

# Factors Affecting the Susceptibility to Bacillary Dysentery\*

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BACILLARY dysentery is an almost constant menace wherever large numbers of people are massed under conditions which hinder the maintenance of proper individual and group standards of hygiene. Armies, refugee camps, orphanages, prisons, and mental hospitals are particularly liable to epidemics of this disease.

A number of factors which bring about the relatively high morbidity in the situations mentioned above have been identified. Among these are the increased opportunity for the completion of the feces, food, feces cycle offered by crowding and by the presence of carriers or mild cases who remain ambulant.

It is generally believed that warm weather and tropical climate, favoring as they do the presence of flies, facilitate the spread of the disease.<sup>1</sup> On the other hand, it has been observed that in one mental hospital the greatest incidence of infection occurred in the winter when the patients were confined indoors, whereas the rate fell to zero during the summer months when it was possible to distribute the patients on open porches during the day, thus relieving crowding.<sup>2</sup>

In addition to climate and crowding, which affect all, conditions such as occupation or mode of life subject certain individuals to particular risks. This

was long ago pointed out by Pringle<sup>3</sup>: "For in general it may be remarked, that this disease *caeteris paribus* prevails mostly among such as are of scorbutic (that is, putrid) habitus or among poorer people, who from their foul air, bad diet and nastiness are most liable to putrid diseases." In mental hospitals the highest incidence was among the "wet and dirty" cases.<sup>4</sup> In a hospital for mental defectives, there was an inverse relationship between the intelligence level and the rate of morbidity.<sup>4</sup>

It has been claimed that attacks of the disease confer immunity. This contention has been used to explain the greater susceptibility of army recruits as compared with veterans, and the promptness with which newcomers to tropical countries develop the condition while the native population remains apparently healthy. The same principle has been invoked to explain the alleged decrease in morbidity with advancing age,<sup>1</sup> natives of tropical countries, army veterans, and older people presumably having survived previous attacks.

There is no close agreement concerning the value of artificially conferred immunity. An authoritative text on immunology<sup>5</sup> states, "We cannot at the present time recommend the use of dysentery vaccine as a general prophylactic measure."

Cathcart and Gordon<sup>2</sup> reported that they had used a vaccine for the Flexner Y type of dysentery with good results

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in a mental hospital. Johns and Chalk<sup>6</sup> continued this work, using a slightly different technique. They gave vaccine orally on four successive days, repeating the treatments periodically. Whereas 37 cases had arisen in the year before treatment, only 31 developed in the subsequent nine years. None of these 31 patients had received vaccine within the two years before their infection.

#### BACKGROUND

For several years prior to the present studies, involving the prophylactic use of vaccination, the Flexner strain of bacillary dysentery had been endemic at the Norwich State Hospital with periodic outbreaks of epidemic proportions. During the two years preceding the study, stools of suspected cases of bacillary dysentery were cultured and records of the results were kept.\* It was found that the majority of cases arose on three wards. These were the wards on which the disturbed women, the deteriorated women, and the elderly women resided. During the period of study, all cases of gastroenteritis were isolated, subjected to at least one stool culture followed immediately by sulfaguanidine given in 1 gm. doses every 4 hours for a week. All cases of dysentery were followed with periodic stool cultures. This program permitted the detection of a large number of cases and possible carriers and also decreased the opportunities for transmission because of the prompt sterilization of the stool by sulfaguanidine.

#### PROCEDURE

The subjects of the current study

were the patients who resided on the three wards for elderly, disturbed, and deteriorated women. The highest incidence of infection had previously occurred on these wards.

Patients who had entered the hospital within five months preceding inoculation were eliminated from consideration. All other patients served as subjects for the experiment, being grouped in the following manner:

Those patients who were too ill or debilitated to be fit subjects for inoculation were listed separately from the control and treatment groups.

The remaining relatively healthy patients were listed alphabetically. Consecutive names were taken from the beginning of the list until the desired number of cases for inoculation had been obtained. All other patients served as controls. The number of inoculated patients was greater than the number of control patients because the original purpose of the study was to determine the effect of inoculation.

