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Evaluation of the effectiveness of cortisone and oxytetracycline alone and in combination in experimental peritonitis in rabbits

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AN EVALUATION OF THE EFFECTIVENESS OF CORTISONE AND OXYTETRACYCLINE ALONE AND IN COMBINATION IN EXPERIMENTAL PERITONITIS IN RABBITS

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AN EVALUATION OF THE EFFECTIVENESS OF CORTISONE AND OXYTETRACYCLINE[1] ALONE AND IN COMBINATION IN EXPERIMENTAL PERITONITIS IN RABBITS[2]

I have evaluated the effect of cortisone in the treatment of experimental peritonitis in rabbits. Our interest was aroused by the differences of opinion as to the value of the administration of cortisone in patients with se ere fulminating infections. Jahn and his collaborators (1) have used cortisone in combination with antibiotics in patients toxic from severe peritonitis. They obtained satisfactory results. Others (2-7) have presented experimental evidence that cortisone is of no value in cases of infection and may even have a deleterious effect. The deleterious effect may be based on two mechanisms: 1) by causing a dissemination of infections throug its anti-inflammatory effect, and 2) by reducing the e fectiveness of antibiotics (8).

An operation designed to produce severe peritonitis of intestinal origin was performed in forty rabbits. These animals wer divided into four equal groups. Group I was treated with oxytetracycline and cortisone; Group II with terramycin; Group III with cortisone; and Group IV was untreated and served as the control. The results suggest th t the addition of cortisone to oxytetracycline in treatment of peritonitis is of little value, if any.

METHODS AND MATERIALS

Rabbits of either sex weighing from five to eight pounds were used. No food was given twelve to twenty-four hours preceding the operation, but water was allowed. Sodium Nembutal in a dose of 20 mg. per kg. of body weight was given intravenously for anesthesia. Using aseptic technique, the abdomen was opened through a midline incision. The appendix was identified, crushed at the base, and ligated with a silk suture approximately 9 cm. from the tip. The vessels to the appendix were ligated. The appendix was then opened through a longitudinal incision from the site of ligation to the tip. Cultures were made from the appendiceal contents. The distal end of the appendix was grasped with an Allis forceps and it was wiped through the peritoneal cavity from the right upper quadrant to the left lower quadrant to the right lower quadrant. The wound was closed in layers with silk sutures. The animals were allowed access to food and water immediately after the operation.

The treatment was started immediately after operation. Oxytetracycline was given as used in Groups I and II intramuscularly in a dosage of 12 mg. per kg. of body weight every eight hours for five days. Cortone acetate as used in Groups I and III was given intramuscularly in an average daily dosage of 4.2 mg. per

kg. of body weight. The dosage was reduced from 8 mg. per kg. the first day to 1 mg. per kg. by the fifth day, after which it was discontinued, as shown in Table I. These sages were chosen because they were comparable to the therapeutic doses of these drugs in man. Animals dying within the first twenty-four hours after the operation were excluded from the experiment. Such deaths were assumed to result from improper anesthesia, hemorrhag , embolism, or other complications. The duration of the experiment was two weeks. Animals surviving for the two-week periods were sacrificed and autopsied. At the time of autopsy cultures were made of the peritoneal fluid and abscesses.

The findings were correlated with qualitative bacteriological studies, gross autopsy findings, and microscopic examinations of the sections of the viscera.

RESULTS

Mortality

Of the rabbits in Group I, which were treated with a combination of cortisone and oxytetracycline, nine were alive at the end of the two-week period (forty-two eight-hour terms) of the experiment. One animal died after six and a ha (twenty 8-hour terms) days. The survival rate was ninety per cent.

Animals in Group II which were treated with oxytetracycline alone survived the two-week period of the experiment. The survival rate was one hundred per cent.

Of the animals in Group III, the cortisone-treated group, five rabbits survived the two-week period of the experiment and five died in a period ranging from one and a half to six days. The survival rate of this group was fifty per cent.

