THESIS ON

"P E R I T O N I T I S"

"SOME EXPERIMENTAL AND CLINICAL OBSERVATIONS

on

ITS PATHOLOGY, PROPHYLAXIS AND TREATMENT."

PRESENTED for the DEGREE of CH. M.

by

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C O N T E N T S .

C O N T E N T S (Contd.)

PREFACE

The impression conveyed to one from a rapid survey of the vast literature on the subject of Peritonitis is that this literature may be divided into two clearly defined and widely differing parts.

The one part dealing with the experimental side of the subject, is chiefly concerned with physiological and pathological questions, and to a less degree with prophylactic measures for peritonitis; this part is highly scientific in its methods and design.

The other part deals with the methods and the results of the surgical treatment of Peritonitis practised in various hospitals and this section bears for the most part singularly little relation to the former one.

This separation and lack of co-operation between the experimental and the clinical workers on the subject has, one feels sure, retarded the progress of our treatment of Peritonitis.

The work recorded in this thesis is an attempt to harmonise and to combine the methods of experimental/

experimental research with those of clinical and practical therapeutics. Whilst this thesis treats essentially of the use of certain prophylactic and therapeutic measures for peritoneal infections, facts of a more purely pathological and bacteriological nature which were brought out during the research are ,however ,also recorded and discussed.

The experimental part of this work was carried out between March 1908 and April 1909 in the laboratory of the Royal College of Physicians of Edinburgh. To Dr. James Ritchie, Director of the laboratory, I would here acknowledge my indebtedness for many suggestions and much valuable advice. The clinical matter in this thesis is drawn entirely from cases under the care of Professor Caird in the Royal Infirmary, and to him I am indebted both for the opportunity of applying clinically the methods which I had found experimentally to be of value, and for the permission to record in this thesis, notes on the cases so treated.

The expense of the experimental part of the work was partly defrayed by a grant from the Carnegie Trust.

INTRODUCTION/

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Among all the advances of modern surgery, there are none so striking as the evolution of surgical methods and the attainment of surgical possibilities within the abdomen.

By the perfecting of operative technique the mortality after operations on the alimentary tract has been reduced to a comparatively low figure. Through an ever increasing knowledge of the limits of helpful surgical interference in acute infections of the peritoneal cavity, through a more definite understanding of the "danger zones" in infections of that cavity, through evolving more perfect methods of drainage by the aid of post operative posturing, and through realising the benefits of saline infusion in lessening the toxaemia in such infections, our treatment of acute peritonitis, whatsoever its cause, has been crowned with ever increasing success.

On the other hand, the death rate after intestinal resections is still over 20%, and more than two thirds of those deaths are from peritonitis, more especially is this the case after operations

on/

on the large intestine. Also we realise that if post operative peritonitis do occur it is generally fatal.

De Bovis collected statistics of results of resections of intestine for neoplasm, and found that in many hundred cases, from all sources, the death rate was 38%. More than one half of this mortality was from Peritonitis.

Also in regard to the results of the treatment of acute peritoneal infections the death rate still remains at about 15%, and of this mortality otherwise healthy young adults form the major part.

The first question with which this thesis has to deal is :- Can anything apart from operative technique be done to prevent fatal peritonitis occurring after intestinal resections, or to assist the protective forces of the patient, should peritoneal infection take place?

The second question with which we have to deal is:- Can anything over and above the methods at present in general use in the treatment of acute peritoneal infections, be done to still further lower the mortality in this class of case?

Before bringing forward the results of my experimental/

experimental work relative to these two questions, several points require consideration.

PERITONITIS IN LABORATORY ANIMALS AND IN MAN ARE THEY COMPARABLE?

Before considering the results of experiments on animals, one must carefully observe the characters of Peritonitis in the animals used, to see in how far peritonitis in them resembles that in the human subject, and whether one is justified in drawing any conclusions from the work done on those animals.

The animals which have been generally employed in this branch of research are the Rabbit and the Guinea pig.

From the literature on this subject one finds that almost invariably Bacillus Coli Communis has been the organism used in inducing peritonitis, partly I suppose because the rabbit and guinea pig are readily susceptible to it, and partly because it is the organism most frequently found in peritonitis in man. Without exception the experimenters confess that whatever value their results may have, the/

the peritonitis they have produced in animals, has never shown the purulent plastic features so characteristic of the peritoneal infection's of man.

Now what are the pathological findings in a rabbit which has succumbed to a Bacillus Coli peritonitis? One finds on opening the abdomen some turbid serous fluid: there is no pus, seldom any lymph, but great congestion of the peritoneum. There is cloudy swelling of the organs and on cultures from the heart blood, one obtains a vigorous growth of B.Coli. The animal has died from a Bacillus Coli septicaemia. The same holds good for the guinea pig. Now it is the exception for the human subject suffering from peritonitis to die of a septicaemia.

Bertelsmann made cultures from the blood during life in fourteen fatal cases of Peritonitis and in no case did any organism grow on his media.

So far I have made cultures from the blood of sixteen patients suffering from acute peritoneal infection. In twelve of these cases the infection was localised to the lower part of the abdomen, in four it was generalised throughout the whole peritoneal cavity. Five of these cases ended fatally/

fatally. All were operated on for the condition and the blood for cultures was withdrawn from the median basilic vein during operation. The bacteriology of the peritoneal infection in these cases was as follows.

Bac. Coli Communis	(pure)	7 cases.
" " " +	Streptococcus	3 "
" " " +	B. Pyocyaneus	2 "
" " " +	Staph. Aureus	1 case
Streptococcus	(pure)	2 cases.
No growth		1 case
		16

In the fatal cases cultures from the blood were taken on two or three occasions between the time of operation and death, and in two of them when the patieht was moribund. In 15 out of the 16 cases, no growth took place in the culture media. In one case (a fatal case of general peritonitis due to B.Coli+ Staphylococcus Aureus) a growth of Staphylococcus Aureus took place in the media on one occasion, but on making fresh cultures from the blood of this case two days later and just shortly before death no growth occurred.

In/

In two of the fatal cases, cultures made from the heart blood post mortem gave very vigorous growths of B.Coli and of B.Coli and B. Pyocyaneous. respectively, although cultures from the blood of both cases shortly before death remained sterile.

One concluded,therefore,that though agony or post mortem infection of the blood stream in peritonitis does occur, death from a septicaemia is quite the exception in peritoneal infections.

In the human subject the fight between the host and the invading bacteria goes on in the peritoneal cavity and the patient dies of toxaemia. The amount of pus which is present in the abdomen of a human being dying of peritonitis is ample evidence of the local nature and is an index of the fierceness of the fight.

That some bacteria are absorbed into the circulation in cases of general peritonitis in man cannot be doubted but that they are very quickly killed off there,is equally beyond doubt.

I had the good fortune to hit on a strain of Staphylococcus Aureus which after passage through several/

several rabbits in large intravenous doses, produced in reasonable dosage a fatal peritonitis in those animals. This form of peritoneal infection is, I believe, much more comparable to human peritonitis than is the Bacillus Coli peritonitis of rabbits. Thus in 50 post mortems on rabbits dying of Staphylococcal peritonitis, in which cultures from the heart blood were made, in 30 the blood was found to be sterile, in 11 cases only one or two colonies of Staphylococcus Aureus developed, and in 9 cases a fairly vigorous growth took place on the tubes. In the latter cases the animals had succumbed very quickly after a large intraperitoneal injection.

The local reaction in the staphylococcal cases was purulent, with flakes of lymph, and in several cases a definite purulent plastic peritonitis was found. More recently I have found that a mixed infection of Staphylococcus Aureus and Pneumococcus produces in rabbits a peritoneal inflammation which still more closely resembles the human type.

The striking difference between the peritonitis of man and that of rabbits however, is the very frequent absence of any appreciable leucocytosis in the/

the blood of the latter, and though the importance of the leucocyte exudation in the rabbit's peritoneal cavity in promoting recovery is undoubted, the leucocytes in the blood seldom rise above 15,000.

The guinea pig unfortunately is not susceptible to staphylococcus, and therefore one is obliged to use Bac. Coli in experiments on this animal.

FRAMING AND REGULATION OF EXPERIMENTS.

THEIR PRACTICAL AND CLINICAL BEARING: THE QUESTION OF CONTROLS: IN VIVO NATURE OF EXPERIMENTS.

In the experimental part of this work it has been made a guiding principle that all preventive and therapeutic measures tried, be of such a nature that they could, if found of value, be practicably used in the human subject. This will to some extent, explain why the results obtained are not nearly so striking as those of some of the Continental observers, who though they succeeded in immunising animals against the intraperitoneal injections of from 10 to/

to even 50 times the lethal dose of different bacteria did so by methods which could not be applied to the human subject.

Before working many weeks at this subject one became convinced that another factor vitiated many of the results of work previously done on this subject. That factor was the estimating the lethal dose of the bacteria used, and dependent on this the controlling of the experiment. In much of the reported work on this subject, one finds that the experimenter, by a series of inoculations, determined the minimal lethal dose of the bacterium to be used in his experiments, and then, employing the figure so obtained as a control, conducted experiments spread out over weeks or months, using this minimal lethal dose or multiples of it. Now this method is entirely untrustworthy and misleading, as a glance at the dosage employed in my experiments will show.

The virulence of an organism varies in the most striking and tantalising manner from day to day, so that one finds that the dose of say Bac. Coli that to-day will kill a rabbit in 16 hours, will, taken from a subculture 3 days later, only cause a similar rabbit a temporary indisposition.

Much/

Much of my time had, therefore, to be spent in ascertaining what was the exact virulence of the bacteria at the time of each experiment. Moreover a fresh control was used for each experiment as thereby only, could results approaching accuracy be obtained.

One other point which I take to be of great importance must still be considered. That is by what criterion is one to judge the results obtained?

In human surgery the all important point is the recovery or death of the patient. This therefore must be the factor deciding the success or failure of an experiment. No in vitro proof of immunity, no high index or striking leucocytosis will avail if the animal receiving treatment dies, and the control lives.

This method though entailing the sacrifice of more animals, is in my opinion the only safe one and it was employed throughout all the experimental part of this work.

THE CELLULAR REACTION OF THE PERITONEUM TO IRRITATION.

The introduction of any foreign substance into the peritoneal cavity is followed by a very definite cycle of changes in respect to the cellular element of the peritoneal effusion. These cellular changes were observed very carefully and worked out very fully in guinea pigs by Beattie. As frequent reference to them will be made throughout this thesis, more especially to the comparative value of films from the peritoneal exudate of different cases, a description of the method employed in making the films, and a brief outline of the cellular changes usually found is here given.

TECHNIQUE EMPLOYED IN MAKING FILMS OF PERITONEAL EFFUSION.

A capillary glass tube is drawn out to a fine point and graduated, a mark being made corresponding to 3c.m.m. capacity from the point. The hair over the rabbit's abdomen is clipped, the skin purified, and the point of the pipette introduced through the abdominal wall. The peritoneal fluid runs up in the/

the capillary tube. When it has reached the mark, the thumb is placed over the end of the tube which is then withdrawn.