Some of the patients had suffered a known infection in the past; these were tabulated separately. Previously infected patients were found in each of the groups described above.

A newly exposed group was made up of those patients who had been admitted to the hospital after the beginning of the study and who had subsequently been transferred to the wards under observation.

The treated and control groups were comparable with regard to the age and habits of their members. There was no attempt to segregate the various groups. All patients lived and ate together, no distinction being made between patients of the various groups. The medical and nursing staff caring for them were not informed as to the manner of classification or the class into which any given patient might fall. In this way uniformity of treatment was obtained.

A polyvalent vaccine which incorporated the "V," "W," and "Z" strains of *B. Flexneri* was prepared through the courtesy of Eli Lilly & Company according to the method outlined by

\* Specimens of stool were plated out directly on Eosin-methylene blue agar, Bismuth sulfite agar, and S.S. agar. Suspected colonies were fished to Kligler's Iron Agar slants. This was followed by plating on a non-inhibitory medium for purity and then re-isolation from a single colony, if necessary. Identification of the organism was completed by serological and biochemical reactions.

TABLE 1

| Group                        | Patients        |                        | Cases of Dysentery |                        | Cases per 100 Patients<br>per Year |                        |
|------------------------------|-----------------|------------------------|--------------------|------------------------|------------------------------------|------------------------|
|                              | Not<br>Injected | Previously<br>Injected | Not<br>Injected    | Previously<br>Injected | Not<br>Injected                    | Previously<br>Injected |
|                              | Inoculated      |                        |                    |                        |                                    |                        |
| Deteriorated                 | 70              | 18                     | 8                  | 3                      | 11.4                               | 17.1                   |
| Elderly                      | 73              | 18                     | 9                  | 3                      | 13.6                               | 16.7                   |
| Total                        | 143             | 36                     | 17                 | 6                      | 12.5                               | 16.9                   |
| Control                      |                 |                        |                    |                        |                                    |                        |
| Deteriorated                 | 65              | 7                      | 6                  | 2                      | 9.5                                | 28.6                   |
| Elderly                      | 47              | 7                      | 5                  | 0                      | 11.1                               | 0.0                    |
| Total                        | 112             | 14                     | 11                 | 2                      | 10.2                               | 14.5                   |
| Ill (not inoc.)              |                 |                        |                    |                        |                                    |                        |
| Deteriorated                 | 12              | ..                     | 2                  | ..                     | 16.6                               | ....                   |
| Elderly                      | 48              | 6                      | 2                  | 1                      | 5.0                                | 16.7                   |
| Total                        | 60              | 6                      | 4                  | 1                      | 7.7                                | 18.2                   |
| Newly exposed<br>(not inoc.) |                 |                        |                    |                        |                                    |                        |
| Total                        | 57              | ..                     | 7                  | ..                     | 40.0                               | ....                   |

Paddle,\*<sup>4</sup> strain "Z" being the homologous strain involved in previous outbreaks within the institution. At weekly intervals, injections of 0.5, 1.0, and 1.0 ml., respectively, of the vaccine containing 500 million organisms per ml. were given subcutaneously to the inoculated group.

#### RESULTS

All cases of dysentery occurring during the year after inoculations were

recorded. In Table 1, the size of the different groups, the number of infections in each, and the corrected case rates per one hundred patients per year are shown. The corrected case rate per year was utilized in order to permit comparison of other groups with the newly admitted group, many of whose members were resident on the wards under observation for only a few months.

The newly admitted patients had a markedly higher case rate per year than either the control or inoculated groups. This difference was statistically significant at the 1 per cent level by the Chi-squared test. The incidence of infection was slightly higher in the inoculated groups than in the comparable control groups both for uninfected and previously infected patients. This difference was not statistically reliable nor was the difference between the infirm patients and the younger deteriorated and disturbed patients. The control group did not differ to a reliable degree from the debilitated patients. Neither was there a significant difference between the previously infected and the previously uninfected groups.