Four of the animals in Group IV, which were untreated, survived through the experiment and six died in a period ranging from one and a half days to eleven days. The survival rate of this group was forty per cent (Fig. 1).

Gross Autopsy Findings

Group I - Oxytetracycline- and Cortisone-treated group.-- The animals which survived in this group at the time of autopsy generally showed a small, well demarcated abscess localized at the site of the previously ligated and devascularized appendix. The loops of the small and large intestine were adherent to this abscess. The adhesions were limited to the site of the abscess and were small in amount. The loops of intestine could easily be detached from the abscess. There was no gross evidence of generalized inflammation. The viscera otherwise were grossly normal in appearance.

The only animal which died in this group showed no evidence of a localized abscess. The devascularized and

ligated appendix showed signs of necrosis. The peritoneal cavity contained approximately 20 cc. of serous and rather malodorous exudates. No adhesions were found between the loops of intestine. The lungs were edematous.

Group II - Oxytetracycline-treated group.--All the animals showed a well-walled-off abscess at the site of the previously ligated and devascularized appendix. The abscess was thought to be of the same size or slightly larger than that in Group I. The loops of the small and large intestine were adherent to this abscess. Adhesions were limited to the site of the abscess. The amount of adhesion was greater than that seen in Group I. The other viscera were grossly normal in appearance.

Group III - Cortisone-treated group.--The animals which lived in this group had the common findings of a very large abscess at the site of the ligated and devascularized appendix. In addition there were multiple small abscesses scattered over the abdominal viscera and abdominal wall. Loops of intestine were adherent to the large abscess The adhesions were relatively large in quantity but limited to the site of the abscess. There was no gross abnormality in the other viscera.

The rabbits which died showed evidence of generalized infection and inflammation. There were moderate

to large quantit es of serosanguinous exudates. The loops of the int stine were moderately adherent to each other. No struc ure as appendix per se could be recognized. Multiple small abscesses, scattered throughout the abdominal vi cera, were found in some of these animals. Lungs ere generally edematous and hyperemic.

Group IV - The untreated group.--The gross autopsy findings in the animals which lived were essentially similar to those found in Group III with the exception of the absence of the multiple abscesses (except one animal) and large amount of adhesions.

The animals which died showed a much larger degree of inflammation and necrosis than Group III. Adhesions were greater in uantity and were binding the loops of the intestine together. Multiple abscesses were, however, absent. Serosanguinous to purulent exudates were found in the peritoneal cavity of most of the animals. The lungs were edematous, firm in consistency, and hyperemic.

Histological Findings

Group I - Oxytetracycline- and Cortisone-treated group.--The general histo ogical pattern of the peritoneum in these animals was that of a healing chronic infection with granulation reaction. The evidence of an acute infection was lacking. Fibrosis was minimal in extent. The sections of the intestine at the site of the ligation

of the appendix showed evidence of slight focal necrosis, granulation reac ion, and chronic inflammation. Serosa was generally no rmal in appearance. No evidence of acute infection was de ected. The sections of the lungs, liver, adrenals, myocardium, kidneys, and portal vein were essentially normal.

Group II - Oxytetracycline-treated group.--The findings in this group wer ess ntially the same as those in Group I. The inflammatory response was, however, greater in extent. The serosa of the sections of the intestine often showed fibrinopurulent exudates.

Group III - The Cortisone-treated group.--The histological pattern of this group was greatly different from that of Groups I and I. Peritoneum and mesentery showed evidences of fi rinopurulent peritonitis. Moderate to large degrees of inflammatory exudates were found on the peritoneal surfaces. The liver in general showed congestion, cloudy swelling, and central zone necrosis. In some of the animals rod-shaped organisms were found in the hepatic venous c annels and sinusoids. The sections of the lungs showed moderate to large degrees of edema, congest on, interstitial hemorrhage, and atelectasis; in some of the animals bronchopneumonia was found in varipus degrees. The sections of the intestine at the ite of the ligated ap endix presented the picture of fi rinop rulent peritonitis. The adrenals,

kidneys, heart, and portal vein were essentially normal.