The 3ccm. of fluid is then blown out on to a cover slip, another cover slip applied to this and the two drawn apart in the usual manner. One thus obtains films from different cases which are comparable, and from which one gets an approximate idea of the relative number of cells present in different cases. There is no doubt that the bowel is frequently punctured by this manoeuvre but I have never seen any evidence of any gross leakage or any mark on the bowel wall post mortem.

CELLULAR CHANGES IN THE PERITONEAL EFFUSION IN PERITONITIS.

For the first 3 hours after an injection of bacteria into the peritoneal cavity there is little cellular response, only a few lymphocytes being added to the large mononucleated cells found in normal peritoneal fluid. About 3 hours after the injection, however, polymorphonuclear leucocytes migrate from the blood-vessels and appear in large numbers in the peritoneal effusion. This migration of polymorphs continues for 48 hours. These cells are actively phagocytic/

phagocytic and apparently produce some substance which is injurious to the life of the bacteria.

These leucocytes are largely destroyed in the fluid either as free cells or in the interior of other cells.

In fatal cases, Beattie found that the polymorphs increased in number, up till the death of the animal.

My observations do not confirm this, as for several hours before death, I have found a gradual decrease in the number of all cells, coincident with an increase in the number of bacteria.

The large mononucleated phagocytes are found at all stages, but commence to be abundant about 24 hours after the injection, and become relatively more numerous till the restitutio ad integrum is complete.

They are amoeboid and are phagocytic for other cells (especially the polymorphs) and for bacteria.

These large mononucleated cells or macrophages do not come from the blood, but are derived from the endothelial lining of the peritoneum, particularly from that covering the omentum, and also probably/

probably from the endothelium of blood-vessels. The presence of a large proportion of these cells in the peritoneal exudate as being associated with the period of recovery, is a sign of some prognostic value.

It must be mentioned, however, that the peritoneum is not entirely dependent on phagocytosis for its protection against bacterial invasion. During the first two hours after the injection of bacteria, before the migration of the microphages, the bacteria injected disappear in large numbers, an active process of bacteriolysis going on in the peritoneal effusion. But for this lytic process the cellular migration would probably be too late to check the bacterial invasion.

The following experiment illustrates the importance of a good cellular reaction in the peritoneal effusion in protecting the animal from death in infections of that cavity.

EXPERIMENT I.

6:1:09. To each of three full grown rabbits, an intraperitoneal injection of a bacterial emulsion consisting of 1500 million Staphylococcus Aureus and 50 million Pneumococcus was given.

7:1:09. Twenty four hours after injection, peritoneal/

peritoneal fluid was drawn off from each rabbit and films made.

Rabbit I. was now found to have been suffering from a subcutaneous abscess in the left haunch; it, however, was practically healed when first noticed. This rabbit appeared quite well the morning after injection; the other two rabbits looked dull. The peritoneal films showed that whereas Rabbit I. had an intense polymorph leucocytosis in the peritoneal cavity, Rabbit II. had very few polymorph leucocytes in its peritoneal fluid and in Rabbit III the polymorphs were present only in small numbers.

8:1:09. Rabbit I quite well to-day.

Rabbit II. distinctly dull and abdominal looking.

Rabbit III is better than II, but is not eating.

Films from peritoneal fluid again made.

Peritoneal fluid from Rabbit I thick and turbid, and film shows vast numbers of polymorph leucocytes, many of them crowded with cocci.

Peritoneal fluid from Rabbit II. is quite clear and film shows few polymorphs and many cocci free in the fluid.

Film from Rabbit III. shows a fair number/

number of polymorphs but also many free cocci.

Rabbit II. died 58 hours after the start of the peritoneal infection and p.m. showed a purulent plastic peritonitis. Heat blood sterile. Examination of the blood of Rabbits I. and III. now showed that the former had a leucocytosis of 19000, the latter no leucocytosis, and differential counts showed that the polymorphs in Rabbit I. averaged 75%, in Rabbit III. only 60%. Rabbit III. died 3½ days after the injection and post mortem, a condition of pyaemia was found with abscesses in lungs and liver.

Rabbit I. lived for 8½ days after infection; post mortem a purulent plastic peritonitis was found; the heart blood was sterile.

The photomicrographs show the striking difference in the cellular reaction in the peritoneal fluid in these 3 animals. (Plate II)

This experiment brings out very clearly several important points.

The first is that the presence of a leucocytosis in the blood favours a good leucocyte emigration into the peritoneal cavity. (That is as one would expect.)

The second is that a good cellular emigration/

emigration into the peritoneal effusion is one of the chief factors making for success in the combat with the invading germs.

Thirdly, that from the naked eye appearance of the peritoneal fluid, one cannot judge as to the extent or virulence of the infection.

It was note-worthy that whilst in Rabbit I. turbid purulent fluid was withdrawn on the second day, in Rabbits II. and III. the fluid was almost clear.

The purulent character of the fluid was evidence, not of the severity of the infection, but of the intensity and vigour of the rabbit's resistive powers.

The practical bearing of this is obvious.

On opening the abdomen of a patient, free sero-purulent fluid is found. (The source of the infection is immaterial.) One cannot tell from naked eye examination, whether that fluid is germ free and is protective, or whether it is germ-laden and a menace to the patient.

The only satisfactory test is an immediate microscopic examination. This can be made in the operating theatre in 3 minutes. If the film shows numerous undegenerated cells and no free micro organisms, then the fluid is protective and should be left/

left alone. If on the other hand, the cells are beginning to degenerate, and free cocci or bacilli are seen, then the fluid is a menace to the patient and douching out of the abdomen is indicated.

To put it briefly:- Before washing out an abdomen, one should know what one is washing out, and before refraining from washing out an abdomen, one should know accurately what one is leaving behind in it.

Artificial/

PART I.

"THE PROPHYLAXIS OF PERITONITIS".

ARTIFICIALLY PRODUCED LEUCOCYTOSIS as a PRELIMINARY To ABDOMINAL OPERATIONS.

ISSAEFF'S WORK and its PRACTICAL BEARING; Mickulicz's Work.
EFFECT of Subcutaneous Injection of Nuclein on the Blood and on the Peritoneum.
CAIRD'S Results with Nuclein.

The wonderful power of reaction to organismal infection or other form of irritation, possessed by the peritoneum has long been a matter of common knowledge. Issaeff[4] showed that the cellular reaction produced by the intraperitoneal injection of such harmless agents as sterile saline and broth, or still more so by nuclein and its allies, would protect an animal 24 hrs later against an intraperitoneal injection of 10 times the lethal dose of the Cholera spirillum.

Isaeff's results have been confirmed and amplified by very numerous observers, especially Borchard[5] and by Diez and Compara[6], and we now know that the intraperitoneal injection of practically any non-lethal substance will protect the animal, 24 hrs later, against the injection of one or more lethal doses of bacteria.

This striking discovery is surely a very strong argument in favour of performing lengthy and serious abdominal operations in two stages if possible. For example, if the abdomen be explored and a large adherent but still removable carcinoma of the caecum/

caecum or ascending colon be found, in the light of Issaeff's work it would be advisable to make a lateral anastomosis between the Ileum and transverse colon, to pour saline into the abdomen, and several days later to excise the diseased portion of bowel. The peritoneum would thus be prepared for any infection which might take place during the more difficult part of the operation. Though well aware of the clinical disadvantages of such a method, one feels sure that the risk of death from peritonitis which in such cases is by no means small, would be considerably lessened.

Mickulicz[7], in one or two cases, gave intra-peritoneal injections of Nucleic acid to the patients the day before performing an operation on them. He very quickly came to the conclusion, however, that the risk and discomfort attending this method, disqualified it for general use.

Mijake[8], working in Mickulicz' laboratory, found that the subcutaneous injection of nuclein producing in guinea-pigs a leucocytosis, protected them to some extent, (2 - 3 times the lethal dose) against peritonitis induced 9 hours later.

This method of subcutaneous injection of 2 - 6cc. of 5% Nucleic Acid, Mickulicz extensively practised as a preliminary measure to abdominal operations,/

operations, with, he thought, improved results. His untimely death, however, cut short his observations.

The subcutaneous injection of nucleic acid in the human subject and in animals is followed fairly constantly by definite changes in the blood. For the first few hours, (1 hour - 6 hours) there is a well marked leucopaenia, the leucocyte count frequently falling from 8000 down to 4000. The leucocytes in the blood then rapidly increase in number and may rise in the human subject 12 hours after the injection to 25000. In rabbits and guinea pigs, they seldom rise above 15000, and frequently do not reach that figure. The increase is found to be almost entirely in the polymorph leucocytes.

Ledingham[9] found that though a leucocytosis following injection of nuclein did not constantly occur, the opsonic index for all organisms tried was always considerably raised 12 hours after the injection, and he ascribes any benefit resulting from treatment with nuclein more to this factor than to leucocytosis.

This striking rise in the opsonic index after the injection of Nucleic Acid I have never found either/

either in animals or in the human subject.

THE EFFECT of the SUBCUTANEOUS INJECTION of NUCLEIC ACID on the PERITONEUM.

It is certainly of interest and importance to know whether, along with the leucocytosis in the blood, any increase in the number of cells in the peritoneal cavity takes place. To ascertain this, the following experiment was carried out.

Two rabbits were each given 2cc. of 5% nucleic acid subcutaneously at 3 p.m.; a third rabbit was used as a control. Peritoneal fluid was drawn off hourly by means of a capillary pipette from one of the "nuclein rabbits" (I), and from the control (III.). The other "nuclein rabbit" (II) was left alone until a leucocytosis in its blood was established.

In Rabbits I. and III. after the first 3 hours, a polymorph leucocytosis in the peritoneal cavity began to be evident, and this, during the next 3 - 4 hours became more and more marked (due no doubt, to the repeated irritation caused by the punctures.) It was, however, much more marked in Rabbit I. which had received the nuclein/

nuclein than in Rabbit III which had not.

After seven hours, (a leucocytosis in the blood being already present) peritoneal fluid was for the first time drawn off from Rabbit II. but not a single polymorph leucocyte was found in the films from the fluid obtained.

This showed that nuclein does not produce a leucocytosis in the peritoneal cavity when injected subcutaneously, unless the factor of some local irritation of the peritoneum be introduced, but, given this latter factor, an emigration of polymorphs into the peritoneal cavity is favoured and hastened by the presence of a leucocytosis in the blood.

This observation has been repeatedly confirmed.

In Rabbits and Guinea pigs one has found that though the preliminary subcutaneous administration of Nucleic Acid does give some protection against Peritonitis, this protection is not very striking nor is it quite constant.

This will be seen from the experimental result detailed later.

During the years 1905 and 1906, Mr Caird employed/

employed this method of preliminary injection of nuclein in most of his abdominal cases in the Royal Infirmary. He has kindly permitted me to look through the notes on these cases. In 60 cases which I looked up, I found that some degree of leucocytosis was invariably produced by the nuclein injection. The leucocytosis varied from 10,000 up to (in one case) 36,000, the average for all the cases being 15,500.

