

The effect of intraperitoneal injections of ozone in animals following injections with virulent bacteria / by S.E. Finch.

Contributors

Finch, S.E.
Royal College of Surgeons of England

Publication/Creation

[New York] : A.R. Elliott, 1914.

Persistent URL

<https://wellcomecollection.org/works/rgwapa86>

Provider

Royal College of Surgeons

License and attribution

This material has been provided by This material has been provided by The Royal College of Surgeons of England. The original may be consulted at The Royal College of Surgeons of England. where the originals may be consulted. Conditions of use: it is possible this item is protected by copyright and/or related rights. You are free to use this item in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s).

P. C. 3

5.

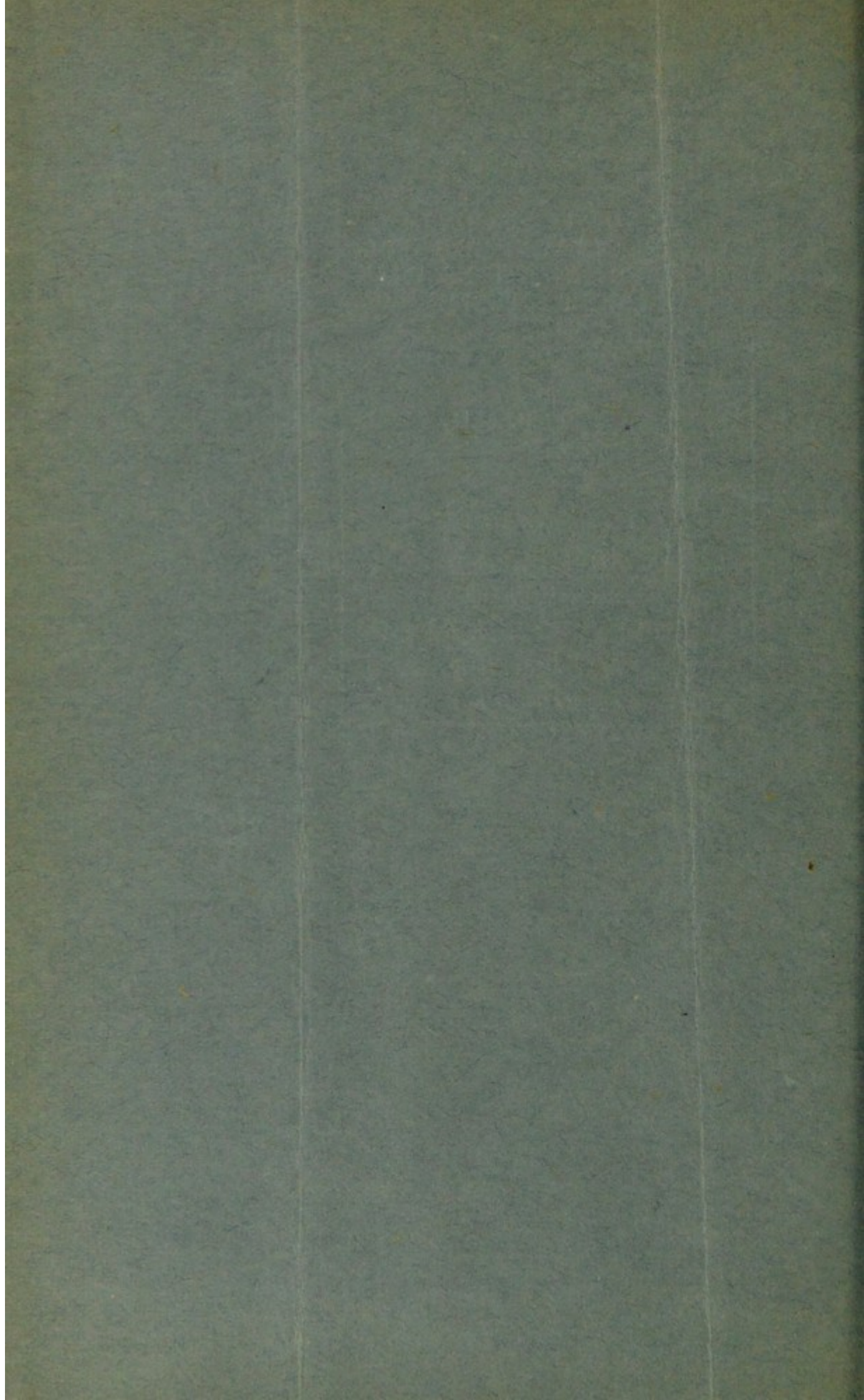
THE EFFECT OF INTRAPERI-
TONEAL INJECTIONS OF
OZONE IN ANIMALS FOL-
LOWING INJECTIONS WITH
VIRULENT BACTERIA.

