For eleven days the temperature remained normal and the abnormal signs in the right lower thorax had practically disappeared, when the temperature suddenly rose to 101 F. Only a mild inflammation of the tonsils and pharynx could be detected on physical examination. The following morning, however, a severe chill was followed by a rise in temperature to over 102 F. The skin was flushed. There were signs suggesting consolidation at the base of the right lung posteriorly. The patient began to vomit. There was evidence of acidosis in the absence of hyperglycemia. The sputum was profuse and bloody, and showed beta hemolytic streptococci on culture. The signs at the base of the right lung soon became those of fluid in the pleural cavity, which were confirmed by roentgenologic examination. Fifty-five cubic centimeters of a serosanguineous fluid was obtained by thoracentesis. Cultures of this fluid showed beta hemolytic streptococci. The patient died on the twenty-third day of her illness.

Postmortem examination was not permitted.

Summary.—A woman, aged 41, was admitted six days after the onset of lobar pneumonia with pneumococcus type VIII (Cooper) in the sputum. Mild diabetes mellitus existed. A critical fall in the temperature occurred on the seventh day of illness, with apparent recovery. A sudden elevation of temperature developed on the nineteenth day with signs of consolidation at the base of the right lung, followed by empyema. Beta hemolytic streptococci were recovered from the throat, sputum and empyema fluid. Death occurred on the twenty-third day of illness.

COMMENT

Case 1 was treated with Felton's concentrated antibody. The dosage was regulated by the demonstration of specific agglutinins in the patient's blood, a method described by Sabin.[12] Agglutinins against the infecting organism were found to persist after the administration of 55 cc. of serum, even after the onset of the streptococcic infection. The pneumococcic infection had been very severe, and the patient had just begun to recover his strength when the fatal streptococcic infection became manifest seventeen days after the onset of pneumonia. This infection progressed rapidly to death three days later.

Cases 2 and 3 were similar in many respects to case 1. The onset of the streptococcic infection in each occurred about twelve days after the subsidence of the original pneumococcic infection and at a time when the patient's recovery seemed assured. The onset in each instance was explosive with a steadily failing course to death within a few days. Cases 1 and 3 were characterized by streptococcic pleurisy on the side of the resolving pneumonia. In case 2, consolidation of the opposite lung was found to have occurred.

The event we have described should be borne in mind in the consideration of febrile complications that occur during convalescence from lobar pneumonia caused by pneumococci. Streptococcic sepsis may be confused with various pneumococcic complications, chief of which are empyema and recrudescence of pneumonia. Pulmonary infarction may also be suspected. Empyema due to the pneumococcus rarely has such an explosive onset; it usually starts in an insidious manner, and signs of fluid in the pleural cavity frequently precede the fever. Recrudescence of lobar pneumonia occurs rarely, usually as the result of infection by a different organism than that originally found and with symptoms more like the onset of the primary pneumonia. Thomas[13] demonstrated that remission of the original type of pneumococcic infection during convalescence is unlikely because of acquired specific immunity. Pulmonary infarction resulting from thrombosis of a large blood vessel in the consolidated or resolving lobe is a not uncommon late complication of the disease. While its onset may be accompanied by violent symptoms, sudden stabbing pain, bloody sputum and dyspnea, it is more commonly an afebrile complication until secondary infection of the necrotic area occurs with subsequent abscess formation or gangrene. The presence of bloody sputum at the time of onset of the streptococcic infection in case 3 suggested the occurrence of pulmonary infarction, and this may have occurred.

The mode of infection by streptococci in convalescent patients is not completely understood. The organisms may be inhabitants in the mouth and nasopharynx of the patient or may be introduced by contact with individuals carrying streptococci, as was suggested by Cole and MacCallum[3] and by Cumming, Spruit and Aten.[4]

CONCLUSIONS

Cases such as the three similar fatal cases of beta hemolytic streptococcic infection during convalescence from lobar pneumonia due to pneumococci that have been reported present a distinct clinical picture. A small proportion of the deaths recorded as due to lobar pneumonia can be attributed to streptococcic sepsis arising during convalescence from lobar pneumonia.

12. Sabin, A. B.: The Microscopic Agglutination Test in Pneumonia: Its Application to Rapid Typing and to Control of Serum Therapy, J. Infect. Dis. **46**: 469-484 (June) 1930.