Group IV - The untreated group.--The microscopic findings were similar to those found in Group III. The inflammatory process was, however, greater in extent. The lungs in some of the animals showed focal bacterial colonies.

Bacteriologic Findings

The type of bacterial organisms found at the time of the operation in the intestinal contents of the animals and the organisms found in the abscesses or peritoneal fluid of the animals at the time of autopsy are given in Table II. Table III was derived from Table II to indicate: 1) the type of the organisms found in the animals which did not survive the two-week period of the experiment; 2) the possible relationship of any one organism to the cause of death; 3) the possible relationship of a symbiotic group to the cause of death.

The organisms most commonly encountered in the animals which died were Escherichia coli, Clostridium species, and Bacterioides species. In general gram-negative rods were the most commonly found organisms. The cortisone-treated group showed the largest number of organisms. Staphylococci and streptococci were also more frequently seen in this group than in any other group. The oxytetracycline-treated group showed the least number of organisms.

The results btained from the bacteriologic data did not seem to be su ficient to lead to any significant conclusions. It could not be determined whether any specific type of acterial organism, or a combination of the most commonly en ountered organis s, were responsible for the virulence of the isease or the effect on the survival rate of the animals. These findings were in agree ent with those of Kay and Lockwood (9) and Zintel et al (10).

DISCUSSION

That ACTH an cortisone play a role in the process of infection and inflammation has been known for a long time. These hormones have been used in a variety of infections both a one a d with antibiotics. The results have been variable.

Kass and his colla orators (11) treated patients with pneumococcal pneumonia and atypical pneumonia with ACTH. They noticed marked symptomatic relief. The bacteremia, however, persisted during the treatment in patients with pneumococcal pneumonia and the patients with atypical pneumonia showed return of the fever after ACTH was withdrawn. Glaser and Loeb (12) treated experimentally produce streptococcal pneumonia in rats with penicillin and c rtisone. They reached the conclusion that the a dition of cortisone was of some value in

limiting the inflammation and reducing concomitant toxic manifestations of e severe infection. Vollmer (13) produced peritonitis in mice using large doses of type I pneumococci; and then treated them with antibacterials and ACE. The hormone seemed to prolong the life of the animals. He concluded that the animals had suffered a relative insufficiency of the substances which were partially relieved by the administration of ACE. Smadel and co-workers (14), Woodward and associates (15), and Wisseman (16) demonstrated that addition of cortisone to chloramphenicol in the treatment of typhoid fever caused more prompt relief of toxic clinical manifestations. There was rapid defervescence and marked feeling of well being. Headache, malaise, and confusion were eliminated. Almost identical results have been obtained in the treatment of rickettsial diseases (17). Some authors (18) have demonstrated that addition of ACTH or cortisone to a sufficient dose of chemotherapeutic agents in cases of experimental tuberculosis may enhance the effectiveness of chemotherapeutic agents and decrease the morbidity and mortality. In this respect the work of Jahn et al (1), (19), and Kinsell and associates (20) has been of interest. They have, through clinical trials, demonstrated that in cases of overwhelming infection, particularly peritonitis, the addition of cortisone or ACTH to antibiotics may be of great value. Beneficial

effects of comb ned ACTH or cortisone and antibiotics have been observed in tuberculous peritonitis (21), tuberculous meni tis (22), pneumococcic meningitis, meningococcemia (19), severe pneumonia, diphtheria, tetanus, and po iomyelitis (20).