BY
S. E. FINCH, M.D.,
NEW YORK.

Reprinted from the
New York Medical Journal

INCORPORATING THE
Philadelphia Medical Journal and
The Medical News

January 10, 1914.



Reprinted from the New York Medical Journal for
January 10, 1914.

THE EFFECT OF INTRAPERITONEAL INJECTIONS OF OZONE IN ANIMALS FOLLOWING INJECTIONS WITH VIRULENT BACTERIA.*

BY S. E. FINCH, M. D.,
New York.

Had oxygen been shown to possess a bactericidal action in vitro, it was proposed to ascertain its value when used intraabdominally in animals following controlled peritoneal infection with pyogenic bacteria. Failing in the demonstration of such an action by oxygen, the finding that under the same conditions in which it showed slight inhibitory action toward two of the types of bacteria used, oxygen, of which a small percentage had been changed to ozone, showed not only an inhibitory but a bactericidal action toward all four microorganisms experimented with,¹ led to its use in a series of animals (rabbits and cats) after they had received intraabdominally fatal doses of *Aurococcus*, *Streptococcus pyogenes brevis*, or of the colon bacillus.

Certain known factors were against this use of the gas, namely, the ease with which ozone is reduced by readily oxidizable organic matter, inability to limit or direct the action of the gas unless passed through fluid medium, and difficulty in raising the temperature of the gas sufficiently high for intraabdominal use without reducing the concentration of the ozone.

The source of the ozone was the same as that previously used in connection with the bacteria in

*From the Research Laboratory of the New York Skin and Cancer Hospital.

¹A Study of the Action of Oxygen, Peroxide of Hydrogen and Ozone Gas upon the Growth of Certain Bacteria.

vitro. The concentrations available were, 0.001 per cent. and 0.015 to 0.0185 per cent. by weight of ozone in ozonized oxygen (22°C.), and 0.005 to 0.012 per cent. by weight of ozone in ozonized air (22°C.). Though the gas was passed through a specially constructed box containing coils of glass tubing surrounding an electric stove, it was found difficult to raise the temperature of the gas to 33°C. for introduction within the peritoneum. In order to have the gas at 30° or 37°C. at the moment of its leaving the aluminum tubing which conducted it from the heating chamber to the abdomen, it was necessary to keep the temperature inside the box at from 42° to 45°C.; this meant reducing the concentration of the ozone from spontaneous change of a varying percentage back to oxygen.

With the exception of two cases, virulent strains of the microorganisms were used, and only those cases considered in a series in which the control animal died from the bacteria injected. The dose of an organism was varied and given, with exception of two instances, from one and one half to four hours before the use of the ozone. All operations were conducted under ether anesthesia. As strict asepsis as possible under existing conditions was observed. The abdomen was entered to one side of the median line by an incision from two to three inches in length, and the ozone introduced through a glass cannula. In some cases a second incision in the opposite groin was made for the escape of the gas, in other cases it was allowed to escape around the cannula. Silk was used for all sutures; the purse string suture used around the cannula included the peritoneum and a layer of fascia or fascia and muscle.