In Table 2, the number of infections per month is shown for each of the major groups without distinction as to age or

\* It contained 500 million organisms per ml., the dosage being 0.5 ml., 1 ml., and 1 ml. subcutaneously, at weekly intervals. Given in this way, no unpleasant reactions occurred. The organisms were isolated in pure culture and identified by morphological, cultural, biochemical, and serological methods. The organisms were agglutinated first against polyvalent serum and finally against monovalent Flexner types. Cultures are kept in stock on agar and when a vaccine is required, heavy inoculation is made on two nutrient agar slopes in 12 oz. medical flat bottles and incubated for 18 hours at 37° C. The resultant growth is washed off under aseptic conditions with as little as possible of sterile 0.5 per cent phenol in normal saline into another sterile 12 oz. medical flat bottle containing glass beads, thoroughly shaken, and heated in a water bath at 60° C. for ½ hour. Cultures are then taken and incubated at 37° C. for 48 hours. The amount is again heated for ½ hour at 60° C. if there is any growth. When the emulsion is found to be sterile, the strength is estimated by comparison with opacity tubes and the vaccine is diluted with 0.5 per cent phenol solution in saline to contain 500 million organisms per ml. This is placed in appropriate rubber-capped bottles and by means of a sterile syringe or glass capillary pipe cultures are again taken from each bottle and grown aerobically and anaerobically for at least 48 hours to check the sterility. After taking this culture, the cap of this bottle can be sealed.

previous infection. The inoculated patients had more infections in the first month than the controls, and the ratio of two to one in that month is approximately that which obtained over the 12 month period. The low incidence of infection for new patients in the first months is not surprising in view of the fact that the majority of the patients comprising this group had not yet been admitted to the wards under observation.

contact with toilets, either in the form of dabbling in the toilet bowl or cleaning the toilets in bathrooms. Table 4, in which the results are shown, includes some patients excluded from the previous tables because they did not fall in any of the groups into which the patients had been subdivided. Some other patients previously reported are excluded from Table 4 because adequate information concerning their habits was not available. By means of the Chi-

TABLE 2  
Incidence by Months

| Groups                 | 1943 |      |      |       |      |      | 1944 |      |      |      |      | Total |     |
|------------------------|------|------|------|-------|------|------|------|------|------|------|------|-------|-----|
|                        | June | July | Aug. | Sept. | Oct. | Nov. | Dec. | Jan. | Feb. | Mar. | Apr. |       | May |
| Inoculated, all groups | 6    | ..   | 6    | ..    | ..   | 1    | ..   | 6    | 1    | ..   | 2    | 1     | 23  |
| Control                | 3    | ..   | 7    | ..    | ..   | ..   | 1    | 2    | ..   | ..   | ..   | ..    | 13  |
| New Patients           | 1    | ..   | ..   | ..    | ..   | ..   | 1    | 5    | ..   | ..   | ..   | ..    | 7   |
| Ill                    | ..   | 1    | ..   | ..    | ..   | ..   | 1    | 2    | ..   | ..   | 1    | ..    | 5   |

In Table 3 the mean age of the infected patients is compared with that of those who were not infected. It will be seen that in both the younger deteriorated group and the older infirm group there was no significant age difference between the infected patients and those who were not infected.

squared test, the incidence of infection in patients showing any behavioral trait was compared with that in those not showing the trait. Where necessary, Yate's correction for small numbers was applied. The "level of confidence," that is, the likelihood that an equally great or greater difference in infection

TABLE 3  
Mean Age of Infected and Non-infected Patients

| Group        | Non-infected Patients |          |      | Infected Patients |          |      |
|--------------|-----------------------|----------|------|-------------------|----------|------|
|              | No.                   | Mean Age | S.D. | No.               | Mean Age | S.D. |
| Control      |                       |          |      |                   |          |      |
| Deteriorated | 59                    | 46       | 12.2 | 6                 | 45       | 11.6 |
| Infirm       | 42                    | 67       | 11.1 | 5                 | 66       | 17.4 |
| Inoculated   |                       |          |      |                   |          |      |
| Deteriorated | 60                    | 45.2     | 7.3  | 8                 | 43.25    | 11.2 |
| Infirm       | 64                    | 69.4     | 10.2 | 9                 | 68.1     | 7.9  |