In contrast, however, many of the experimental observations have pointed in a different direction. Mogabgab and Tho nas (2), using cortisone in rabbits infected with roup A nemolytic streptococci, noticed marked dissemina ion o' the infection, multiple systemic involvement, and incre sed mortality rate. Others (23) reported increas d susceptibility of rabbit to pneumococcal infection and t ndency for the development of fulminating bact remia. Many investigators believed that administrat on of cortisone with chemotherapeutic agents in pulmonary tuberculosis would cause a lysis of the fibrous and ranulation tissue and hence make the hidden organisms more accessible to the antituberculous chemotherapeutic agents. Spain et al (4), however, believe that cortisone has no effect on the granulation tissue already formed, and has no fibrolytic action. Actually by produ ing t berculosis in guinea pigs they demonstrated that anima s reated with cortisone and streptomycin show d les localization of lesion than those treated with stre tomycin alone. This observation has been confirmed ani amplified by other investigators (6),

(24), (25), (5), (3). Jawetz (8) tested the effect of cortisone on the efficacy of antibiotics. In his experiments he inf cted mice with Klebsiella pneumonia and/or Streptoco cus pyogenes. He reached the conclusion that the efficacy of antibiotics was decreased when cortisone was simultaneously administered. He stated that this depressing effect of cortisone on antibiotics may not be seen in ordinary clinical cases due to the fact that clinically the antimicrobial agents are used greatly in excess of the necessary curative dose. The depressing effect would be best manifested when one is dealing with res stant organisms.

Perplexed by this variety of opinions as to the usefulness of cor isone as an adjunct to antimicrobial therapy, the question presents itself: What are the mechanisms of the action of ACTH and cortisone and their effects?

1. Cortisone has no bacteriostatic or bacteriocidal effect.--Studies vitro of the effect of cortisone on the growth of Salmonella typhosa has shown no bacteriocidal or bacteriostatic action (15). Jahn and associates (19) believe that ACTH and cortisone have no inhibitory effect on the growth of the infectious agent. Germuth et al (23) have experimentally shown that pneumococcal organisms locally injected to cortisone-treated rabbits exhibited an incr ased tendency to survive and proliferate.

They also noticed that one of the characteristics of cortisone-treated animals was a tendency to develop bacteremia. This bacteremia was due to increased bacterial growth and not the result of interference with the blood clearing mechanism of the host. Some workers, however, believe that bacteremia is not due to increase in the growth rat of b cteria and is rather due to inhibitory effect o' cort sone on macrophages and hence on phagocytosis. The work of Cra be (26) is of interest. He has experimentally shown that the degree of the inhibition of phago osis is not directly related to the amount of cortisone.

2. Cortisone and ACTH do not interfere with the specific antibody formatio .--The time of the appearance of antibodies and their iter appeared to be the same in patients with pneumococcal pneumonia who received ACTH and those who did not (27). Mirick (28) has shown that following vaccination of human subject with a mixture of pneumococcal polysaccharide, dministration of cortisone and ACTH fails to sup ress the antibody formation. Germuth et al (23) testin the influence of cortisone on the development of immunity reached the conclusion that treatment during infect on does not interfere with the subsequent development of acquired immunity. There are, on the other hand, some authors who believe that cortisone

and ACTH inhibit anti dy formation (29), (30). It seems to be the eneral opinion, however, that the effect of cortiscne or ACTH on the formation of antibodies, if any, s negligible. These hormones, however, are capable of reducing the amount of antibodies already present in the blood.

3. Cortisone and ACTH do not counteract the bacterial and viral toxins.--It is generally agreed that cortisone and ACTH in ordinary therapeutic doses do not counteract or neutralize bacterial and viral toxins. Kass and his co-workers (31) using s spensions of rickettsiae or influenza viruses in rats or mice were not able to demonstrate an antitox c protective effect of ACTH. Thomas and Good (32) and Thomas and Mogabgab (33) used bacterial toxins in cortisone-tre ted ra bits and untreated rabbits. They reached the conclusion that cortisone did not counteract the toxins and the Shwartzman reaction occurred in either group in the same proportion. Smadel and his associates (14) al so think that the beneficial effect of cortisone in cc bina ion with chloramphenicol in treatment of typhoid fever is not due to the counteraction of the lib rated bacterial toxins.