13. Thomas, H. M., Jr.: Recurrent Type I Pneumonia: Serum Treatment of Two Attacks One Month Apart, Am. J. M. Sc. **161**: 103-109 (Jan.) 1921.

AMIDOPYRINE IN THE TREATMENT OF MEASLES

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In recent years, medical literature has included several reports on the specificity of amidopyrine (pyramidon) in the treatment of measles.

Amidopyrine as a therapeutic agent in measles was first mentioned by Loewenthal[1] in 1924. In his report he stated that amidopyrine, when administered at or before the appearance of the rash, will cause (1) reduction of temperature to normal or nearly normal within twelve hours; (2) inhibition of eruption, at times completely, almost always partially; (3) immediate euphoria; (4) clearing up of conjunctivitis, coryza and cough within a day or two.

On these studies Loewenthal concluded that "the drug acts as promptly in measles as quinine does in malaria, or the salicylates in rheumatic fever. A drug which checks the onward march of the symptoms, and particularly the development of the rash, surely has the right to be called a specific drug."

Independent of Loewenthal's observations and discovery of amidopyrine as a "specific for measles," Dr. Hoyne[2] had used this drug in a small outbreak of measles in Chicago and later on as a routine treatment of the disease in various hospitals of this city. In a report of his observations (1929) he mentioned that amidopyrine is a most remarkable remedy in the treatment of measles and that he thought it acted as a "specific." He considered amidopyrine the most important therapeutic agent in the treatment of measles

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1. Loewenthal, Max: Brit. M. J. **2**: 51 (July 12) 1924; **1**: 1198 (June 28) 1930.

2. Hoyne, Archibald: Illinois M. J. **56**: 254 (Oct.) 1929.

because (1) it reduced temperature without injury to the patient; (2) it allayed cough and appeared to lessen the irritation of all mucous membranes; (3) it was of value in lessening complications and therefore tended to shorten the course of the disease and to lower the mortality rate.

Following the reports of Loewenthal and Hoyne, several other reports dealing with amidopyrine as a therapeutic agent in measles appeared in the British medical literature. Thus, Gladstone,[3] in 1930, reported a series of twenty-four cases treated with amidopyrine. He reported a temperature drop within the first twenty-four hours with no respiratory complications and further stated that nearly all patients were well on the fourth day. He also stated that when the drug was given in the Koplik spot stage a rash was scarcely evident. He believed that the drug was of particular value for younger individuals, but not so effective for older patients.

In support of Gladstone's observations, Urquhart and Winchester [4] reported six cases treated with amidopyrine, in which there was also a fall in temperature within twenty-four hours and disappearance of the cough and bronchitis. They thought the drug almost a "specific" but thought that it might cause a hemorrhagic rash.

Collier,[5] in reporting a group of twenty-six cases of measles treated with amidopyrine, states that, of five patients who were thus treated during the stage of invasion on appearance of Koplik spots, only two developed a rash and all were well in two days. Sixteen patients treated at the onset of the rash showed an immediate reduction of temperature, and they were well in from three to four days, while five cases treated in various late stages showed only little, if any, beneficial effect. On these observations he concluded that the marked features of this use of amidopyrine are (1) fall of temperature within the first day, (2) alleviation of cough, and (3) absence of complications. He believed that, if the drug is administered in the stage of Koplik spots, the disease is aborted. He stated, however, that the type of the case, mild or severe, determined the result.

In a later paper, Collier, in collaboration with Ronaldson,[6] reported 150 cases of measles treated with amidopyrine and concluded that amidopyrine is of most value in early cases, that it lessens the tendency to pneumonia, and that it prevents complications. They stated that they could not substantiate the claim that the drug exercises a specific action or that it causes an abortion of the rash. They believe that the drug has no constant effect on the exanthem of measles. They therefore consider amidopyrine a valuable adjuvant in the treatment of measles and think that its action is chiefly antipyretic but that it appears to have some influence on other symptoms of the disease.

Attlee [7] reported 129 cases, in 9 of which amidopyrine was given. In the cases in which amidopyrine was not administered there was a rise in temperature with the appearance of the rash and then an abrupt fall within twenty-four hours; only six cases showed some complications (bronchitis in four, bilateral otitis in two). In the nine cases in which amidopyrine was given there was a slower appearance of the rash with a longer duration of the fever, while the complications were much more frequent. He concludes, therefore, that amidopyrine should not be given in measles.

