvement of the stomach was not clearly shown in this experiment, 2 animals given 10^7 or 10^8 cells of a fimbriate descendant vomited on the 1st day and one animal given 10^8 cells vomited on the 4th day. Autopsy was performed on only 2 cases excreting bloody mucous stool. Major gross changes were almost similar to those in humans and monkeys, except the formation of intussusception in the ileum in one case. The intussusception might be produced as secondary change due to severe diarrhea.

From the results obtained in this experiment, it is considered that cynomolagus
monkeys can serve as an animal model for Salmonella gastroenteritis in humans. The authors emphasized also that the size of Salmonella organism needed to produce an acute gastroenteritis occurring naturally in humans should be smaller than that proved by the experiments with volunteers. The view is supported also by the epidemiological data that a small number of Salmonella organism has been recovered from the incriminated materials in certain cases.

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References


要約

S. typhimurium の鼻内投与によるカニクイザルの実験的腸炎: 勝部泰次・田中 鍾（国立子防衛生研究所細菌部）——人に胃腸炎を発症させるに要する菌量を知るための基礎研究として、絶食などの前処置を受けていない、外見上健康的なカニクイザルに、S. typhimurium の野生株（線毛株の鼻内投与により敗血症死したマウスの腸管乳剤）および非線毛株（非線毛株の培養菌）を鼻内投与した。野生株を投与した例では、10⁶ 個群 3 頭中 3 頭、10⁸ 個群 6 頭中 5 頭、10⁹ 個群 6 頭中 6 頭に腸管感染の成立をみた。感染例のうち、10⁷ 個群では全例、10⁸ 個群では 4 頭、10⁹ 個群では 2 頭が腸炎を発症した。これに対し、非線毛菌投与例では、わずかに 10⁷ 個群 3 頭中 1 頭、10⁸ 個群 3 頭中 1 頭に腸管感染の成立と腸炎の発症をみたのみであった。主要な症状は水様性下痢であったが、個体によっては粘血便、あるいは軟便を排出するものもみられた。水様便は 2〜3 週間、粘血便は 2 または 5 日、軟便は 1 または 2 日、それぞれ排泄された。病初の大便中の菌量は 10⁶〜10⁹/g であり、多くの例において、経過中に排泄菌量が増加した。粘血便を排出した 2 頭を剖検したところ、病変は回腸、結腸などにみられた。野生株と非線毛株の間にみられた感染性の差異は、線毛が関与している腸管定着能の有無によるものと考えられた。人のサルモネラ腸炎は、分離株を用いた人体実験で証明されたものよりもはるかに少ない菌量でおきているものと推定される。