4. Cortisone and ACTH have marked anti-inflammatory effect.--The anti-inflammatory effect of cortisone and ACTH is an accepted fac . The exact mechanism of the action is not, however, known. The therapeutic use of

these substances in rheumatoid arthritis, as well as many other diseases, has shown a reduction of edema, necrosis, deposition of fibrin, and inflammatory exudates. This very anti-inflammatory action of cortisone and ACTH is the main basis of the difference of opinion as to the use of ACTH and cortisone with antibiotics in the treatment of the infectious diseases. It is quite probable that inflammation represents an effective mechanism for resistance a ainst infection in tissues and for the limitation of the infection. If so, cortisone and ACTH, by decreasing the inflammatory reaction, would tend to enhance t e infection and prevent its localization. On he ot er hand, those who advocate the use of cortisone or ACTH with antibiotics (1) in certain infectious diseases believe that the extensive and uncontrolled inflammation can cause the destruction of the important and vital organs. Such diseases are iritis, mumps orchitis, meningitis, and peritonitis. Hence, by using cbrtisone or ACTH the inflammation would be checked and de ressed and the addition of antibiotics would prevent the dissemination of the infection.

5. The benefici effect of cortisone or ACTH may be due to the action on the host cell rather than the offending organism.--The work of Selye (34) on adaptation and stress indicates th t the adrenal cortical hormones play an important part in modifying the alarm mechanism

of the host in various conditions. Through the help of these hormones, the host may survive severe and deleterious situations which would otherwise lead to destruction and death. Smadel (14) and Woodward (15) using cortisone in cases of typhoid fever believe that the beneficial effect of cortisone as an adjunct to chloramphenicol results from its action on the patient as a whole. It causes defervescence, decreases the malaise, and gives the host a lift to overcome the infection.

6. The effect of cortisone and ACTH on reticuloendothelial system.--The reticuloendothelial system is considered a major daily defense mechanism. This system seems to play a great role in removal of the bacteria from blood (35). Cortisone is believed by some to interfere with the functioning of this system, reducing its capacity for removal of the bacteria and bacterial products. Uncontrolled infection may result. Furthermore, other tissues which ordinarily are not concerned with the function of the reticuloendothelial system may try to take over these functions, and this would lead to their destruction (36).

In the present experiment I have produced peritonitis of intestinal origin in rabbits. The method used has been simple and effective. The aim has been the evaluation of the effectiveness of cortisone and oxytetracycline alone and in combination in this disease. The exact

mechanism or mec nisms of death and morbidity in cases of peritonitis is not known. The growth of bacteria in the peritoneal cavity and liberation of toxins may be an important fac r. Absorption of bacteria from peritoneal surfaces and subsequent bacteremia may also play an important part. Kay and Lockwood (37) believe that peritonitis is a l calized disease with marked systemic manifestations which cause death by producing shock.

The type of rganisms responsible for adverse effects of peritonitis is also subject to controversy. However, Escheric ia coli, Clostridium welchii, streptococci and staphylococci seem to be the main offenders responsible for mc rbidi y and mortality.

The use of a timicrobials has markedly reduced the mortality of peri oniti and today these agents are considered essential in the therapy of patients with peritonitis. Domagk as the first to demonstrate the value of sulfonamides i the reatment of peritonitis in mice. Prontosil was use in mixed type of peritonitis by Bower (38). Later the effect of penicillin in cases of peritonitis of appendiceal origin was tested and reported by Crile (39). The ffect of streptomycin was reported by Murphy and his as ociates in the treatment of experimental peritoniti in dogs. Favorable results were obtained by using streptomycin. It was found to be particularly effe tive in cases of spreading peritonitis