There is apparently a conflict of opinion as to the value of amidopyrine in the treatment of measles. One group thinks that amidopyrine is a "specific," while another believes that it should not be used at all. A third group considers amidopyrine merely an adjuvant in the treatment of this disease, influencing it only as would any other antipyretic.

In order to observe the action of this drug first hand in the prophylaxis and treatment of measles, a series of 194 cases was studied in the contagious department of Cook County Hospital during the first six months of 1931. Alternate patients entering the institution received amidopyrine, 1 grain (0.065 Gm.) for each year, up to 5 grains (0.3 Gm.) three times a day for ages above 5 years. The series includes ninety-five patients who received amidopyrine and ninety-nine to whom the drug was not administered.

TABLE 1.—*Day of Return to Normal Temperature Level in Group of Patients Receiving and Those Not Receiving Amidopyrine*

Stage of Eruption on Admission	Number of Patients with Day of Return to Normal Temperature Level									
	1st	2d	3d	4th	5th	6th	7th	8th	9th	15th	16th
First day, 80 patients											
41 without amidopyrine treatment	3	10	13	8	4	2	0	0	1	0	0
39 with amidopyrine treatment	1	19	5	8	2	0	2	0	0	1	1
Second day, 30 patients											
10 without amidopyrine	4	2	3	1	0	0	0	0	0	0	0
20 with amidopyrine	1	9	5	2	2	0	0	1	0	0	0
Third day, 11 patients											
7 without amidopyrine	1	4	1	1	0	0	0	0	0	0	0
4 with amidopyrine	1	1	2	0	0	0	0	0	0	0	0
Fourth day, 3 patients											
1 without amidopyrine	1	0	0	0	0	0	0	0	0	0	0
2 with amidopyrine	0	1	0	0	0	0	0	0	0	0	1
Sixth day, 2 patients											
1 without amidopyrine	0	1	0	0	0	0	0	0	0	0	0
1 with amidopyrine	0	0	1	0	0	0	0	0	0	0	0

On entrance the majority of patients bore the usual symptoms of measles: characteristic rash, coryza, conjunctivitis and bronchitis. One patient had bronchopneumonia on admission. In all cases an attempt was made to determine the duration of the rash, but in sixty-nine this could not be learned. Eighty entered the hospital on the first day of the appearance of the rash, thirty within forty-eight hours, eleven within seventy-two hours, three within ninety-six hours, and two on the sixth day after the eruption. One patient entered without an eruption but developed the rash on the fourth day after admission (this patient received amidopyrine).

Of the eighty patients who entered on the first day of the eruption, thirty-nine received amidopyrine while forty-one did not. In the nonamidopyrine cases the temperature dropped to normal as follows: three on the first day, ten on the second, thirteen on the third, eight on the fourth, four on the fifth, two on the sixth, and one on the ninth day. The average duration of fever was 3.3 days.

3. Gladstone, M. B.: Brit. M. J. **1**: 1198 (June 28) 1930; **2**: 1103 (Dec. 27) 1930.
4. Urquhart, G. H., and Winchester, A. H.: Brit. M. J. **1**: 1153 (June 21) 1930.
5. Collier, J. I.: Brit. M. J. **1**: 1093 (June 14) 1930.
6. Ronaldson, G. W., and Collier, J. I.: Brit. M. J. **2**: 994 (Dec. 13) 1930.
7. Attlee, W. H. W.: Brit. M. J. **2**: 996 (Dec. 13) 1930.

In the amidopyrine treated cases the temperature dropped to normal as follows: one on the first day, nineteen on the second, five on the third, eight on the fourth, two on the fifth, two on the seventh, one on the fifteenth, and one on the sixteenth day. The average duration of fever was 3.6 days.

Of the patients who entered with a rash of two days' duration, ten had not been given amidopyrine and twenty had received it. In the former, the average duration of temperature was 2.1 days; in the latter, 3 days.

Of eleven patients who entered the hospital on the third day of rash, seven did not receive amidopyrine and showed an average duration of fever of 2.3 days, while four who did receive amidopyrine had fever for an average of 2.25 days.

Of the three patients who entered on the fourth day of rash, the one who did not receive amidopyrine was afebrile the following day. Two received amidopyrine; one became afebrile on the second day; the other developed a complication and a fever of sixteen days' persistence.

Of the two patients who supposedly had a rash for six days, the one who did not receive amidopyrine became afebrile on the second day; the one receiving amidopyrine became afebrile on the third day.