Normal animal.—The introduction of 0.001 per cent. ozone into the peritoneal cavity of a normal rabbit was accompanied by the following symptoms: Temporary bleaching at the site of introduction of the gas, followed by injection of the bloodvessels about the wound and on the perito-

neum, more especially those near the point of entrance of the gas into the abdomen. There immediately followed a slight increase in the rate of respirations and the heart beat, which continued during the operation and with diminishing rate for the subsequent four hours. A slight increase in the amount of anesthetic was at first required to maintain second degree anesthesia; to be remembered, however, was the high percentage of oxygen in the gas ozonized. No increase in the amount of peritoneal fluid was observed. With distention short of serious embarrassment of the respirations by pressure upon closing the abdomen, there was restlessness and uneasiness of the animal for four to six hours after the use of the ozone. Twenty-four hours after introduction of the gas, the animal's appearance and actions were quite normal; its abdominal girth was much reduced. No inhibition of peristalsis was noted. Upon investigation of the peritoneum forty-eight hours after the use of from fifteen to twenty milligrams of ozone no odor of ozone could be detected, and, aside from a possible slight hyperemia of some peritoneal vessels near the wound or point of introduction of the gas, the abdominal condition was macroscopically normal.

First series.—Ozone 0.001 per cent. was employed in a series of ten animals, four of which had received intraperitoneally a fatal dose of aurococci; five, colon bacilli; one, colon bacilli with aurococci. The results were: Sixty per cent. of the animals lived, forty per cent. died. The ozone was used within three hours of the introduction of the microorganisms in nine cases; in the tenth, twenty-four hours after the injection of the bacteria. On closing the abdomen moderate distention with the gas was employed in seven cases, firm distention in three cases. The maximum amount of ozone, 0.001 per cent. dilution, introduced at one time was 22.5 milligrams, the minimum in any given case, twelve milligrams.

Finch: Ozone Injections.

The amount of ozone used was in seven out of the ten cases probably sufficient to have killed these same bacteria in vitro, if in suspension in fluid medium, as one half a culture or less was the dose injected. Of these seven animals five lived and two died. The latter two had received virulent strains of the bacteria, the ozone had been used two and two and a half hours later, and the animals died four and five hours before the controls. As seen at autopsy no sterilization of the peritoneum had been effected, and good growths of the bacteria were obtained on culture from the heart blood. As regards the three cases in which the amount of ozone used could not have been sufficient to have killed all the bacteria, as two and three cultures were injected, two animals died and one lived. The one that lived had been injected with a less virulent organism, and received twelve milligrams of ozone twice twenty-four hours apart. Its control died in ninety-six hours.

Concerning the microorganisms used in the seven cases above referred to, results seemed to be dependent, not upon the type of the microorganism, but upon its virulence, whether the infection had extended beyond the peritoneum, and the circumstances under which pressure distention of the abdomen with the gas was resorted to on closing the peritoneal cavity. In no case did the animal survive the intraperitoneal use of ozone in which, 1, the infection had extended beyond the peritoneum, or in which, 2, the animal showed symptoms of more than slight toxemia before the use of ozone, or in which, 3, the sterilization of the peritoneal cavity was only partial and distention with the gas resorted to. Using distention of the abdomen in a severe infection seemed to hasten the death of the animal; but, using distention after sterilization (determined by operator) in a slow infection, no ill effects were noted to result from such distention when oxygen was the gas ozonized and the ozone concentration was not greater than 0.001 per cent. by weight.

In the animals that did not recover, death took place in from three to twenty hours after operation. Consciousness was regained very slowly after discontinuing the anesthetic, respirations and heart beat continued rapid, the animal later showing abdominal distress and great weakness. No inhibition of peristalsis was noted. On post mortem examination in the case of colon bacillus infection, a purulent peritonitis was present. In the case of aurococcus, there was either simply an intense injection of the peritoneal vessels, or congestion of these vessels with a slight amount of fibropurulent exudate. There was never any odor resembling ozone in the free gas in the peritoneal cavity at autopsy. The microorganisms were in all cases recovered from the heart blood, though death after operation might occur as soon as five or six hours from the time of inoculation with the bacteria.