Mr. Caird did not consider, however, that his results were influenced by this preliminary nuclein treatment.

More work will require to be done before the clinical value of this method can be definitely judged.

VACCINE THERAPY AS A PROPHYLACTIC MEASURE AGAINST POST-OPERATIVE PERITONITIS.

It is found where after an operation on the intestinal tract, peritonitis has occurred, either from infection of the peritoneum at the time of operation or from a leak in the suture line subsequent to the operation, that the predominating organism in the purulent exudate is the Bacillus Coli Communis. Many observers have regarded this organism as being of secondary importance and have attributed the fatal issue so frequent in such cases, to the presence of the Streptococcus or to some anaerobe.

There is now, however, no room for doubt that these observers greatly under-estimated the virulence of the Bac. Coli when it is multiplying rapidly in the peritoneal cavity.

It has been of late frequently demonstrated that in a generalised peritonitis Bac. Coli may be the only organism discoverable by both film preparations and cultures, and moreover, that in such cases, a fatal issue is the rule.

The investigations of Dudgeon and Sargent[10] give strong support to this view. We have also every/

every reason to believe that should a quantity of a certain strain of Bac. Coli of comparatively low virulence escape into the peritoneal cavity, and gain a hold and be permitted to multiply there, the Bacillus will increase in its virulence and in its toxicity and will eventually kill the host.

The important point in such cases is, then, that the protective forces of the host shall be capable of dealing with the initial infection, and of stamping out the bacteria before any extensive multiplication of them has occurred. One therefore naturally wondered whether by injecting a Bac. Coli vaccine subcutaneously some days before operation, one could prepare the protective forces of the patient so that, should some infection of the peritoneum occur at the operation, they might be in a better position to promptly deal with it, than would otherwise be the case.

EXPERIMENTAL EVIDENCE AS TO THE VALUE OF VACCINE TREATMENT AS A PROPHYLACTIC MEASURE and as to the VALUE of OPSONIC EXAMINATIONS IN PERITONITIS.

Numerous experiments were carried out on Rabbits/

Rabbits and Guinea-pigs to test the degree of protection given by a dose of a suitable vaccine several days before the induction of Peritonitis, and frequent opsonic examinations of the blood of these cases were made.

To give detailed descriptions of all these experiments would occupy too much space. Therefore only those experiments which brought out special points of interest, especially with regard to the value of the opsonic index, are recorded in detail, the results of the other experiments being then summarised.

EXPERIMENT I. Illustrating how the Opsonic Index cannot be taken as an Index of the Animal's resistive power during an infection.

RABBIT I. full-grown buck.

17:5:08.

Under ether anaesthesia abdomen opened, vermiform appendix removed; abdominal wound closed, but at conclusion of operation, a suspension of 1200 million living Staphylococcus Aureus injected into peritoneal cavity.

Complete recovery.

For/

For state of Opsonic Index during period of recovery. See CHART I.

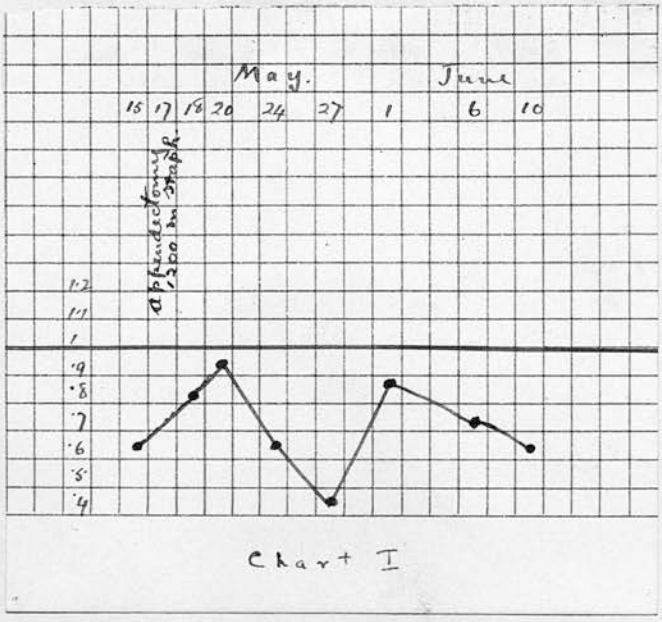


Chart I

RABBIT II. full-grown buck.

17:5:08. Exactly the same procedure as in Rabbit I.

From the day of operation, this rabbit looked ill, got very thin, and died 3 weeks later.

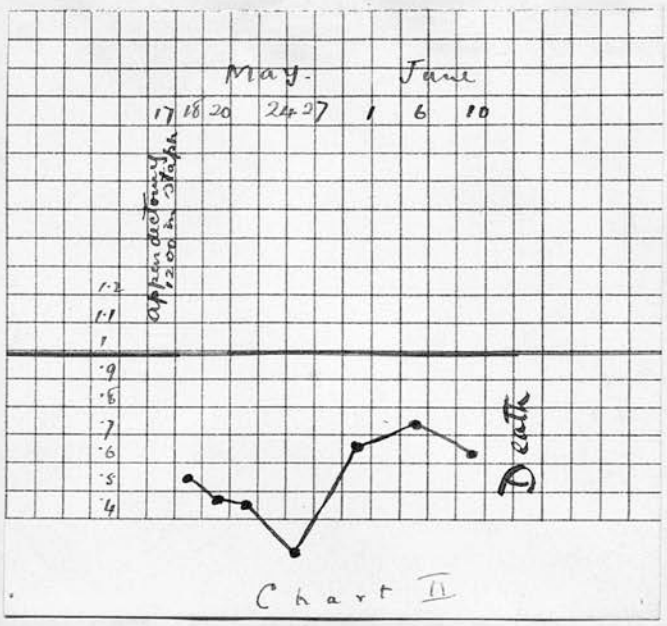
P.M. Chronic plastic peritonitis, vig.growth of Staph. Aureus on cultures from peritoneal cavity.

No growth on culture from Heart blood.

For record of Opsonic Index for Staphylococcus from time of operation till death,

See/

See CHART II.



In this experiment both rabbits had a low index, yet one made a perfect recovery and the other died. This, one has repeatedly found to be the case and one has come to put very little trust on the opsonic index as a prognostic test.

Another chart, showing how misleading the opsonic index might be if taken as a prognostic sign, is here given.

EXPERIMENT II.

RABBIT.

14:5:08. Given an intraperitoneal injection of 1000 million Staphylococcus Aureus.

Complete recovery.

For/

For record of Opsonic Index and leucocytosis for the 10 days following injection, See CHART III.

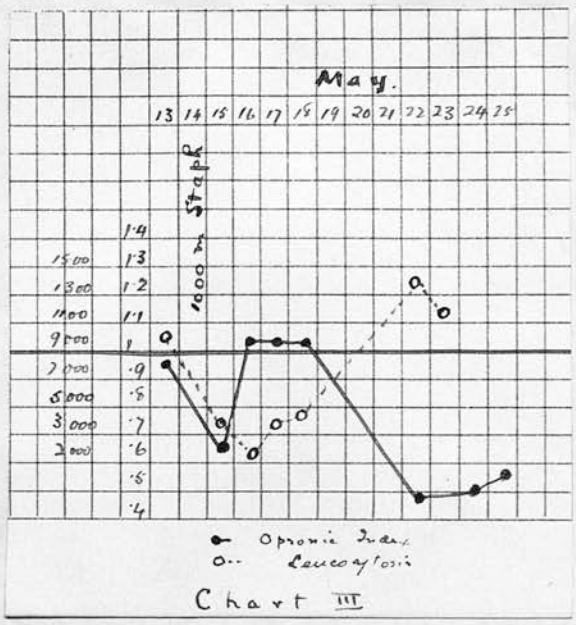


Chart III

On the other hand, a high index may indicate a high resistance and a low index a diminished resistance, as the following two experiments show.

EXPERIMENT III. Illustrating high Opsonic Index with increased resistance to Infection.

RABBIT I. ¾ grown buck.

During 7 weeks had received at different times 4 injections of B. Coli vaccine and 2 injections of live B. Coli. (See Chart.)

On/

On May 31st 1908, Opsonic Index for B. Coli = 3·81. The Rabbit was put under ether anaesthesia, its abdomen was opened, its vermiform appendix removed, and at the conclusion of the operation, 1500 million living B. Coli Communis injected into the abdominal cavity.

The animal made a prompt recovery though the opsonic index fell markedly during the few days following operation. See CHART IV.

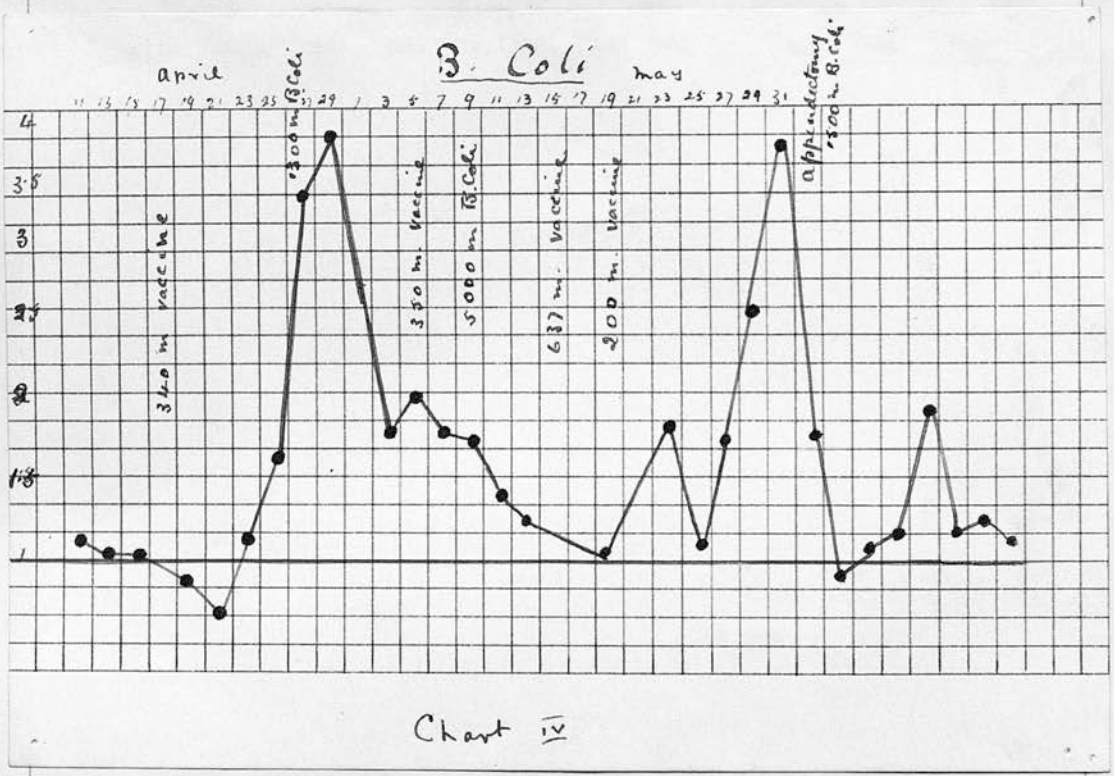


Chart IV

RABBIT II. (control) $\frac{3}{4}$ grown buck.