and localized peritonitis without a palpable mass. Zintel and collaborators (10) tested the efficacy of penicillin therapy alone and in combination with streptomycin and sulfonamide in experimental peritonitis in dogs. They reached the conclusion that penicillin therapy alone was as effective as a combination of penicillin and streptomycin or combination of penicillin, streptomycin and sulfonamides. Streptomycin alone was not as effective as penicillin or a combination of penicillin and streptomycin Several other antibiotics such as bacitracin, aureomycin, chloromycetin, and terramycin have been used in peritonitis; all being more or less effective. Several investigators have tested and compared the relationship of the route of the administration of antibiotics to their efficacy. Intraperitoneal administration was found to be very effective in destroying the organisms and sterilizing the peritoneal cavity. This method of administration, however, had its own disadvantages. Streptomycin caused death due to streptomycin intoxication and aureomycin caused chemical peritonitis. Schlotten and Abbott (40) have tested the intraperitoneal use of terramycin in experimental peritonitis and have obtained very good results.

Recently the addition of cortisone or ACTH to antimicrobials has been advocated in the treatment of severe peritonitis. The basis for such a treatment is the

assumption that these hormones increase the resistance of the host to infection and reduce the toxic manifestations of the disease. Furthermore, the reduction and the control of the inflammatory process allows adequate and ear surgery. Such beneficial effects would tend to reduce the morbidity and mortality of peritonitis.

The results presented in this paper do not give support to the above assumptions. The animals receiving a combination of oxytetracycline and cortisone showed a higher mortality rate than those which received oxytetracycline alone. In general the bacteriological and histological findings were similar in the animals receiving oxytetrac cline either alone or in combination with cortisone. In comparison with these two groups, the cortisone-trea ed group (Group III) and the untreated group (Group IV) showed a much higher mortality rate. The gross autopsy and histological findings in contrast to Groups I and II were that of an acute fibrinopurulent peritonitis with large a scesses and in many cases multiple abscesses throughout the peritoneal cavity.

Summary

1. Experimental peritonitis was produced in forty rabbits. The appendix was ligated at the base, devascularized, and opened through a longitudinal incision. The

peritoneum was contaminated by appendiceal contents and the abdomen was closed.

2. The animals were divided into four equal groups. Group I was treated with oxytetracycline and cortisone, Group II was treated with oxytetracycline alone, Group I I was treated with cortisone, and Group IV was left un reated as control. The duration of the experiment was two weeks. The animals dying within the fir t twenty-four hours were excluded from the expe ment.

3. Oxytetracycline was ven intramuscularly in a dose of 12 mg. per kg. of body weight every eight hours for five days. Cortone acetate was given intramuscularly for the same period of time in a dose of 4 to 4.2 mg. per kg. of body weight per day.

4. The survival rate of Group I was 90 per cent, that of Group II was 100 per cent, Group III 50 per cent, and Group IV 40 per cent (Fig. 1).

5. Groups I and I showed a well localized abscess and evidence of chronic healing infection. Groups III and IV showed ocalized abscesses, multiple abscesses, and evidence o widespread fibrinopurulent peritonitis. The amount of adhesions seem to be less in groups receiving cort sone.

6. Bacteriologica studies were not conclusive. The oxytetracycl e-treated group had the least number

of bacterial types and the cortisone-treated had the largest number. The type of organisms most commonly encountered in animals which died during the experiment were Escherichia coli, Clostridium species, and Bacterioides species.

7. The addition of cortisone to oxytetracycline in treatment of experimental peritonitis in rabbit is of no va e and has no deleterious effect.