Normal animal.—The introduction of ozonized air, the ozone 0.008 to 0.01 per cent. by weight into the abdomen of a normal rabbit was accompanied by the following symptoms: Dryness at the edges of the wound; transient bleaching followed by moderate congestion of the visible peritoneal vessels; respirations quickly increased from 120 to 180 and 200 a minute, with pauses at irregular intervals, of from one to three seconds' duration; heart action 120 to 140 or 160 a minute, the latter dependent upon increase in abdominal pressure. No increase in the amount of anesthetic was necessary to maintain second degree anesthesia. When not more than 140 to 190 milligrams of ozone of this dilution were used, with moderate distention of the abdomen upon closing the wound, the respirations fell within twenty-four hours of operation, also the pulse rate. Recovery of consciousness after discontinuing the anesthetic was slow, requiring from one to one and one half hour. Restlessness and some abdominal uneasiness marked the next twelve to twenty-four hours, with abdominal girth, rate of

respirations, and heart beat normal forty-eight hours after the use of this strength of ozone. The peripheral circulation showed poor aeration under prolonged use of ozonized air. If bled from the ear before the use of ozone, the serum separated clear from the clot. Following the introduction of 100 milligrams or more of ozone of this concentration, on the other hand, the blood obtained from the ear yielded a serum slightly tinged with hemoglobin which could not be centrifuged clear.

Second series.—Ozonized air, the proportion of ozone varying from 0.005 to 0.01 per cent. by weight was used intraabdominally on four rabbits that had received fatal doses of *Streptococcus brevis*. This organism was selected, as its growth was found to be readily influenced by ozone in vitro. The results were: Twenty-five per cent. lived, and seventy-five per cent. of the animals died. The control animals for the two different strains died, one fifty-four hours after inoculation and the other after sixteen days. With the first microorganism, the case that was operated in within one and one half hour of injection with the bacteria, lived. At that time the animal was not noticeably ill and from 170 to 175 milligrams of ozone were circulated among the intestines and passed through the small amount of fluid present. The prostration after operation was of shorter duration, and the return to the normal rate of respirations and heart beat was within a shorter period than in the case of the test animal and ozone. No hemolysis was noted in the peripheral circulation. In another rabbit which had received an injection with the same strain of streptococcus, same dose, but the time of operation was two hours after inoculation, the amount of ozone introduced was about fifty milligrams; a sufficient amount under certain conditions to have killed these bacteria in vitro. The animal died five and one half hours later. At autopsy a light growth of streptococcus was recovered from the perito-

neum and a luxuriant growth of this microorganism from the heart blood.

In a third case and the same strain of streptococcus, the animal was operated upon forty-eight hours after the inoculation, at which time the rabbit showed marked symptoms of general peritonitis and refused all food. About 170 milligrams of ozone were used; it was then discontinued, owing to the marked depressing action of the gas on the respirations and heart that followed its use. This animal died within eighteen hours of operation, and the peritoneum showed that no sterilization had been effected by the ozone, as there was a purulent peritonitis present from which streptococcus was the organism isolated. The streptococcus was also isolated from the heart blood. No hemolysis was noted in the peripheral circulation.

In the fourth case a much less virulent streptococcus was used and peritoneal flushing with the ozone gas, 250 milligrams, was undertaken two weeks after inoculation with the bacteria and two days before the death of the control animal from general pyemia. In this case again, the peritoneum, from which a light growth of the bacteria was obtained by culture at the time of operation, was not sterilized by the amount of ozone used, as was shown at autopsy when the animal died two days later of general pyemia, and a good growth of streptococcus was recovered from the peritoneum. Reinfection might have occurred, however, from one of several foci beneath the peritoneum that were present at the time of operation but not removed.