31:5:08. Opsonic Index for B. Coli ·81. Under ether Anaesthesia abdomen opened, appendix removed. At/

At conclusion of operation, 1500 million living B. Coli injected into peritoneal cavity.

Died 20 hours after the operation.

P.M. General peritonitis with turbid seropus and great congestion. B. Coli grown on cultures from peritoneum and from heart blood.

EXPERIMENT IV. Illustrating low opsonic Index accompanying diminished resistance to infection. "Summation of Negative Phases."

RABBIT I. full grown buck.

During a period of 2 weeks this rabbit received two injections of Staphylococcus Aureus vaccine and one injection of living Staphylococci which it survived. Its opsonic index, two days after this injection was found to be ·92. On the following day, a very large dose of Staphylococcal vaccine (3000 million) was given. Ten days later its opsonic index was found to be ·68. Another large dose of vaccine, (2000 million) was given. The day following this, the Index had fallen still lower to ·46. At this point, (May 17th, 1908) the abdomen was opened under ether anaesthesia, the appendix was removed and 1200 million living Staphylococci injected into the abdomen/

abdomen at the conclusion of the operation.

The next day the animal was very dull, and the index to Staphylococcus was .48. On the second day after operation the animal died.

P.M. Well marked general plastic peritonitis. Vigorous growth of Staphylococcus Aureus on culture from peritoneal cavity, a few colonies on culture from heart blood. See CHART V.

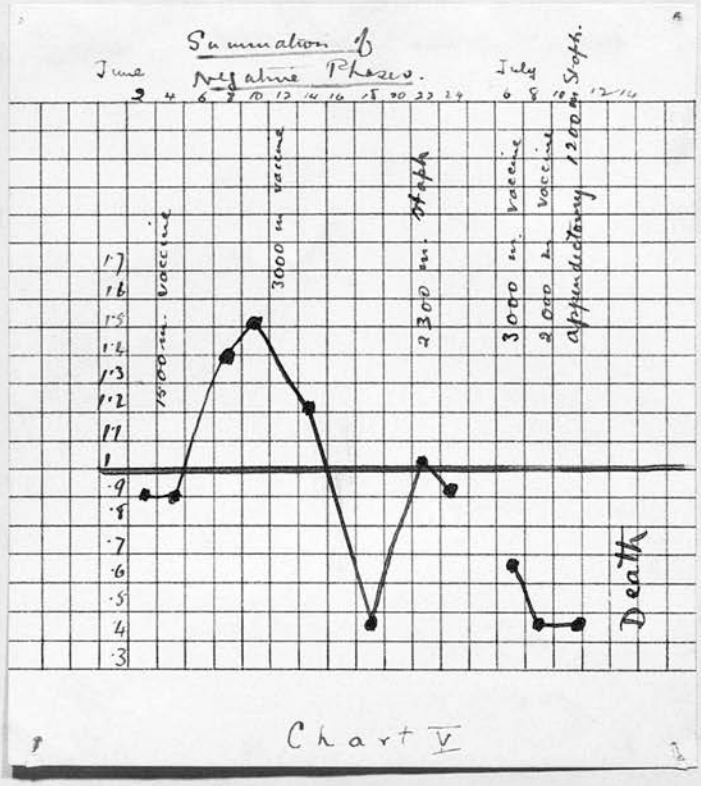


Chart V

RABBIT II. (control.)

Had two weeks previously, had an intra-peritoneal injection of Staphylococcus Aureus and had recovered. No vaccine.

17/

17:5:08.

Opsonic Index for Staph. Aureus = ·82.

Abdomen opened, appendix removed. At conclusion of operation, 1200 million Staph. Aur. injected into peritoneal cavity.

Complete recovery.

In this experiment, large doses of vaccine producing marked negative phases, lowered the animal's resistance to infection.

VARIATION in OPSONIC INDICES for DIFFERENT STRAINS of the SAME BACTERIUM.

Another point brought out in the course of these vaccine experiments was the fact that the opsonic index of an animal's blood may vary for two different strains of the same organism. In many of the experiments, one tested the opsonic index both for a virulent strain of the bacterium and for one taken from an old stock laboratory culture, and one found often very marked difference in the two indices, the difference being especially marked if the animal had been previously given a dose of a vaccine made from one of those strains.

This/

This point was brought out chiefly in working with Bac. Coli Communis, but was present in a lesser degree with different strains of Staphylococci.

The following table shows some of the results obtained.

TABLE SHOWING OPSONIC INDEX TAKEN SIMULTANEOUSLY FOR STOCK EMULSION AND A VIRULENT EMULSION OF BAC. COLI.

		Index for Stock culture	Index for Virulent culture
RABBIT	I. after dose of Stock Vaccine	·99	·61
"	II. " "	3·81	1·09
"	III. " "	2·21	·92
"	IV. " "	1·83	·98
"	V. " "	1·05	·84
"	VI. " "	·88	·73
"	VII " "	·86	·61
"	VIII. " "	·90	·81
GUINEA PIG.	I. " "	1·32	1·05
"	II. " "	·90	·67
"	III. " "	1·10	·98
"	IV. " "	·94	·86
GUINEA PIG	I. after dose of Virulent Vaccine	·83	·90
"	II " "	·63	·98
"	III " "	·74	1·00
"	IV. " "	1·25	1·56
"	V. " "	·80	1·36

The following clinical case brings out the foregoing/

foregoing point, and also emphasises how unreliable the Opsonic Index is as a prognostic sign during an acute infection.

CASE I.

Woman 42.

Operated on for Acute Appendicitis.

A gangrenous appendix removed and a large abscess in R. iliac fossa and in pouch of Douglas evacuated and drained.

Culture from abscess gave a growth of pure B. Coli Communis.

The day following operation, patient was very ill with a pulse of 130.

Opsonic Index for Stock B. Coli = 1·64. She was given 200 million of a Stock B. Coli vaccine. The following day she was still worse, P. 140.

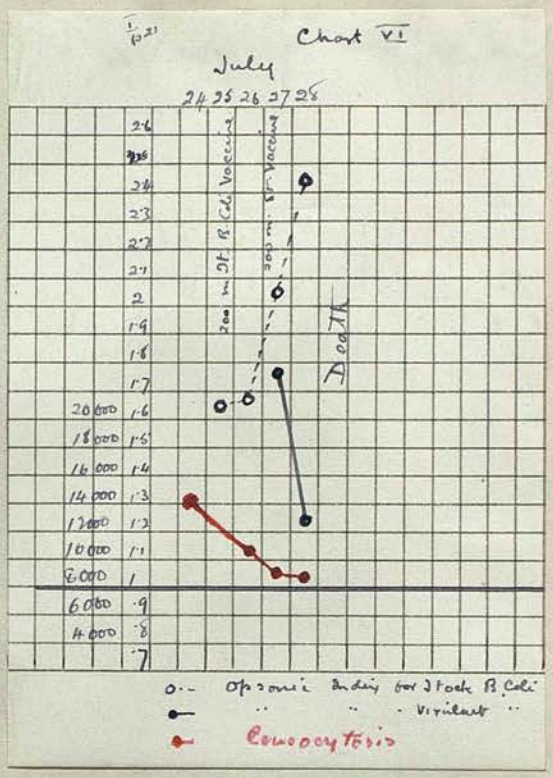
Index for Stock B. Coli 1·68. given another dose of 200m. stock B. Coli vaccine.

She died two days later with a very high index for B. Coli but no leucocytosis.

It is interesting to note (see CHART VI) that though after the injection of vaccine, her index for the Stock B. Coli rose, that for the B./

B. Coli grown from her abdomen, fell.

CHART VI.



At the post mortem an abscess was found extending upwards in the right renal pouch. The rest of the Peritoneal cavity was healthy.

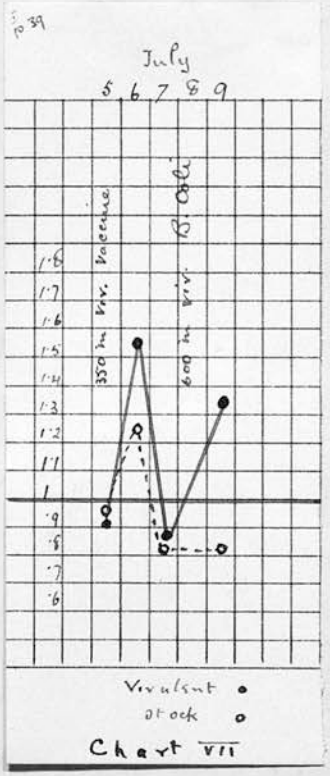
This case was very instructive, as showing that in a fat woman who obviously had a low resistive power, with no leucocytosis, and who went down rapidly under an acute infection, still one found a high opsonic index to the causal organism.

It strikingly confirmed the results one had seen in animals namely, that during an acute/

acute infection, the opsonic index is no guide as to the resistance of the patient.

It was found, however, that as a rule the opsonic indices for two strains of the same organism rose and fell together, and that as a rule, a dose of stock vaccine, if it caused a marked rise in the opsonic index for the stock organism, caused also a slight rise in the index for the virulent organism.

The appended CHART (VII) demonstrates this point.



WHAT AMOUNT OF PROTECTION IS GIVEN BY PRELIMINARY VACCINE TREATMENT?

In all, 10 experiments were carried out to test/

test this. I will not give them all in detail but merely state the results.

In three experiments the animals which had received the vaccine injection lived, whilst the controls died of Peritonitis.

In two experiments, the vaccinated animals made a prompt recovery, whilst the controls were ill for two or three days but then recovered.

In two experiments, both controls and vaccinated animals made prompt recoveries. In one experiment, both animals died at practically the same length of time after the induction of peritonitis.

In two experiments the vaccinated animals died whilst the controls lived. In one of the latter, however, enormous doses of vaccine had been given and the animal was given peritonitis during a marked negative phase. In the other the rabbit died of Acute Enteritis which may or may not have been caused by the peritonitis.

From these experiments one concluded that the preliminary injection of a vaccine did give some protection against death from peritonitis, provided the vaccine was given in reasonable dosage, and provided a sufficiently long interval was allowed to elapse/

elapse between the vaccine injection and the onset of the peritonitis, to allow the negative phase to pass by.

One there-fore felt justified in using this method in the human subject before operation in cases where an intestinal resection was anticipated.

CLINICAL USE OF PROPHYLACTIC VACCINE INJECTIONS.

Eight cases were treated in this way. In seven of them, one succeeded by the injection of a B. Coli Vaccine in raising the opsonic index to this organism in such a manner that on the morning of operation, the index for B. Coli was considerably above normal.

