

blood pressure. Observations on the size of the heart, as determined by roentgenograms, failed to show any appreciable change during diathermy. Electrocardiographic studies also showed either no change whatever, or such minor alterations as we considered insignificant. The amplitude and the rate of respiration were essentially unaltered.

These experiments suggest that appreciable changes within the chest could be obtained only when such intense diathermy currents were employed that serious burns and sloughing of tissues would be liable to occur.

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THE ANTITOXIN TREATMENT OF ERYSIPELAS

OBSERVATIONS IN ONE HUNDRED AND THIRTY-ONE
PATIENTS AT BELLEVUE HOSPITAL*

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In the past twenty-three years, 15,277 cases of erysipelas were admitted to the isolation pavilion of Bellevue Hospital. During that time almost every conceivable form of treatment was practiced, most of it based on the application of local remedies. None of them appeared appreciably to shorten the course of the disease—and erysipelas, although commonly regarded as a self-limited process, seldom, in our experience at least, brings itself to an abrupt end, but is apt to pursue a leisurely course, sometimes consuming weeks. Within the past year, Birkhaug¹ introduced the antitoxin treatment of erysipelas, employing it in a series of sixty cases with results that were astonishing. In Bellevue Hospital, which maintains, perhaps, the largest and most active erysipelas service in the world, we are now using the antitoxin treatment to the exclusion of other methods. As our first trial, we employed an unconcentrated product provided gratuitously by the Lederle Antitoxin Laboratories, through Dr. R. O. Clock, assistant director. Thus far, 131 cases have been treated by this antitoxin and the results have been remarkable. At the commencement of this work, it was agreed, as a control, that every other case of erysipelas was to be treated by antitoxin under the supervision of one of us (Symmers) while every alternate case was to be treated by Dr. William C. Lusk, using methods with which he had been working for years. After a period of critical observation, Dr. Lusk requested that all of the cases be treated by antitoxin—this after an experience in the treatment of erysipelas as large as, perhaps larger than, that of any other physician on the American continent.

PREPARATION OF SERUM

In the preparation of the unconcentrated antitoxin, as outlined by Dr. Clock, horses are immunized by subcutaneous injections with gradually increasing amounts of erysipelas toxin; also by intravenous injections of cultures of the erysipelas streptococcus isolated from typical cases of erysipelas. The toxin is obtained from broth cultures of the erysipelas streptococcus grown at

37 C. Phenol (carbolic acid) is added up to 0.5 per cent and the material allowed to sediment at room temperature. The supernatant fluid is siphoned off and used for injection into horses. After the immunizing treatment has continued for a period sufficient to produce a potent antitoxic serum, as indicated by potency tests applied to trial bleedings, blood is drawn under aseptic conditions from the jugular vein and allowed to clot and the clear serum siphoned off. The serum is then clarified by Buchner filtration and sterilized by Berkefeld filtration, after which the necessary tests are made.

Potency tests are made as follows:

Serial dilutions of the antitoxic serum are made with physiologic sodium chloride solution and these dilutions are mixed in equal volume with a dilution of erysipelas toxin of such strength that 0.1 cc. of the toxin-antitoxin mixture will contain one skin test dose of toxin.

The skin test dose of toxin is determined by intradermal tests applied to Saanen goats, 0.1 cc. of various dilutions of erysipelas toxin being injected.

Intradermal injections of 0.1 cc. of the various toxin-antitoxin mixtures are applied to Saanen goats. The highest dilution of antitoxin serum in the toxin-antitoxin mixture giving a negative skin reaction indicates the potency of the antitoxic serum. These tests are applied to trial bleedings of the horses as well as to all batches of the finished product.

INJECTION

For the introduction of the antitoxin into the body we now employ the intramuscular route exclusively. At the outset we essayed to use the antitoxin intravenously, and in five cases the results were little short of wonderful. In the sixth case, however, the patient, an alcoholic subject, immediately developed an alarming degree of anaphylactic shock from which, however, he rallied in the course of one and one-half hours. The seventh case was that of an obese woman whose muscles could not be reached by the hypodermic needle. Erysipelas involved almost the entire trunk. Her son, a physician, asked that antitoxin be given intravenously as a last resort. Two hours after injection the patient developed cyanosis and edema of the lungs, and death occurred in a short time. Taking all things into account, therefore, we feel that the intravenous use of antitoxin is not only unnecessary in the great number of cases, but dangerous, and that the intramuscular is the route of preference.