With the duration of the fever as a criterion, we found that the temperature dropped the first day after admission in 22 patients: 11 to whom amidopyrine had been administered and 11 to whom it had not been given. On the second day the temperature dropped in 63 patients, of whom 37 had received amidopyrine while 26 had not. Forty-two cases became afebrile on the third day: 18 with amidopyrine dosage, 24 without it. On the fourth day the temperature dropped in 29 patients, of whom 15 had and 14 had not been given amidopyrine. The temperature dropped in 15 cases on the fifth day, of which 5 were treated with amidopyrine, while 10 were not. Six cases became afebrile on the sixth day: 2 with amidopyrine, and 4 without it. Of 10 cases that had an afebrile course, 8 were in the group that did not receive amidopyrine and 2 among those which did receive the drug. Of the cases with prolonged fever, 2 were in the nonamidopyrine group

TABLE 2.—*Day on Which Temperature Returned to Normal in One Hundred and Eighty-Three Cases*

Days on which temperature dropped to normal.....	1st	2d	3d	4th	5th	6th	8th	9th	15th	16th
Number of cases treated with amidopyrine	11	37	18	15	5	2	1	1	1	1
Number of cases without amidopyrine	11	26	24	14	10	4	0	1	1	0

—nine and fifteen days, respectively—while 4 were in the amidopyrine group—eight, nine, fifteen and sixteen days, respectively (table 2).

Twenty-seven patients in this series developed complications. Of these, 11 received no amidopyrine, while 16 were given the drug. Among the 11 in the nonamidopyrine group, there were 4 with bronchopneumonia (one having entered the hospital with this complication), 5 cases of unilateral otitis media (1 of these being in a patient with bronchopneumonia), 1 bilateral otitis media, and 1 abscess of the thigh.

Among the amidopyrine group, bronchopneumonia developed in 2 cases, unilateral otitis media in 9, a bilateral otitis media in 1 case, diphtheria and cervical adenitis in 2 cases each.

Since, as already stated, all cases entered the hospital when the rash had already appeared, the effectiveness or noneffectiveness of amidopyrine in the prevention of the rash could not be observed. Only one case entered in the Koplik spot stage, before the appearance of the rash. This case in the amidopyrine group developed a full blown eruption on the fourth day after admission. No marked difference in the persistence of the rash was noted in the two groups, nor was there any striking difference in the symptoms of conjunctivitis or coryza, among the patients of the two groups.

COMMENT

In 194 unselected cases of measles in which amidopyrine was given in alternate cases (dosage as stated), no striking difference was noted in the clinical course of the two groups. Nothing that would indicate therapeutic value was noted in the cases in which amidopyrine was given. The same clinical picture appeared in those in which this drug was not given and in those in which other antipyretics were given. There were no appreciable differences in the duration of fever or speed of convalescence among the two groups. Complications were about evenly distributed in the two groups.

TABLE 3.—*Patients with Complications*

Type	Bronchopneumonia	Unilateral Otitis	Cervical Adenitis	Diphtheria	Bilateral Otitis	Abscess of Thigh	Total
With amidopyrine treatment.....	2	9	2	2	1	0	16
Without amidopyrine treatment.....	4*	5	0	0	1	1	11

* One patient had bronchopneumonia on entrance.

In our investigation we have obtained results which make us believe that amidopyrine should be used as an adjuvant in the treatment of measles similar to any other antipyretic. This drug proved neither a "specific" nor a harmful agent in the treatment of measles.

SUMMARY

1. Of 194 patients with measles admitted to the contagious division of the Cook County Hospital during the first six months of 1931, about one half received the amidopyrine treatment, while the remainder did not.

2. The morbidity, duration of fever, and complications were about equal in the two groups.

3. Amidopyrine did not prevent the appearance of the rash (one patient who entered the hospital and received amidopyrine developed a rash on the fourth day).

4. Complications occurred with equal frequency and severity in the two groups.

5. No marked drop of temperature was noted in the amidopyrine group as compared with the nonamidopyrine group, although a greater number of those in the amidopyrine group became afebrile on the second day.

6. Amidopyrine is not a specific for measles. It is a valuable antipyretic adjuvant in the treatment of the disease but should not be considered a specific.

CONCLUSIONS

1. Amidopyrine did not prevent the eruption of measles in the one case in this series seen in the preeruptive state.

2. It did not lessen complications.

3. It did not shorten the course of the disease.

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