In the eighth case the index was still low on the morning of operation, but as the case was one of resection of small intestine for Sarcoma, and the operation was conducted almost altogether outside the peritoneal cavity, any infection of the latter was unlikely and the patient made a rapid recovery.

I shall give notes of two of the cases to indicate the method adopted and merely give charts of the others showing the effect of the vaccine injection on the Opsonic Index.

CASE I. Carcinoma of the Rectum: Excision by the Abdomino-perineal method.

J. C. 48. Gamekeeper.

History of passage of blood and mucus by bowel with frequent calls to stool and great loss/

loss of weight for 6 months before admission.

On examination found to have a large interesting carcinoma of Rectum the upper limit of which was beyond the reach of the examining finger.

The growth was on the right lateral and anterior aspects of the rectal wall and was somewhat fixed, but it was decided that an attempt to remove it was justifiable.

On 23:X:08, Opsonic Index for B. Coli = 1·20; on this day a subcutaneous injection of 200 million B. Coli vaccine was given.

(The vaccine was made from a culture obtained from a case of Acute Appendicitis.)

24:X:08 Op. Index for B. Coli = 1·04.

26:X:08 Op. Index " " " = 1·41.

On this morning operation performed.

Under spinal anaesthesia the abdomino-perineal operation was performed, the entire Rectum and 4 inches of the pelvic colon being removed, and the sacral fat and glands cleared out.

The operation was prolonged and difficult and the rectum ruptured during removal, considerable soiling of the wound with faeces taking place.

For/

For ten days following operation, patient was very ill from post operative ileus & caecostomy had to be performed. Thereafter, however, he made a rapid recovery and 4 months after operation had gained 3 stones in weight, and was doing full duty as gamekeeper.

The Opsonic Index 10 days after operation was found to be 1·08. See CHART VIII.

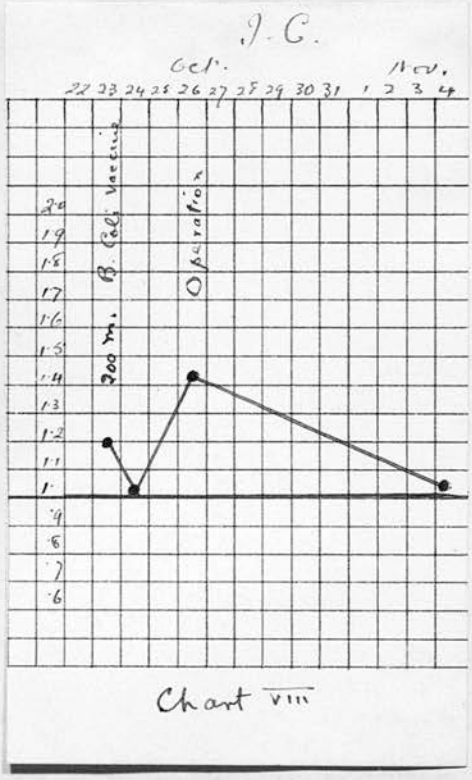


Chart VIII

CASE II. Acute Obstruction due to Annular Carcinoma of Pelvic colon.

Two Stage Operation.

J.B. aet 58.

History. On Nov. 5th 1908, patient was suddenly seized with acute abdominal pain while walking home/

home from work. The pain came on in spasms, and has continued intermittently till admission to Hospital on Nov. 16th. Vomiting commenced on Nov. 5th, and has persisted for 10 days. Repeated enemata have occasionally brought away a little flatus, but there has been no motion for 14 days."

Previous to Nov. 5th, patient had been losing weight but bowels acted fairly regularly.

STATE on ADMISSION.

Emaciated man with yellowish sallow complexion, sunken eyes and anxious expression. Tongue very dry and crusted, P. 64, leucocytes 20,000. Considerable general distension of the abdomen and peristaltic waves made out every now and then.

OPERATION.

Mesial incision below umbilicus. Free fluid with some lymph in peritoneal cavity. Great distension of colon above an annular carcinoma of Pelvic colon. Abdomen irrigated.

The pelvic colon above the tumour was brought out through an incision in the left iliac region, and a Pauls-tube inserted. Mesial wound closed.

For five or six days after this operation/

operation, patient was very ill suffering from the prolonged toxaemia, then he began to improve somewhat.

On Nov. 13th, 1908 five days after the colotomy operation, his opsonic index for B. Coli was 1·03. On this day he was given subcutaneously 200 million B. Coli Vaccine.

Seven days later, Opsonic Index for B. Coli = 1·23.

Again given 200 million B. Coli vaccine. A week later i.e. on Nov. 27th. Opsonic Index for B. Coli = 1·46.

On this morning the abdomen was reopened in the mid line and the tumour of the pelvic colon resected.

The operation presented special difficulties owing to the tumour being very close to the colotomy opening. Most of the operation had thus to be performed within the peritoneal cavity and some soiling of the peritoneum could not be prevented. After resecting the tumour the ends of bowel were closed and a lateral anastomosis performed between the transverse colon and Rectum.

Patient made an uninterrupted recovery

and/

and left hospital on the 25th. day.

The colotomy wound was closed at a later date.

The accompanying CHART (IX) shows the method of vaccine treatment and course of the Opsonic Index.

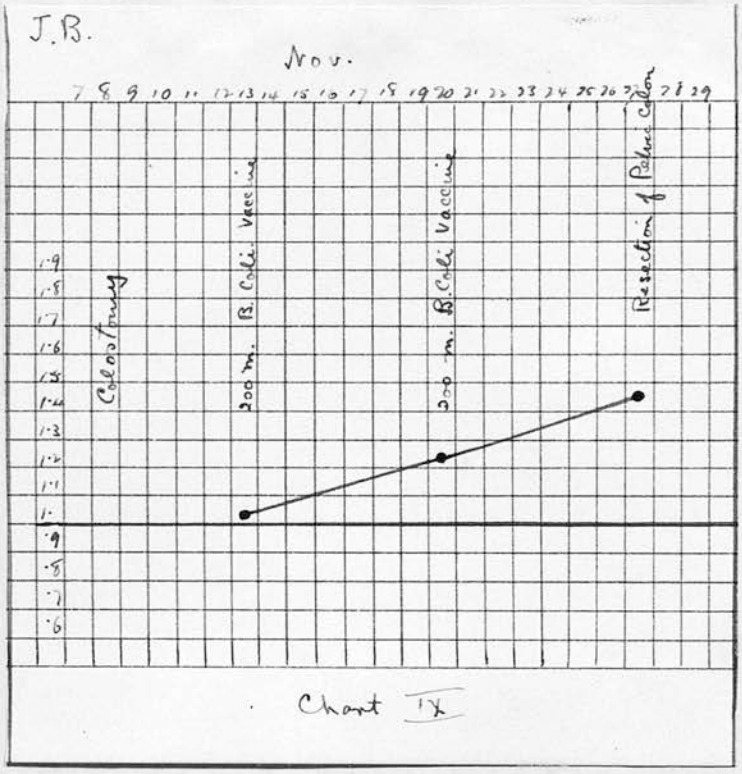
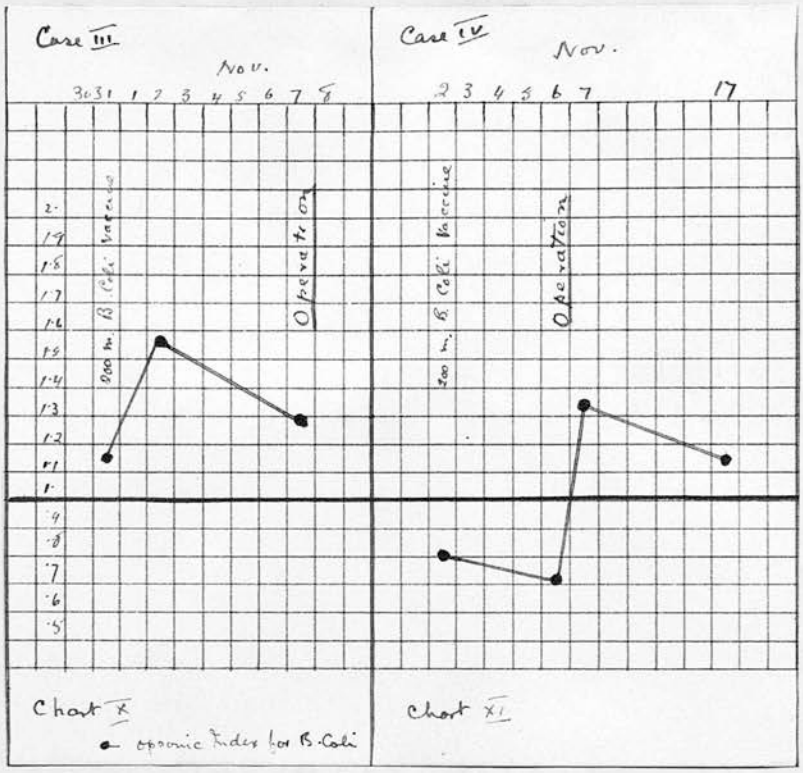
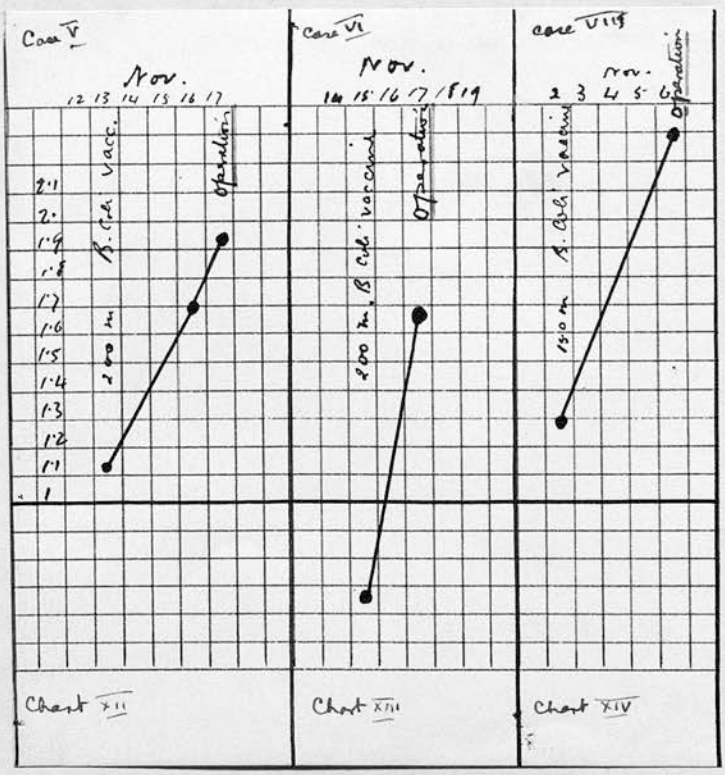
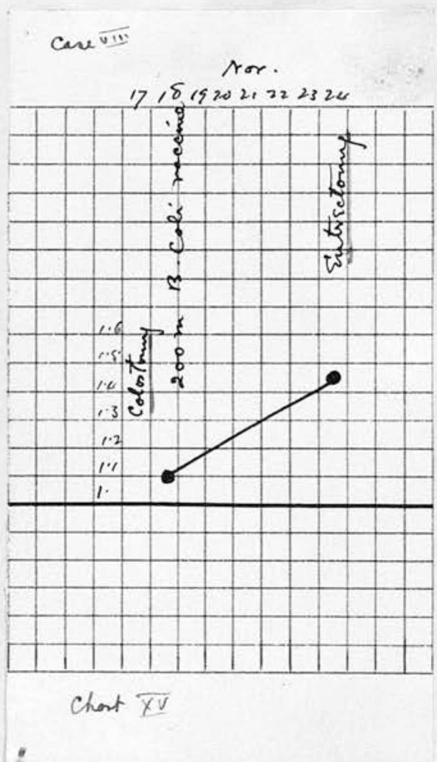