DOSAGE

The dosage of the antitoxin is to be determined in each case since there are several factors which enter into the patient's reaction, such, for example, as the duration of the disease before the institution of treatment, the patient's resistance, the virulence of the infective agent, and perhaps most strikingly of all the part of the body involved. The earlier a patient comes under treatment, the more promptly is arrest of the disease to be expected, and it is likewise to be anticipated that the young, the vigorous and the temperate will yield to treatment more easily than the old, the debilitated and the debauched. In Bellevue Hospital, unfortunately, we have to deal with the latter type more often than with the former and, for that reason, we venture to predict that our results, although gratifying, will be surpassed. Finally, in the matter of dosage, we have but one fixed practice to commend, namely, to administer the antitoxin in excess rather than to attempt to minimize the dose. Consequently, as a routine, we have

* From the Fourth Surgical Service, Dr. Carl G. Burdick, director, and the Third Surgical Service, Dr. George D. Stewart, director, Bellevue Hospital.

1. Birkhaug, K. E.: Erysipelas, J. A. M. A. 86: 1411 (May 8) 1926.

injected 25 cc. of the unrefined antitoxin at the moment of the patient's admission to the hospital, repeating the amount, usually at intervals of twenty-four hours, until the erysipelatous blush disappears, the edema is dissipated and the temperature is normal. As a result of this practice, we have sometimes been able to control

TABLE 1.—Facial Erysipelas.

111 Cases of Facial Erysipelas Treated with Antitoxin at Bellevue Hospital Between May 5, 1927, and June 23, 1927			92 Cases of Facial Erysipelas Treated Without Antitoxin at Bellevue Hospital Between May 5, 1926, and June 23, 1926		
85.6% cured in 3-7 days 9.9% cured in 8-21 days 4.5% of the patients died			33.7% cured in 2-7 days 47.8% cured in 8-18 days 12% cured in 23-54 days 6.5% of the patients died		
Cured in Days—	No. of Cases	Per Cent of Total	Cured in Days—	No. of Cases	Per Cent of Total
3	19	17.1	2	2	2.17
4	26	23.4	4	8	8.69
5	22	19.8	5	5	5.43
6	14	12.6	6	8	8.69
7	14	12.6	7	8	8.69
8	6	5.4	8	6	6.52
9	2	1.8	9	6	6.52
11	1	.9	10	14	15.21
13	1	.9	11	2	2.17
21	1	.9	12	4	4.34
Deaths—	5	4.5	13	5	5.43
			14	2	2.17
			15	1	1.08
			16	1	1.08
			17	2	2.17
			18	1	1.08
			23	1	1.08
			24	1	1.08
			26	1	1.08
			27	1	1.08
			28	2	2.17
			30	2	2.17
			34	1	1.08
			40	1	1.08
			54	1	1.08
			Deaths—	6	6.52

the disease by a single injection. Oftener two injections have been necessary, but most often we have used three injections of like amount, while in occasional instances from 100 to 150 cc. or even more has been given to a single patient. We have not observed any ill effects from this dosage other than nine cases of serum sickness coming on in from two to seven days after treatment and lasting from two days to a week.

RESULTS

In the present series of 131 cases, the length of the patients' stay in the hospital has been reduced somewhat over 53 per cent. The individual figures vary, of course, depending on such factors as have already been pointed out, among which, however, the most striking is to be found in the part of the body involved. In this series, the facial cases outnumbered those of the extremities and trunk in the proportion of 5½ to 1. Of the 111 cases of facial erysipelas, as shown in table 1, 85.6 per cent were cured in from three to seven days and 9.9 per cent in from eight to twenty-one days, with a mortality of 4.5 per cent; whereas, in a series of ninety-two cases of facial erysipelas treated without antitoxin during the corresponding season of 1926, 33.7 per cent were cured in from two to seven days, 47.8 per cent in from eight to eighteen days, and 12 per cent in from twenty-three to fifty-four days, the mortality being 6.5 per cent. Of the twenty body cases treated by antitoxin, 60 per cent were cured in from three to seven days and 30 per cent in from eight to sixteen days, with a mortality of 10 per cent; whereas, of the fifteen cases of body erysipelas treated without antitoxin during the corresponding season of last year, 46.6 per cent were cured in from seven to fifteen days and 13.3 per cent in from twenty-five to fifty-eight days, the mortality being 40 per cent.

As far as the complications of erysipelas are concerned, the only one that developed in this series after the use of antitoxin consisted of subcutaneous abscesses occurring, usually, immediately under the skin corresponding to the distribution of the rash and varying in size from those of negligible proportions to extensive infiltrations of pus. The incidence of abscesses seems to be about the same whether antitoxin is used or not.