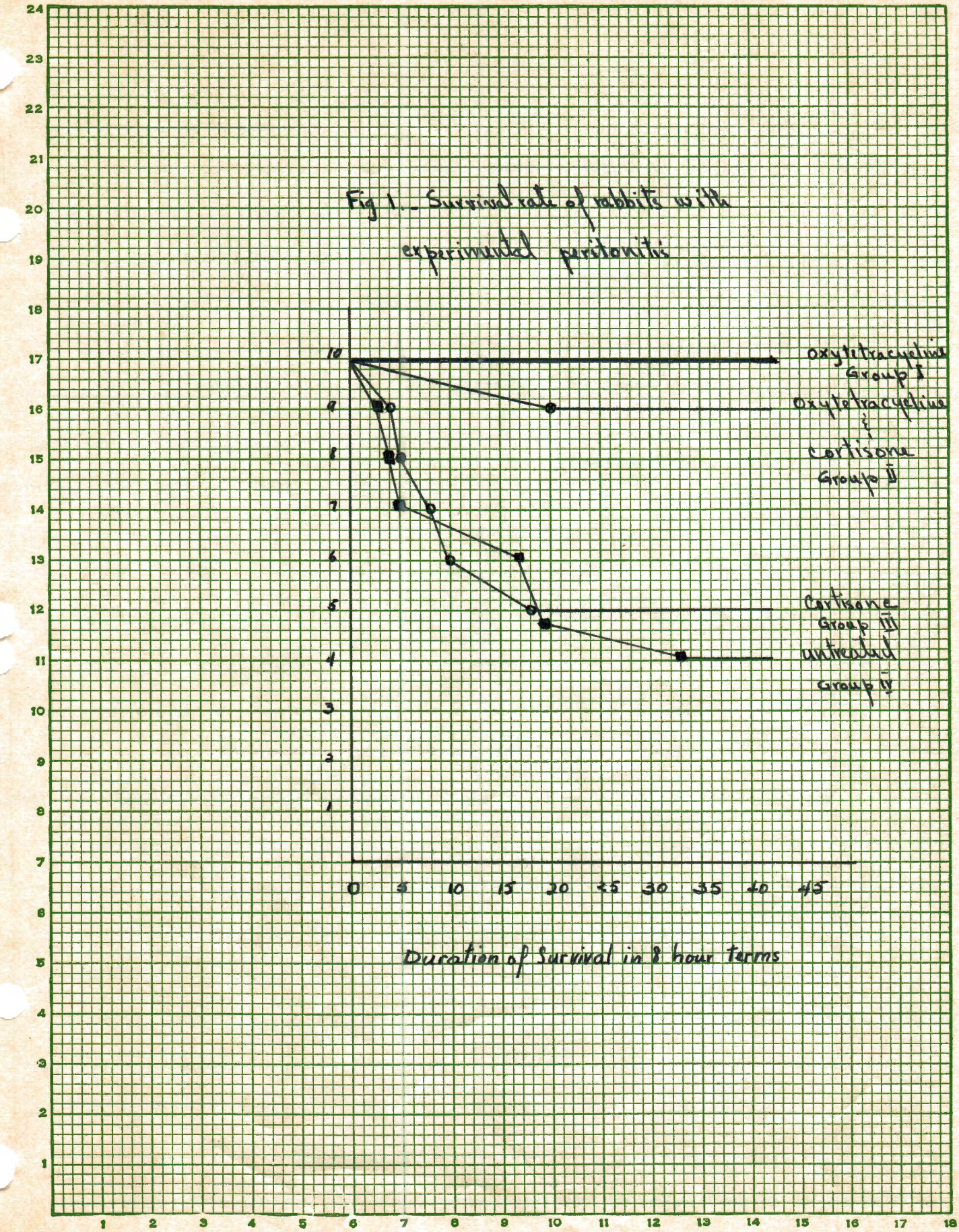
Fig 1.- Survival rate of rabbits with experimental peritonitis
Oxytetracycline Group I
Oxytetracycline & Cortisone Group II
Cortisone Group III
Untreated Group IV
0 5 10 15 20 25 30 35 40 45
Duration of Survival in 8 hour terms

Table I.--Dosage Schedule for Cortisone

Days	Dose per day
First	8 mg. per kg. body weight
Second	6 mg. per kg. body weight
Third	4 mg. per kg. body weight
Fourth	2 mg. per kg. body weight
Fifth	1 mg. per kg. body weight

Total: 21 mg. per kg. of body weight in five-day period.