Chart IX


Case III
Nov.
30 31 1 2 3 4 5 6 7 8
200 m. B. Coli. vaccine
Observation
Case IV
Nov.
2 3 4 5 6 7 17
200 m. B. Coli. Vaccine
Observation
Chart X
Opsonic Index for B. Coli
Chart XI


Case V
Nov.
12 13 14 15 16 17
200 m. B. Coli. vacc.
Operation
Case VI
Nov.
14 15 16 17 18 19
200 m. B Coli. vaccine
Observation
case VII
Nov.
2 3 4 5 6
150 m. B. Coli. vaccine
Operation
Chart XII
Chart XIII
Chart XIV


Case VIII
Nov.
17 18 19 20 21 22 23 24
Colostomy
200 m B. Coli vaccine
Enterostomy
1·6
1·5
1·4
1·3
1·2
1·1
1·
Chart XV

C O N C L U S I O N S.

1. In Rabbits and Guinea pigs, injection of vaccine frequently fails to cause any appreciable rise in the opsonic index for the bacterium injected.

2. Injection of a suitable vaccine previous to infection of the peritoneal cavity, does increase the resistance of the animal to the resultant peritonitis; the increase of resistance is, however, not very striking.

3. In a case of Peritonitis the Opsonic index is not an index of the animal's resistance and is of no value as a prognostic test; an animal may die with a high index, and conversely may recover with a low index.

4. The opsonic index of an animal may differ widely for 2 strains of the same bacterium.

5. Subcutaneous injection of B. Coli vaccine in the human subject almost invariably produces a rise in the opsonic index to this/

this organism.

6. Injection of vaccine is unattended by risk or pain.

7. It probably is of some value as a prophylactic measure when given before intestinal operations on the human subject.

THE COMBINATION OF VACCINE & NUCLEIN INJECTIONS AS A PROPHYLACTIC MEASURE AGAINST PERITONITIS.

By first raising the opsonic index, and then by producing a leucocytosis in the blood, of an animal one hoped to increase its resistance to a peritoneal infection.

The method employed was to give a subcutaneous injection of a suitable vaccine 3 days before and a subcutaneous injection of Nucleic Acid 12 hours before inducing peritonitis.

As will be seen from the experiments detailed below, it was found that the combination of Vaccine and Nuclein gave much greater protection than did either by itself, so much so, that one is encouraged to hope that this combination may prove clinically to be of considerable value.

EXPERIMENT I.

Four Rabbits used.

Rabbit I was given vaccine and Nucleic Acid.

Rabbit II " " vaccine alone.

Rabbit III " " Nucleic Acid alone.

Rabbit IV was control.

Rabbits I, II, and III. were of equal size and weight.

Rabbit/

Rabbit IV. was larger, weighing 100 grms. more; it was therefore made the control.

4:12:08. 12 noon. Rabbits I and II. each given subcutaneous injection of 660 million Staphylococcus aureus vaccine.

6:12:08. 5 p.m. Rabbits I and III. each given subcutaneous injection of 2ccm. 5% Nucleic acid.

7:12:08. 2·30 p.m. All four Rabbits given an intraperitoneal injection of 14000 million living Staphylococci.

Thereafter peritoneal fluid was drawn off, by the method previously described, every hour till the death of Rabbits II, III, & IV, and films stained and examined.

(One was thus enabled to follow exactly the cellular changes occurring in the peritoneal cavity throughout the entire fight between the bacteria and the protective phagocytes. Photos from some of these slides are appended.)

Plates III IV V & VI

Rabbit I. never showed signs of being ill and made a complete recovery.

Rabbit/

Rabbit II. 2 hours after injection began to look ill and never picked up, dying 7 hours after injection.

P.M. 20 minutes after death.

General Peritonitis with sero-pus and great injection of peritoneum.

Culture from peritoneum gave a vigorous growth of Staph. Aureus.

Culture from heart blood gave numerous colonies of Staph. Aureus.

Rabbit III. remained well for 3½ hours. It then began to be dull and gradually got worse, dying 10 hours after injection.

P.M. At once.

General Peritonitis with a large quantity of turbid fluid and flakes of lymph and great congestion of peritoneum.

Culture from fluid in peritoneal cavity gave a vigorous growth of Staph. Aureus.

Culture from heart blood gave one or two colonies of Staph. Aureus.

Rabbit IV. looked ill for the first 3 hours after injection, then it brightened up till 10 hours after injection when it became very dull. It died 16 hours after the induction of peritonitis.

P.M./

P.M. General peritonitis, more lymph, and less fluid than in II, and III. Culture from peritoneum = vigorous growth of Staph. Aureus.

Culture from Heart blood = sterile.

EXPERIMENT II.

Four Rabbits.

Rabbit I given Vaccine and Nucleic Acid.

Rabbit II " Vaccine alone.

Rabbit III " Nucleic Acid alone.

Rabbit IV Control.

15:12:08. 1 p.m. Rabbits I and II. each given 400 million Staphylococcus Aureus vaccine subcutaneously.

16:12:08. 8 p.m. Rabbits I and III. given 2ccm. 5% Nucleic Acid subcutaneously

17:12:08. Under complete anaesthesia (Ether), laparotomy was performed on all four rabbits. In each case the appendix was removed and the abdomen closed. At the conclusion of the operation an intraperitoneal injection of 3000 million living Staphylococci was given to each Rabbit.

Rabbit I. made an uninterrupted recovery.

Rabbit II. got over the operation and 10 hours later looked well; thereafter it became dull and died 20 hours after the injection.

P.M./

P.M. General peritonitis with turbid fluid and some lymph.

Culture from peritoneum, vigorous growth of pure Staph. Aureus.

Culture from Heart blood, sterile.

Rabbit III. recovered from operation and 3 days later was eating well. Then it became much thinner and died 8 days after injection.

Daily leucocyte counts showed a steadily increasing leucocytosis up till death.

P.M. General purulent plastic peritonitis. Fatty changes in organs and pyaemic abscesses in kidneys and Heart muscle.

Culture from peritoneum = vigorous growth of Staph. Aureus.

Culture from Heart blood = one or two colonies of Staph. Aureus.

Rabbit IV. began to look ill shortly after recovering from the anaesthetic and died 18 hours after injection.

P.M. General peritonitis, turbid fluid and lymph, cloudy swelling of organs.

Culture from Heart blood = numerous colonies of Staph. Aureus.

In this experiment the element of an abdominal operation was introduced in order that the subsequent peritonitis might more closely resemble post operative peritonitis in the human subject.

EXPERIMENT III. 4 RABBITS.

Rabbit .I given Vaccine + Nucleic Acid.
Rabbit II " Vaccine alone.
Rabbit III " Neucleic Acid alone.
Rabbit IV. Control.

2:1:09. 3 p.m. Rabbits I. and II. given 1300 million Staphylococcus Aureus Vaccine.

3:1:09. 9'30 p.m. Rabbits I. and III. given subcutaneous injection of 2cc. of 5% Nucleic Acid.

4:1:09. 3 p.m. All four Rabbits given 4500 million living Staphylococcus Aureus intraperitoneally. At 12 midnight, Rabbits I, II, and IV. looked well. Therefore were given a second intraperitoneal injection of 6000 million Staph. Aureus. Rabbit I. made a perfect recovery and at no time did it look ill.

Rabbit II. was fairly well the morning following injection, but thereafter became dull and died on the 5th day with a purulent plastic peritonitis.

Numerous colonies of Staph. Aureus were grown/

grown from the heart blood.

Rabbit III. 2½ hours after the first injection began to look ill and got steadily worse. It was killed 10 hours after injection as recovery was out of the question.

Rabbit IV. was ill for one day after the second injection but eventually recovered.

VACCINE AND NUCLEIN EXPERIMENTS ON RABBITS SUMMARISED.

EXPERIMENT I.

ANIMAL	PRELIMINARY INJECTION of	INTRAPERITONEAL INJECTION of	RESULT.
Rabbit I.	Vaccine & Nuclein	14000 mill. Staph. Aur.	Recovery.
Rabbit II.	Vaccine only	"	D.7 hrs. after inj.
Rabbit III.	Nuclein only	"	D.10 hrs. aft.injec.
Rabbit IV.	Control	"	D.16 hrs. aft.injec.

EXPERIMENT II.

Rabbit I.	Vacc. & Nuclein	3000 mill. Staph.Aur.	Recovery.
Rabbit II.	Vaccine only	"	D.20 hrs. aft.injec.
Rabbit III.	Nuclein only	"	D. 8 hrs. aft.injec.
Rabbit IV.	Control	"	D.18 hrs. after.

EXPERIMENT III.

ANIMAL	PRELIMINARY INJECTION OF	INTRAPERITONEAL INJECTION of	RESULT.
Rabbit I.	Vacc. & Nuclein	4500 mill. Staph.Aur.	Recovery.
Rabbit II.	Vaccine only	"	D.5 dys. later.
Rabbit III.	Nuclein only	"	D.10hrs. aft.inj.
Rabbit IV.	Control	"	ill but recovd.

EXPERIMENTS ON GUINEA PIGS

to test the

PROTECTIVE EFFECT OF VACCINES AND NUCLEIN

SINGLY and COMBINED.

In these experiments the degrees of protection given by vaccines made from stock cultures and from virulent cultures of Bac. Coli, were tested and compared; also the effect of combining these two kinds of vaccine with nuclein was compared with the effect of simply giving the vaccines by themselves.

Peritonitis was induced by the intraperitoneal injection of a bacterial emulsion made from a culture/

culture of virulent B. Coli.

Three experiments were carried out, six guinea pigs being used in each experiment. In each case the vaccine injection was given 2 days before, and the Nuclein injection 12 - 14 hours before peritonitis was induced.

Daily leucocyte counts and opsonic estimations were made, but as they were chiefly of negative value, they need not be detailed here. It will be sufficient to state that in no case was a marked leucocytosis produced during the course of the peritonitis whether it resulted in recovery or death.

The nuclein injections invariably produced a certain degree of leucocytosis, which 12 hours after injection averaged 13000, but a marked leucocytosis was never found.

EXPERIMENT IV.