MORTALITY

In the 15,277 cases treated at Bellevue Hospital during the last twenty-three years, the mortality from all causes was 10.1 per cent. In the present series of 131 cases treated by antitoxin, the mortality was 5.3 per cent. The value of the figure obtained from the larger series is impaired by the fact that it is humanly impossible to review such a vast array of records, to eliminate the contributing factors in the production of death, and to deduce from the remainder an intelligent conception of erysipelas as a direct cause of death. On the other hand, to draw any conclusions from such disproportionate numbers is hazardous. Suffice it to say that, in this series of 131 cases, death from all causes occurred seven times, or in 5.3 per cent; whereas, in a series of 107 cases treated without antitoxin during the corresponding season of last year, the mortality from all causes was 11.2 per cent.

CONCLUSIONS

1. The antitoxin treatment of erysipelas marks an advance, the results of which are commensurate with those obtained in the treatment of diphtheria. As far as the immediate attack is concerned, erysipelas is now a vanquished disease. Beyond the immediate attack, however, the antitoxin treatment does not promise anything—it does not, for example, confer immunity, and

TABLE 2.—Body Erysipelas.

20 Cases of Body Erysipelas Treated with Antitoxin at Bellevue Hospital Between May 5, 1927, and June 23, 1927			15 Cases of Body Erysipelas Treated Without Antitoxin at Bellevue Hospital Between May 5, 1926, and June 23, 1926		
60% cured in 3-7 days 30% cured in 8-16 days 10% of the patients died			46.6% cured in 7-15 days 13.3% cured in 25-58 days 40% of the patients died		
Cured in Days—	No. of Cases	Per Cent of Total	Cured in Days—	No. of Cases	Per Cent of Total
3	1	5	7	2	13.3
4	3	15	8	1	6.6
5	4	20	12	1	6.6
6	2	10	14	1	6.6
7	2	10	15	2	13.3
8	1	5	25	1	6.6
10	1	5	58	1	6.6
11	1	5	Deaths—	6	40
13	2	10			
16	1	5			
Deaths—	2	10			

Percentage of deaths from all causes in patients treated with antitoxin	5.3%
Percentage of deaths from all causes in patients not treated with antitoxin	11.2%
Average number of days in hospital of all patients treated with antitoxin	5.6 days
Average number of days in hospital of all patients not treated with antitoxin	12.1 days

recurrent attacks occur with the same freedom as in erysipelas treated by other methods; nor does it appear to diminish the incidence of complications, such as the abscesses which so frequently follow in the wake of this disease. Moreover, the antitoxin method confers enormous economic benefit on both patient and hospital, the patient's period of disability being reduced by slightly more than 50 per cent. At the same time it permits reduction in the personnel of the nursing staff

to the extent of about 60 per cent and effects a notable saving of bed linen and sleeping garments by doing away with the destructive effects of ointments and similar local applications.

2. Facial erysipelas responds more readily to treatment by antitoxin than erysipelas of the trunk or extremities. In a series of 111 facial cases treated at Bellevue Hospital, 85.6 per cent of the patients were cured in from three to seven days, 9.9 per cent were cured in from eight to twenty-one days, and 4.5 per cent died. In a series of ninety-two cases of facial erysipelas treated at Bellevue Hospital without antitoxin during the corresponding season of 1926, 33.7 per cent of the patients were cured in from two to seven days, 47.8 per cent were cured in from eight to eighteen days, 12 per cent were cured in from twenty-three to fifty-four days, and 6.5 per cent died. In a series of twenty cases of erysipelas of the trunk or extremities treated by antitoxin, 60 per cent of the patients were cured in from three to seven days, 30 per cent were cured in from eight to sixteen days, and 10 per cent died. In fifteen cases of body erysipelas treated without antitoxin at Bellevue Hospital during the corresponding season of last year, 46.6 per cent of the patients were cured in from seven to fifteen days, 13.3 per cent were cured in from twenty-five to fifty-eight days, and 40 per cent died.

3. The intramuscular route offers the best method of introducing the antitoxin. Intravenous injection, we think, is dangerous and is to be employed only in desperate circumstances.

IODODERMA FROM IODIZED OIL*

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Since the introduction by Sicard and Forestier¹ of iodized oil as an aid in roentgen-ray diagnosis, it has been very widely used in connection with the roentgen ray, not only in the spinal canal but also in various other organs and structures of the body as a diagnostic procedure.

The French preparation lipiodol, and the Danish preparation iodumbrin, are said to be very closely similar in that they contain approximately equal amounts of iodine (40 per cent), and in that they are both highly stable. The relative stability of these compounds is evidenced by the few reports of untoward symptoms following their use during the five years of their employment.

