

of insanity commonly heard of as one takes the history of the patients with severe forms of constitutional inadequacy are shiftlessness, eccentricity, vagabondism, solitariness, dipsomania, suicide, stammering, enuresis, pathologic temper and feeble-mindedness.

Often I have been impressed by the fact that in certain families constitutional inadequacy, psychopathy or neurosis, and abnormalities in the functions of the glands of internal secretion seem to be inherited, sometimes together and sometimes sorted out. From this I gain the impression that the genes for these defects are sometimes linked and sometimes separated.

TREATMENT

As already pointed out, we physicians must become more conscious of the importance of this problem of constitutional inadequacy, and we must become more adept at recognizing the victims when they first begin to break down. We must spot them soon after they come into the office. After recognizing them we must spend much time with them, trying to get them to understand the situation, to acquiesce to it and to stop hunting for a complete cure. When they will permit us to use our judgment as to the tests worth making and the treatments worth trying, we can save them from the wastage of much money.

We must learn the technic of explaining the situation to them so that they will accept our verdict without annoyance or rebellion and will decide to mend their bad psychic ways, to hoard their energies and to live within their limited means of strength. Oftentimes we can make these persons self supporting or at least less of a burden to their relatives than they were before, by encouraging them to find work that they can do without breaking themselves down. Often we can give them hope and encouragement by telling them what is true, and that is that some of the best work of the world has been done by frail persons who suffered from poor health all their days. I often point to Darwin, who, by working only a few hours a day, published a long series of papers and books and changed the thought of the world.

Sometimes the constitutionally inadequate man greatly needs the physician's help in getting his family or, more important yet, his wife's family, to understand the situation so that they will stop blaming him for his failures to work steadily and to succeed well in life. Women often need similar help so that the husband will understand the situation and will be more sympathetic and helpful.

SUMMARY

Many of the chronically ailing patients seen daily by medical consultants are constitutionally inadequate persons, unable to stand up well to the strains of life. They cannot be cured, as they hope to be, by the discovery and eradication of any one local disease.

By grasping desperately at diagnostic straws, by carrying out extensive treatments and performing operations on these persons, we physicians, with the best of intentions, often do them injury, and waste their money and our time.

We must learn to recognize these persons and their symptoms more often and more quickly so as to save them expense and trouble. In many cases the basic weakness is in the nervous system. In bad cases the disease seems to be an equivalent of insanity. In other cases it goes with an inheritance of a frail body and defective glands of internal secretion.

Treatment must consist mainly of keeping the patients from doing foolish things and wasting money. They

must be taught, if possible, to acquiesce to the situation, to stop hunting for a complete cure, to hoard their energies and to find a job that can be done without too much fatigue.

In times of war every effort must be made to keep the constitutionally inadequate out of the army. All they do is to break down and go on the pension roll.

STUDIES ON THE CONTROL OF  
ACUTE RESPIRATORY  
INFECTIONS

I. PRELIMINARY REPORT ON THE ORAL ADMINISTRATION OF SULFADIAZINE AT THE ONSET OF ACUTE RESPIRATORY ILLNESSES

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The successful treatment of pneumococcal, streptococcal and other bacterial infections of the respiratory tract with sulfonamides has led to a consideration of their use in the prevention of these infections and their complications. For this purpose sulfadiazine<sup>1</sup> was chosen because of the early reports on its relatively low clinical toxicity and its high therapeutic effectiveness<sup>2</sup> against different bacterial pathogens of the respiratory tract. This preliminary report deals with the clinical conditions found in patients treated at the onset of symptoms of acute respiratory infections as compared with those who were not treated with sulfadiazine.

PLAN OF STUDY

The study has been conducted at Letchworth Village, a New York state institution for mental defectives. It was carried out among the group of children

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The physicians at Letchworth Village, particularly Dr. Harry C. Storrs, superintendent, Dr. Herman Alpert and Dr. Nathaniel Bernstein, aided in this work.

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with the lowest mental rating who were highly susceptible to respiratory infections and who usually had an annual pneumonia incidence of more than 10 per cent. These children were confined to two cottages, the boys to cottage Iota and the girls to cottage Y. Each cottage had about 130 inmates varying in age from 2 to 14 years, the average being about 8 years.

In cottage Iota the inmates were allocated to a sulfadiazine treated and a control group in alternate order of admission to the institution. The average number in each group throughout the test period was about 65. The groups were comparable in respect to physical and mental characteristics, age, weight, duration of residence at the institution and incidence of endemic respiratory infections and pneumonia.

In cottage Y definitive test groups were not chosen for the duration of the study. Instead, alternate patients with acute respiratory illnesses were treated with sulfadiazine.

The sick children in each cottage were put to bed in their respective dormitories as soon as any symptoms of infection were recognized. They received the routine type of treatment employed in the cottage. This consisted of bed rest, enemas, fluids, acetylsalicylic acid and local applications as needed. In addition, the group treated with sulfadiazine received the drug from the time of onset of recognizable symptoms of respiratory illness.