G.P. I given "Virulent" Vaccine + Nucleic Acid.
" II given "Virulent" Vaccine alone.
" III " "Stock" Vaccine + Nucleic acid.
" IV " "Stock" Vaccine alone.
" V " Nucleic Acid alone
" VI Control.

12:10:08. 12 noon. G.Pigs I. and II. given 350 million virulent B. Coli vaccine, subcutaneously. G.Pigs III. and IV. given 400 million stock B.Coli vaccine/

vaccine.

13:10:08. 10 p.m.

G.Pigs I. III. & V. given 1cc. of 5% Nucleic Acid subcutaneously.

14:10:08. 12 noon.

All six G.Pigs given an intraperitoneal injection of 600 million live virulent B. Coli.

G.Pig I. never looked the least bit the worse for the injection.

G.Pig II. looked ill for a few hours but made a perfect recovery.

G.Pig III. looked ill for 24 hours but recovered.

G.Pig IV. was very dull for two days but recovered.

G.Pig V. was very ill and died 20 hours after injection.

G.Pig VI. was very ill for 3 days but eventually recovered.

In this experiment the only animal which was not affected to some extent by the intraperitoneal injection of live Bacteria was that one which had received the virulent vaccine + Nucleic acid.

The other two experiments I shall give in tabular form to save space.

EXPERIMENT/

EXPERIMENT V.

ANIMAL	PRELIMINARY TREATMENT.	INTRAPERITONEAL INJECTION of	RESULT.
G.P. I	"Virulent" Vacc. + Nuclein.	1100 mill. Virulent B. Coli.	Recovered & was well 8 dys.aft.inj.
G.P. II	"Virulent" Vacc. alone	"	Died 15 hrs. after injec.
G.P. III	"Stock" Vaccine + Nuclein	"	Died 19 hrs. after injec.
G.P. IV.	"Stock" Vaccine alone.	"	Died 11 hrs. after injec.
G.P. V.	Nuclein alone.	"	Died 13 hrs. after injec.
G.P. VI.	Control.	"	Died 10 hrs. after injec.

Here again, the animal which received the "Virulent" vaccine and nuclein differed markedly from all the others.

EXPERIMENT/

EXPERIMENT VI.

ANIMAL	PRELIMINARY TREATMENT	INTRAPERITONEAL INJECTION of	RESULT.
G.P. I.	Virulent Vacc. + Nuclein	1100 mill. virulent B. Coli.	slightly ill for 24 hrs. Recovery.
G.P. II.	Virulent Vacc. alone.	"	ill for 30 hrs. Recovery.
G.P. III.	Stock Vaccine + Nuclein	"	slightly ill for 30 hrs. Recovery.
G.P. IV.	Stock vaccine alone.	"	very ill for 3 days. Recovery.
G.P. V.	Nuclein alone	"	very dull for 3 days. Recovery.
G.P. VI	Control	"	Died 30 hrs. after injection

Recognising that the injection of a virulent vaccine + Nuclein did give considerable protection against death from Peritonitis, one next wished to ascertain what the extent and limits of that protection were. The following experiment was therefore carried out with that purpose.

EXPERIMENT VII.

The minimal lethal dose of a virulent B. Coli for a guinea pig of a certain weight was ascertained by giving graduated doses to a series of

/

of those animals.

Multiples of this dose of B. Coli were then injected into eight guinea pigs, four of which had received preliminary treatment with virulent vaccine and nuclein, the other four acting as controls.

	ANIMAL	WEIGHT	PRELIM. TREATMENT.	INTRAPERIT. INJECTION of	RESULT.
I.	G.P. I.	410 grm.	Vir. Vacc. + Nuclein.	1000 mill. vir.B.Coli	Prompt recovery.
	G.P.(Control)	405 grm.	Nil.	"	D.19 hrs. aft.injec
II.	G.P. II.	480 grm.	Vir. Vacc. + Nuclein	1500 mill. vir B.Coli	very ill for 2 dys. Recovery.
	G.P.(Control)	500 grm.	Nil	"	D.17½hrs. aft.injec
III.	G.P. III.	440 grm.	Vir. Vacc. + Nuclein	2000 mill. vir.B.Coli	ill for 24 hrs. but rec.
	G.P.(Control)	490 grm.	Nil.	"	D.16 hrs. aft.inj.
	G.P. IV.	600 grm.	Vir. Vacc. + Nuclein	2500 mill. vir.B.Coli	ill for 3 dys. but recovered
	G.P.(Control)	680 grm.	Nil.	"	D.25 hrs. aft.injec

The results obtained with this combination of vaccine and Nuclein were sufficiently striking to encourage one to hope that this method of preliminary treatment may be found of value in human abdominal surgery.

CASES/

CASES ILLUSTRATING THE USE OF PRE-OPERATIVE INJECTIONS OF A VACCINE AND NUCLEIN IN ABDOMINAL SURGERY.

CASE I. Acute Intestinal Obstruction following on chronic obstruction due to an annular Carcinoma of the Pelvis Colon.

Mrs. F. Aged 48.

History. For 2 months had been losing flesh and had been troubled with obstinate constipation and spasms of abdominal pain.

For 3 - 4 weeks before admission to hospital, troubled with frequent vomiting and attacks of griping pain.

For 3 days before admission constant vomiting, latterly dark in colour, great abdominal pain, and complete stoppage of the bowels.

STATE on ADMISSION.

"Patient is a very emaciated woman with sallow complexion, sunken eyes and listless expression. Tongue dry with brown crust. Breath faecal odour. Pulse 146. T. 97·6. Patient is evidently suffering from profound toxaemia. Abdomen greatly distended. No patterns - tympanitic all over on percussion, splashing elicited over the region of the ascending and transverse colon/

colon. Leucocytes 12000.

Can retain barely 1½ pints of fluid per rectum.

OPERATION. Mesial incision below the umbilicus.

Free fluid in abdomen, slightly turbid straw-coloured. Greatly distended small intestine, also greatly distended and partially gangrenous caecum with a small perforation on its outer side found.

An annular carcinoma of the Pelvis colon found to be the cause of obstruction.

A fresh wound made in Right iliac region and the gangrenous caecum with a portion of Ileum brought out and left outside, a Pauls-tube being inserted into caecum. Mesial incision closed.

Patient was practically pulseless at the conclusion of the operation.

For several days following this operation, patient was very ill and it was recognised that a further operation to remove the cause of obstruction, and then an excision of the sloughing caecum, were urgent.

On Jan. 2nd., two days after the first operation, patient's opsonic index for B. Coli was 1·05 and on this day she was given subcutaneously 250 million of B. Coli vaccine from a virulent strain/

strain of that organism. On Jan. 6th., her Opsonic Index for B. Coli was 1·43 and the leucocyte count was 10000. At 9 p.m. on the 6th, she was given a subcutaneous injection of 4cc. of 2% Nucleic acid.

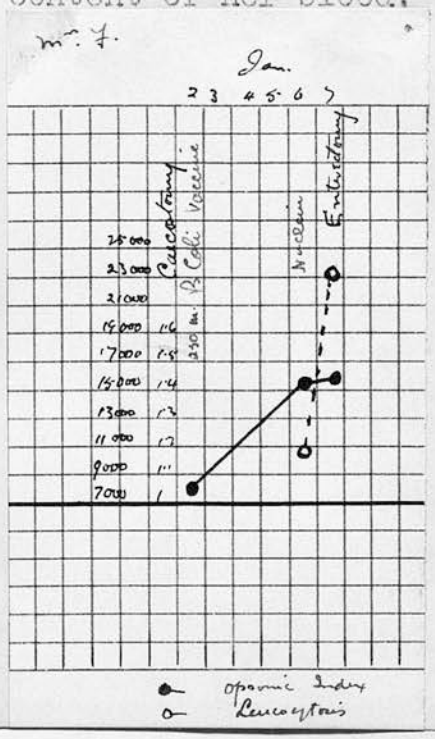
On Jan. 7th. at 10·30 a.m. her opsonic index for B. Coli = 1·45.

Leucocytes had risen to 23000.

On this morning, abdomen again opened and the Pelvic colon resected.

Patient's pulse at the start of the operation was 120, and though she stood the operation well, she apparently never got over the initial toxaemia and gradually wasted and died 10 days after the second operation.

The appended CHART (XVI) illustrates the effect of vaccine and Nucleic acid on the opsonic and leucocyte content of her blood.



CASE/

CASE II.

Acute Intestinal Obstruction from an Annular Carcinoma of the Pelvic colon.

1st Operation. Caecostomy, resection of the Neoplasm, colostomy.

2nd Operation, lateral anastomosis between Transverse colon and Rectum.

Vaccine and Nuclein Treatment before 2nd operation.

John J. aet 64.

Had suffered from constipation, flatulence and pains in the abdomen for 2 months.

Acute symptoms for one week.

STATE on ADMISSION.

Patient suffering from profound intestinal toxaemia. Abdomen greatly distended.

OPERATION. Feb, 27th 1909.

Incision as for Inguinal colotomy.

Tumour of the fixed Iliac colon discovered.

During manipulation the tumour tore across, necessitating immediate resection. Open ends of colon brought out in left lumbar region.

Incision made over caecum and a caecostomy performed.

Patient survived this operation and bowels acted well through both openings.

On March 5th. his Opsonic Index for B. Coli = ·83.

He/

He was given a subcutaneous injection of 200 million B. Coli Vaccine.

On March 11th. Index for B. Coli = 1·13.
" 16th " " = 1·14. Given a 2nd injection of 200 million B. Coli vaccine.

March 17th. 8 p.m. Leucocytes 6500. Given a subcutaneous injection of 4cc. of a 2% solution of Nucleic Acid.

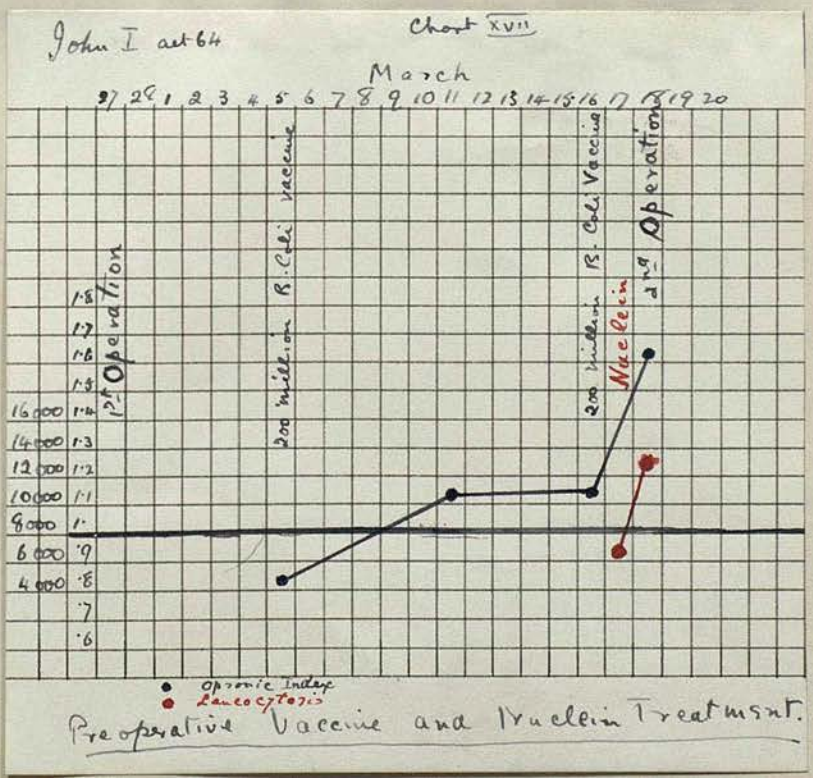
March 18th. 10·30 a.m. Leucocytes 13000.