All patients were rated with regard to the usual presence of the following behavioral traits: ambulant (as opposed to bedridden), carelessness with regard to cleanliness, stealing of food, urinary incontinence, fecal incontinence, smearing of feces, eating food from the trays of other patients, eating of the patient's own feces, eating the feces of others, eating rubbish or licking the floor, and

would arise from chance is shown. A level of confidence greater than 10 per cent is usually considered not reliable. Table 4 indicates that the greater opportunity for exposure offered by the ambulant status was not a critical factor nor was the stealing of food of other patients. Patients who were characterized as uncleanly were much more likely to develop infection; when this

TABLE 4.

| Traits                       | Infected<br>(94 Patients) | Not Infected<br>(281 Patients) | Level of<br>Confidence |
|------------------------------|---------------------------|--------------------------------|------------------------|
| Ambulant                     | 91                        | 260                            | 30%                    |
| Careless of cleanliness      | 49                        | 110                            | 5%                     |
| Urinary incontinence         | 48                        | 104                            | 5%                     |
| Fecal incontinence           | 47                        | 97                             | 2%                     |
| Fecal smearing               | 44                        | 76                             | 1%                     |
| Eats own feces               | 14                        | 15                             | 1%                     |
| Eats feces of others         | 10                        | 10                             | 2%                     |
| Eats rubbish—licks floor     | 17                        | 28                             | 10%                    |
| Eats food of others          | 32                        | 76                             | 30%                    |
| Cleans or dabbles in toilets | 35                        | 107                            | 90%                    |
| One or more uncleanly trait  | 72                        | 199                            | 40%                    |

uncleanliness was related to excreta, particularly the handling or ingestion of excreta, the likelihood of infection was tremendously increased. An overall impression of cleanliness or uncleanliness distinguished much more sharply between the infected and uninfected than did a separation based on the absence of all uncleanly traits.

#### DISCUSSION

Our data confirm objectively the generally held opinion that poor personal hygiene on the part of many mentally ill individuals facilitates the spread of bacillary dysentery through institutions for the mentally ill and mentally defective. We have demonstrated that uncleanly individuals are more readily infected than cleanly ones. It is highly probable that, once infected, the uncleanly patient is a greater menace than a cleanly one.

It is possible that undetected carriers and subclinical cases played an important part in spreading the infection prior to the liberal and repeated use of sulfaguanidine and the taking of repeated stool cultures following clinical recovery. We favor the use of this relatively insoluble drug because it gives rise to fewer renal and hematological complications than the more readily absorbed sulfonamides, and can therefore be used with greater safety for mass treatment under conditions in which repeated blood and urinary studies are not always possible.<sup>7</sup>

Among the previously exposed, immunity was not enhanced by inoculation or by previous infection. The previously exposed, whether they had suffered a known previous infection or not, were more immune than the newly admitted patients.

The degree of immunity was not affected by age differences or by extreme variations in general health. It may be that the debility of the aged and severely ill patients was offset by their inactivity which afforded them fewer contacts.

The greater susceptibility of newly admitted patients cannot be explained conclusively. One can only conjecture that repeated exposure confers some kind of immunity. In the administration of an institution in which bacillary dysentery is encountered, the difference between immunity of the recently admitted and the stable population is of the greatest practical importance.

#### CONCLUSIONS

1. Patients who were newly exposed to infection by the Flexner type of bacillary dysentery were markedly more susceptible than those who had previously been exposed by residence on wards where the disease was endemic.

2. General uncleanliness was associated to a highly reliable degree with increased morbidity. Of the group of uncleanly traits, the handling or eating of feces showed the most definite relationship with infection.

3. The incidence of clinical infection in a group inoculated with vaccine was slightly higher than in a comparable control group. This difference was not statistically reliable.

4. Age difference was not attended by a significant difference in morbidity.

#### SUMMARY

In the presence of Flexner dysentery, neither inoculation with a polyvalent vaccine nor a previous history of infection resulted in a lowering of incidence compared with control patients. Age and general health did not affect susceptibility. Absence of previous exposure and the presence of uncleanly personal habits were attended by increased morbidity, other conditions being equal.

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