Here and there one finds fever and dyspnea reported immediately after the use of these oils. O. Lichtwitz² reported a rapidly progressive pulmonary tuberculosis which flared up after their use, and Moeller and von Magnus³ and Armand-DeLille and Moncrieff⁴ have reported acute iodism, the case of the latter having been accompanied by edema of the larynx.

* Studies and Contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Sicard, H., and Forestier, J.: *Méthode générale d'exploration radiologique par l'huile iodée (lipiodol)*, Bull. et mém. Soc. méd. d. hôp. de Paris **46**: 463 (March 17) 1922.

2. Lichtwitz, O.: *Injury by Lipiodol as Contrast Substance in Pulmonary Tuberculosis*, Wien. klin. Wchnschr. **39**: 133 (Jan. 28) 1926; abstr. J. A. M. A. **86**: 1104 (April 3) 1926.

3. Moeller and von Magnus: *Investigation of Bronchial Affections by Means of Iodine Preparations (Iodumbrin and Lipiodol)* Acta med. Scandinav. **63**: 174, 1924.

4. Armand-DeLille, P. F., and Moncrieff, A.: *The Use of Lipiodol in the Diagnosis of Bronchiectasis*, Brit. M. J. **2**: 7 (July 5) 1924.

Iodized oil when introduced into the body is supposed to be eliminated mechanically, that is, by coughing, expectorating, etc., or by absorption and elimination through the regular body channels. That an amount sufficient to be injurious can be absorbed is shown by the cases of acute iodism already reported. By acute iodism I presume is meant symptoms referable to the gastro-intestinal and upper respiratory tracts. In none of the cases reported have I been able to find any reference to an accompanying iododerma.

Moeller and von Magnus,³ in their work with iodumbrin, found iodine in the urine six hours after the injection of the oil; its elimination reached its peak at twenty-four hours, and no trace could be found after six days. Iglauer⁵ also states that iodine is found in the urine no later than six days following the use of lipiodol. It is well known from statements already published⁶ and from the experience in our own roentgen-ray department, however, that this substance may remain in the lungs, at least, many weeks.

I recently saw a case of iododerma in which lipiodol is the most likely source of the iodide skin reaction.

D. C., a white man, aged 57, was referred on April 13, 1927, to the department of dermatology and syphilology from the tuberculosis unit for diagnosis and advice regarding a skin eruption. Examination revealed an acneform eruption involving the face, upper trunk and arms, such as is commonly caused by iodide or bromide, and several members of the staff, including our chief, corroborated the diagnosis.

Because the halogen group is at this time under investigation in our clinic, bromine and iodine were searched for in the patient's urine. No bromine was found, but iodine was present in large quantities, and we were especially interested to learn why a patient in the tuberculosis unit was receiving iodide.

No iodide was being given the patient, and iodized salt was not being used in the unit. Close questioning of the patient failed to obtain a history of taking medicine not given him by the physician in charge.

Thorough investigation of the patient's record since his admission on Dec. 22, 1926, reveals three possible sources of iodine. Dec. 29, 1926, he received gallbladder dye (tetraiodophenolphthalein) by mouth; from Jan. 11 to Jan. 16, 1927, he received potassium iodide, 15 grains (1 Gm.), three times a day, and on March 29 his lungs were injected with lipiodol. The eruption for which the patient was referred appeared, April 6 or 7.

Examination of the urine and saliva, April 13, 14 and 15, were strongly positive for iodine, and reexamination of the chest by roentgen ray, April 14, showed the presence of lipiodol in the lung bases.

Since this patient had received iodine from sources other than lipiodol, it might be argued that this case is not clearly due to lipiodol. However, all other iodine preparations had been administered by mouth, at least three months previous to the appearance of the eruption. It is definitely established that iodine preparations administered by mouth are rapidly absorbed and eliminated, and it is not possible that these preparations could have caused the eruption. On the other hand, this eruption appeared about nine or ten days following the injection of lipiodol, and at the time of the examination tests of body fluids gave evidence of continued absorption of iodine from some source. Roentgen-ray examination demonstrated the presence of lipiodol in the lungs.

Whether the iodine was actually being absorbed from the lungs, or whether it was coming from sputum swallowed and broken down in the gastro-intestinal canal, is impossible to determine. The fact remains that the patient was absorbing enough iodine to give him an iododerma, with lipiodol the most likely source.

5. Iglauer, Samuel: *Use of Injected Iodized Oil in Roentgen-Ray Diagnosis*, J. A. M. A. **86**: 1879-1884 (June 19) 1926.

6. Iglauer, Samuel, in discussion on paper referred to in footnote 5.