Average: 4.2 mg. per kg. of body weight.

Table II.--Bacterio ogic Studies of the Organisms Found at the Time of Operation and the Time of Autopsy

Organisms	At Operation	Oxytetracycline & Cortisone		Oxytetra-cycline		Cortisone		Untreated	
		Died	Survived	Died	Surv.	Died	Surv.	Died	Surv.
STAPHYLOCOCCI									
Hemolytic micrococcus pyo enes var. aureus	1	.	.	.	.	1	.	.	.
Nonhemolytic micro-coccus pyog es var. aureus	6	.	.	.	1	2	.	.	.
Nonhemolytic micro-coccus pyogenes var. albus	1	.	1	.	2	.	.	.	.
Sarcina lutea	1	.	.	.	.	.	.	.	.
STR TOCOCCI									
Alpha hemolytic streptococci	2	.	1	.	.	.	.	1	1
Beta hemolytic streptococci	0	.	1	.	.	.	.	.	.
Nonhemolytic streptococci	6	.	.	.	.	3	.	.	.
Anaerobic streptococci	3	.	.	.	.	.	.	.	.
AM-NEG TIV RODS									
Escherichia coli	16	.	3	.	4	3	4	4	3
Pse domonas aeruginosa	1	.	.	.	.	1	.	.	.
Aerobacter aerogenes	2	.	1	.	.	1	.	.	.
Paracolobacterium species	3	.	.	.	.	1	.	1	.
Alkaligenes species	2	.	.	.	.	.	.	.	.
Esc erichia freundii	1	.	.	.	.	.	.	.	.
Aerobacter cloacae	1	.	.	.	.	.	.	.	.
Anaerogenic paracolon bacillus	0	1	.	.	.	1	.	.	.
ANA BES									
Veillonella species	0	.	2	.	.	.	1	1	.
Clostri ium species	3	1	1	.	1	2	.	2	.
Fusobacterium species	2	.	.	.	.	.	.	.	.
Bacterioides species	8	.	1	.	2	.	1	1	.
OTHERS									
Bacillus species	29	.		.	5	3	1	5	.
Dipht eroid	3	.	.	.	.	.	.	.	.

Table .--Bacterio Studies on the Animals Which Did o Surv ve t ek Period of the eriment

	Cortisone- reated Grdup					Untreated						Oxytetracycline & Cortisone-treated Group
Animal Number:	21	24	25	26	27	31	32	34	35	36	38	1
STAPHYLOCOCCI:												
Hemolytic M. pyogenes var. aureus	.	.	*	.		.	.		.	.	.	.
Nonhemolytic pyogenes var. aureus	*	.	*			.			.			.
STREPTOC CCI:												
Alpha hemolytic streptococci	.	*	.	.	.	.	.		.	.	*	
Nonhemolytic streptococci	.	.	*	*	.	.	.	.	.	.	.	
GRAM-NEGATIVE RODS:												
Escherichia coli	.	*	*	.	*	*	*	*	*	*	.	
Pseudomonas aeruginosa	.	*	.	.	.	.	.	.		.	.	.
Aerobacter aerogenes	*	.				.	.	.	.	.		
Paracolobacterium species	.	.	.	*			*	.	.	.	.	
Anaerogenic paracolon bacillus	*	.				.	.		.	.	.	.
ANAEROBES:												
Veillonella species		.					.		*	.		.
Clostridium species	.		.	*	*	.		.	*	*	.	*
Bacterioides species	.	.	.	.	.	.		.		.	*	.
OTHERS:												
Bacillus species	*		*	*	.		*	*		*	*	*	.

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Footnotes

1. The trade name of Chas. Pfizer and Co., Inc., for oxytetracyc ine is Terramycin.
2. Supported part by Chas. Pfizer and Co., Inc., Brooklyn 6, New Ycrk.

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