Patients requiring hospital care were transferred to the hospital maintained at the institution. Here the type of treatment depended on the nature and severity of the illness and not on the test group to which the patient had been assigned in the cottage.

The dosage of sulfadiazine employed in this study varied with the weight of the affected child and the temperature. For children weighing less than 50 pounds (23 Kg.) and having a rectal temperature of less than 102 F. at the onset, the initial dose was 1 tablet of 0.5 Gm., followed by two doses each of 0.5 Gm. at four hour intervals. After the first day, 1 tablet of 0.5 Gm. was given three times a day at 8 a. m., noon and 4 p. m. For children weighing more than 50 pounds or for those having a temperature of 102 F. or more at the onset, the initial dose was 1 Gm., followed by three doses each of 0.5 Gm. at four hour intervals. Their daily maintenance dose was 4 tablets (2 Gm.) given in four doses between 8 a. m. and 8 p. m. The drug was given for at least three or four days or until the rectal temperature had been less than 100 F. for twenty-four hours.

#### RESULTS

The test period in cottage Iota began on Dec. 14, 1941, and from this date to Jan. 17, 1942 79 patients with colds were observed, 8 the first week, 7 the second, 10 the third, 35 the fourth and 19 the fifth.

There were 39 in the sulfadiazine treated group and 40 in the control group.

The number of clinical infections was equally distributed between the test groups. The frequency and severity of the acute respiratory illnesses increased after December 28 and reached epidemic proportions between January 4 and January 17, when about 40 per cent of each group was affected. During this period the predominant symptoms were coryza and cough. Many of the infections of the upper respiratory tract were severe and were associated with a high incidence of acute bronchitis and pneumonia.

Hospitalization was required by 12 (30 per cent) of the control group and 2 (5 per cent) of the sulfadiazine treated group. In 1 case of the treated group the temperature was 105.6 F. on the first day of illness when pneumonia was suspected, 99 F. on the second day and 103 F. on the third day, when a definite diagnosis of pneumococcus type XVIII A (Dougherty)<sup>3</sup> lobar pneumonia was made. In the other case the temperature was 106 F. when the illness was first recognized, and the patient was at once transferred to the hospital after having received an initial dose of 1 Gm. of sulfadiazine.

Of the 12 control patients who were hospitalized, 6 had pneumonia. Type I pneumococcus pneumonia occurred in 4 of these cases: 2 were recognized within twenty-four hours after the first signs of illness were observed, the third within seventy-two hours after the onset and the fourth case after nineteen days of intermittent fever, nasal discharge and cough. In the remaining 2 cases of pneumonia, signs of consolidation were recognized two and six days, respectively, after the first symptoms of illness were noticed. The latter patient died shortly after admission to the hospital. Of the remaining 6 hospitalized control patients, 3 had acute bronchitis and 3 nasopharyngitis.

Hospitalization was not required in 37 (95 per cent) of the sulfadiazine treated group and 28 (70 per cent) of the control group. A fall in temperature after the first day's treatment with sulfadiazine occurred in 35 (90 per cent) cases, while in 2 (5 per cent) there was a transient exacerbation of fever within seventy-two hours after withdrawal of the drug. After the first day's treatment in the control group there was a fall in temperature in 14 (35 per cent) cases, while an equal number showed a rise in temperature after routine treatment in bed had been instituted.

When the temperature remained below 102 F. there was no significant difference in the duration of fever between treated and control groups. However, the difference was considerable among those whose maximum temperature was 102 F. or over. In these cases fever persisted for only one to two days in 60 per cent of the treated group as compared with 10 per cent of the controls, for three to five days in about 30 per cent in each group and for more than five days in about 10 per cent of the treated group as compared with 60 per cent of the controls. The average duration<sup>4</sup> of fever after the first day's treatment had been instituted was 1.6 days in the sulfadiazine treated group and 4.2 days among the controls.

In cottage Y, the test period began on Jan. 19, 1942 during the latter part of an outbreak of severe acute respiratory infections with a high incidence of pneumonia and acute bronchitis. During a two week period of observation from January 19 to January 31 there were 18 cases, 9 each in the control and sulfadiazine treated groups.

In the sulfadiazine treated group of cottage Y, the temperature of every patient treated for at least one full day dropped within twenty-four hours. On the second day of illness, all but 1 had temperatures below 100 F. throughout the day and did not appear toxic. In 1 patient pneumonia was suspected at the onset, and the child was transferred at once to the hospital after an

3. The typing was done by the Pneumonia Division of the Department of Health of New York City.

4. In the calculation of the average duration of fever, illnesses of ten days or longer were each considered as ten days to offset the influence of extreme values. This favored the control group, which had 6 such cases as compared with 1 in the sulfadiazine treated group.

initial dose of 1 Gm. of sulfadiazine had been given. Two patients had secondary rises in temperature for one day on the fourth and sixth days, respectively, within twenty-four to forty-eight hours after discontinuation of sulfadiazine.