Normal animal.—With greater concentration of ozone 0.015 to 0.0185 per cent. by weight in ninety-five per cent. oxygen, results were fatal, a normal animal dying within eight hours of its intraabdominal use, though the number of milligrams was not greater than 190 and no distention of the abdomen with the gas was employed. Some difficulty was experienced in giving the anesthetic, respira-

tions becoming very rapid upon beginning the use of this strength of ozone in oxygen medium with frequent pauses of several seconds' duration, and the heart action was very rapid. Poor aeration of the peripheral circulation and the development of muscular tremors were noted during or within a half hour of the operation. The return to consciousness was very slow, two and one half to three hours; the respirations and the heart action continued very rapid, animal feebly restless, extremities cold, with the appearance before death of small hemorrhages or dark, blood tinged extravasations in the skin of the ears (rabbit). At autopsy, gas was noted but no odor of ozone, intestines distended, liver and spleen and peritoneal vessels intensely congested, two areas half inch in diameter acutely congested and edematous, one on the small and one on the large intestine near the wound, two drams of blood tinged peritoneal fluid, many small hemorrhages in the peritoneal coat, scattered hemorrhages in the skin (ecchymotic areas) and subcutaneous tissues, and, aside from intense congestion, small hemorrhages into the lungs and an emphysematous condition of the two lower lobes.

SUMMARY.

Ozone, 0.001 per cent. in oxygen dilution, can be introduced with impunity as a continuous current into the abdomen of a normal rabbit until from twenty to twenty-two milligrams have been passed through the peritoneal cavity. Distention short of pressure embarrassment of the respirations can be used, and the symptoms produced differ from those produced by ninety-five per cent. oxygen only in the following way: the time required for recovery from the anesthetic may be prolonged instead of shortened as when using plain oxygen; the pulse and respirations continue rapid over a longer period, and the animal may show some abdominal uneasiness. The first effect of introducing this con-

centration of ozone is to cause an increase in the amount of anesthetic necessary; but after use for five minutes or longer this effect is no longer observed.

The introduction of ozonized air, the ozone representing ten times the foregoing concentration, i. e., 0.008 to 0.01 per cent. by weight, into the peritoneal cavity, causes very rapid respirations; and if the pressure is increased as by the use of distention, respirations become so rapid that respiratory pauses of one to four seconds punctuate them. The heart action likewise becomes very rapid, but shows no arrhythmia unless the respirations are embarrassed. There is no increase in the amount of anesthetic required while using this gas, and a stupor or semiconscious state exists for one hour or longer after discontinuing the anesthetic when 100 milligrams or more of the ozone have been used. Aside from this action on respirations and heart, there occurs a slight grade of hemolysis in the general circulation following the use of this number of milligrams or more of the gas. This is noticed in the serum of blood drawn from the ear of a normal animal after use of the gas, and, while only of a slight grade, still awaits accurate explanation.

With still higher concentrations of ozone, as the use of 0.015 per cent., oxygen dilution, the introduction of but 190 to 200 milligrams without ballooning the abdomen, causes death of a normal animal within six to eight hours of its use with symptoms as described above.

The use of ozone gas within the peritoneal cavity of animals following general peritoneal infection, may be without harm to the animal if the concentration is very weak, not greater than 0.001 per cent. by weight and in oxygen dilution. Under the following conditions the animals survive the use of a continuous current of 0.001 per cent. ozone: Use within three hours of a general peritoneal infection, limitation of the infection to the peritoneum,

Finch: Ozone Injections.

a low grade of toxemia, use of a continuous current of the gas, and, according to the judgment of the operator, the use of a greater number of milligrams of ozone than would actually be required to kill the bacteria if brought into intimate contact with them, finally, the use of but very moderate, or no distention upon closing the abdomen.

The use of the following concentrations, 0.005 to 0.012 per cent. by weight, when introduced into the peritoneal cavity of normal animals, produces symptoms other than those due to the physiological action of oxygen, and in connection with general peritoneal infection, unless the amount of ozone used and the bacteria are nicely balanced and under the conditions above mentioned, its use insures a rapid and fatal termination.

NEW YORK SKIN AND CANCER HOSPITAL.