Of the 9 control patients, only 2 recovered promptly after the first day's observation. The others were quite sick for a few days; they were restless and apathetic and refused to eat. They lost considerable strength and weight during the illness and had a prolonged convalescent period. Two control patients were sent to the hospital, 1 on the fourth day of illness with an acute bronchitis of undetermined etiology, the other on the first day of illness with bronchopneumonia attributable to pneumococcus type V. This same type of pneumococcus was responsible for at least 2 other cases of pneumonia in the early part of the outbreak.

On February 21 a second outbreak of respiratory infections occurred which affected 12 inmates within ten days in cottage Y. They all had a nasopharyngitis with considerable coryza; a few also had bronchitis. There were no cases of pneumonia and little evidence of toxicity. Most of the affected children were usually active and playful and maintained good appetites throughout these illnesses.

The dramatic drop in temperature that was observed within twenty-four hours after the use of sulfadiazine during the first outbreak did not occur with the same regularity again. In 2 cases the initial infection did not seem to be modified by the use of sulfadiazine, and the temperature remained high for three days. In one of these cases the sulfadiazine level on the third day was 5.1 mg. per hundred cubic centimeters and in the other case it was 3.8 mg. per hundred cubic centimeters. At the end of five days the temperature was normal and remained normal. The controls recovered without difficulty except for 2 patients. One had a nasopharyngitis of undetermined etiology while the other had an acute bronchitis attributable to pneumococcus type V. Significant organisms were isolated in only 2 other cases—pneumococcus type XI A (Gorman) in one and *Streptococcus hemolyticus* in the other. Single throat smears in the early acute stage in the remaining 9 cases were negative.

After the first day's treatment, the blood level of free sulfadiazine<sup>5</sup> usually varied from 4 to 6 mg. per hundred cubic centimeters during the period in which the drug was employed. The maximum level reached was 12 mg. on the fifth day of treatment in a child weighing 47 pounds (21 Kg.) and receiving 1.5 Gm. daily. With the dosage employed there were no gross ill effects except for a transient rash which developed in 1 case after five days of treatment.

#### COMMENT

In this preliminary study on the use of sulfadiazine at the onset of symptoms of respiratory illnesses, it was found that most of the patients receiving sulfadiazine improved after twenty-four hours, a few had a secondary rise in temperature within seventy-two hours after premature withdrawal of the drug and some showed no evidence of improvement.

For the first twelve hours after treatment was begun there was often no perceptible difference between treated and control cases. Within twenty-four to thirty-six hours, however, there were usually signs of improvement in the treated group. The temperature fell and remained low. The patient appeared less toxic.

5. Determined through the courtesy of Dr. Jesse G. M. Bullowa at Harlem Hospital, New York.

His appetite returned and he was no longer restless and apathetic but brighter and more cheerful. Signs of infection, such as coryza and cough, still persisted in many cases, but the infection appeared to be subsiding, as if the inflammation had abruptly passed the acute stage. Most patients showed no exacerbation of the infection when the drug was discontinued after four days of treatment. Some children, particularly those who appeared to be seriously sick at the onset or who had persistent discharge and other evidence of infection, required treatment beyond the four day period. Premature withdrawal of sulfadiazine in these cases resulted in a secondary rise in temperature within seventy-two hours, which usually dropped to normal on reintroduction of the drug. On the whole, therefore, the infection usually appeared to be checked within twenty-four to forty-eight hours after administration of the drug and usually remained under control.

On the other hand, the course in the control group was unpredictable. An occasional patient with high fever at the onset quickly recovered, while other patients who started with low temperatures developed secondary complications. In general, although most of the control children recovered promptly and without complications, some did not, while 1 died. There was usually no way of foretelling the outcome in this group. Those whose temperatures remained below 102 F. usually did as well as those in the treated group. However, there was no way of telling who would have a rise in temperature, when it would occur and what the course of infection would be.

In one small outbreak of relatively mild infection of the upper respiratory tract, the course of the initial infection did not appear to be modified by the use of sulfadiazine. A secondary rise in temperature was not noted. It is a reasonable assumption that this outbreak was due to some agent, probably a virus, not susceptible to the action of sulfadiazine.

The favorable results obtained with sulfadiazine are attributable to its effectiveness against many of the pathogenic organisms which are active in acute respiratory infections. The role of these infecting agents in producing respiratory illnesses under various conditions is not thoroughly understood at present. Any measure, however, which is effective against the pathogens at their source should contribute to the control of these infections. The extent to which respiratory infections can be safely controlled by the use of sulfonamides remains to be investigated on an etiologic basis.

#### SUMMARY AND CONCLUSION

Clinical observations on the value of sulfadiazine when administered at the onset of recognizable symptoms of respiratory illness in a highly susceptible group of mentally defective children—the group being divided into 54 children treated with sulfadiazine and 55 control patients observed between Dec. 14, 1941 and March 2, 1942—show that usually those treated with sulfadiazine appeared less toxic after twenty-four hours and recovered more promptly than the controls. In some cases, however, the initial infection was not modified by sulfadiazine therapy in the dosage employed.

Judging from these preliminary observations among highly susceptible children, it appears that sulfadiazine can be advantageously employed early in the course of many acute respiratory illnesses. In some cases such a procedure might be an early form of therapy, in others a prophylactic measure.

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