Opsonic Index for B. Coli = 1·62.

11 a.m. 2nd Operation. Abdomen opened in mid line. The transverse colon and the pelvic colon were both cut across, all four ends closed and a lateral anastomosis between the transverse colon and the rectum performed.

Patient never gave any cause for anxiety after this operation and made a rapid recovery.

Appended CHART (XVII) shows course of Vaccine and nuclein treatment.



These/

These two cases merely serve to illustrate the application of this method in human surgery and no conclusions as to the value of the method can be drawn from them.

NATURAL PREVENTION OF THE SPREAD OF PERITONITIS. THE "PROTECTIVE" ACTION OF THE STAPHYLOCOCCUS ALBUS.

The property of forming adhesions round a focus of infection and thus preventing a general diffusion of the mischief is the most striking and the most beneficent quality of the peritoneum.

Within the past few years we have learned from Dudgeon and Sargent[10] that this barrier of adhesions is called forth by the benign action of the Staphylococcus Albus, which emigrates into the peritoneal cavity when danger threatens from some more virulent infection, and causes a mild and harmless plastic peritonitis round the site of the more deadly infection, walling off the latter.

Dudgeon and Sargent came to this remarkable conclusion, partly as the result of a series of intro-vitam observations on cases of localised and spreading peritonitis and partly as the result of a series of experiments on Rabbits. They succeeded in isolating the Staphylococcus Albus from the boundary zone of the peritonitis in a considerable number of cases of appendicitis; they found it also always present in the/

the blood in the peritoneal cavity in cases of ruptured tubal gestation and also very frequently in cases of acute intestinal obstruction.

They noticed also, that when this organism was found on the boundary line of a localised peritonitis that the case did well, but when some other organism such as B. Coli was found, the course of the case was by no means so favorable.

They thereupon carried out some experiments on rabbits, the results of which they consider as clear evidence in favour of this benign action of the Staphylococcus Albus.

They injected a non-lethal dose of Staphylococcus Albus into the peritoneal cavity of a rabbit 24 hours before injecting a lethal dose of Bac. Coli. Communis, and found that the rabbit recovered whilst a control which had not received the preparatory Staphylococcal injection, died as a result of the B. Coli injection.

This experiment they repeated several times with the same result.

They found, however, that when the Staphylococcus was injected along with the Bac. Coli, it afforded no protection.

This theory of Dudgeon and Sargent's one finds/

finds quoted in most of the recent works on Peritonitis where it passes unchallenged.

Now whilst much of Dudgeon and Sargent's work on Peritonitis is of great value, I venture to think that their theory in regard to the protective action of the Staphylococcus Albus is unwarrantable, not being supported by sufficient clinical evidence and being based on several worthless experiments.

Since reading their papers, I have made cultures from the boundary zone in over 50 cases of localised and spreading peritonitis (chiefly Appendicitis) in the human subject, and only on one occasion have I been able to isolate the Staphylococcus Albus. The one case in which I found the coccus was one of double Salpingitis with pelvic peritonitis.

With regard to their experiments, one need only recall the original experiments of Issaeff, who showed that any material such as saline, broth etc. injected into the peritoneal cavity 24 hours before infection, protected an animal against a lethal dose of Bac. Coli or other organism.

I carried out three experiments of a converse nature to those of Dudgeon and Sargent with similar results, that is to say, I made B. Coli the protective organism against a lethal dose of Staphylococcus.

I/

I shall give them briefly.

EXPERIMENT I.

6:8:08. 10 a.m.

Rabbit I. given an intraperitoneal injection of 800 million B. Coli.

7:8:08. 10 a.m. Given intraperitoneal injection of 2500 million Staphylococcus Aureus.

Rabbit II.

7:8:08. 10 a.m. Given 2500 million Staph. Aureus, intraperitoneally.

Rabbit I. made a perfect recovery.

Rabbit II. died 25 hours after injection from Staphylococcal Peritonitis.

EXPERIMENT II.

8:9:08. 10 a.m.

Rabbit I. given 800 million B. Coli intraperitoneally. (This was about ½ lethal dose)

9:9:08. 10 a.m. Given intraperitoneally 3000 million Staphylococcus Aureus.

10:9:08. Perfectly well, lively and eating.

Remained well for 8 days, but died on 10th day.

P.M. No sign of peritonitis; an abscess in heart-wall and a basal Pneumonia found.

Rabbit II.

9:/

9:9:08. 10 a.m. Intraperitoneal injection of 3000 million Staphylococcus Aureus.

10:9:08. Has been very dull since 2 hours after injection; recovery doubtful.

After two days the animal picked up, but 2 weeks later developed paralysis of hind limbs and was killed.

EXPERIMENT III.

2:9:08. 9 p.m.

Rabbit I. Intraperitoneal injection of 1000 million B. Coli.

3:9:08. 9 p.m. Intraperitoneal injection of 1000 million Staphylococcus Aureus.

Immediate recovery.

Rabbit II.

3:9:08. 9 p.m. Intraperitoneal injection of 1000 million Staphylococcus Aureus.

Was ill for 1½ days but recovered.

It will be seen from these experiments that a non-lethal dose of B. Coli gives protection from a subsequent lethal dose of a Staphylococcus, just as readily as the non-lethal dose of Staphylococcus protects from the subsequent lethal dose of B. Coli.

Before/

Before ascribing to the Staphylococcus Albus a benign and almost philanthropic action within the abdomen, one must have much stronger evidence than any which has yet been brought forward in support of this theory.

P A R T II.

ON THE USE OF CERTAIN THERAPEUTIC MEASURES IN CASES OF ACUTE INFECTION OF THE PERITONEUM.

THE INTRAPERITONEAL ADMINISTRATION OF OIL TO DELAY ABSORPTION AS A THERAPEUTIC MEASURE IN PERITONITIS.

The rationale of this method of treatment, advocated by Glimm[12] is that when sterilised oil is poured into the peritoneal cavity, the oil globules are absorbed into the lymphatics and by plugging the lymph vessels, retard the absorption of bacteria.

Several questions require investigation and decision before the intraperitoneal use of oil in peritonitis can be put on a sound scientific basis. These questions are:-

I. The Physiology of Peritoneal Absorption?

II. How is absorption from the peritoneal cavity influenced by inflammation of the peritoneum?

III. Which is the more favorable for the patient suffering from peritonitis: Rapid or slow absorption?

IV. If retarded absorption be a favorable occurrence in peritonitis, does the intraperitoneal administration of oil bring about this retardation?

PHYSIOLOGY/

PHYSIOLOGY OF PERITONEAL ABSORPTION.

A great amount of experimental work has been done to elucidate this question, and we now possess fairly accurate knowledge on the subject.

An enormous capacity for absorption of fluid has long been recognised as a striking characteristic of the peritoneum. Wegner[13]'s work on this absorptive capacity revealed the fact that an animal can absorb from its peritoneal cavity, within an hour, fluid equivalent to 5% of its body weight. This fact has been repeatedly confirmed by later observers.

Route by which Absorption takes place.

There are two channels by which absorption may take place namely, by the blood stream, and by the lymph stream.

Absorption of Fluids.

Starling and Tubby[14] injected solutions of Indigo carmine and Methyline blue into the peritoneal cavity and demonstrated that the pigment was present in the urine a considerable time before it could be found in the thoracic duct, showing the absorption of fluid occurred chiefly by way of the blood stream.

Meltzer/

Meltzer[15] in similar experiments found the pigment in the thoracic duct long before it was demonstrable in the urine.

Mendel,[16] however, confirmed the results of Starling and Tubby.

The work of Klapp[17] put this question beyond the region of doubt. He injected a solution of lactose into the peritoneal cavity of a rabbit and estimated by quantitative analysis how long it took for it to be secreted by the urine. He then ligatured the thoracic duct of the animal and repeated the experiment, and found that no delay was caused in the absorption of the lactose by the ligature. Oslow[18] and Heidenhain[19], after much work on this subject also came to the conclusion that the chief route for the absorption of fluids and soluble substances from the peritoneal cavity was by way of the capillary blood-vessels.

Absorption of Solid Particles. (including Bacteria)

When particles of solid matter are introduced into the peritoneal cavity they are also very rapidly absorbed and may within a few minutes, be found in the lymphatics of the diaphragm.[20] (Durham found them in the phrenic lymphatics 5 minutes after injection), and within an hour in the mediastinal lymph/

lymph glands.

The vexed question of whether there be stomata in the poreital peritoneum is not yet definitely settled, and though in the writings of Muscatello[21] and others the presence of stomata is denied, yet from the rapidity with which solid particles injected into the peritoneum enter the lymphatics of the diaphragm, one inclines to the belief that there are stomata, at least on the under-surface of the diaphragm. McCallum's[22] histological work on this subject also favours this latter view.

The experiments of Buxton and Torrey[23] placed almost beyond a doubt the fact that solid particles can by themselves enter the lymphatics of the diaphragm and are not necessarily carried in by leucocytes.

Oil globules resemble solid particles in that they are absorbed only by the lymphatics.

It has been shown by experiment that the absorption of solid particles from the peritoneal cavity takes place chiefly through the lymphatics of the diaphragm and to a less extent through those of the omentum, the rest of the peritoneum participating only in a very much smaller degree.

By painting collodion over the diaphragm

of/

of a rabbit, Peiser[24] was able to delay the absorption of organisms to a very great extent, in fact almost to prevent the absorption altogether.

The constant respiratory movement in the upper part of the abdomen by a sort of pumping mechanism, plays a considerable part in bringing about rapid absorption.

From these facts, it becomes very clear why infections of the upper abdominal zone should be so much more fatal than those in which only the lower abdominal zone is involved.

ABSORPTION from the PERITONEAL CAVITY in PERITONITIS.

Schnitzler and Ewald[25] tested the effect of a bacterial infection of the peritoneum on the absorption of Potassium Iodide from that cavity. They tested the urine qualitatively for the appearance and the disappearance of the Iodide in the urine. They found that absorption was delayed in Peritonitis.

Clairmont and Haberer[26] repeated this work with Potassium Iodide, but got just the opposite result, finding absorption increased by a bacterial peritonitis, except in the very late stages of the inflammation when absorption was slightly retarded.

Glimm,/

Glimm,[27] not satisfied with the methods of the above observers, carried out elaborate experiments on this subject, using lactose and making quantitative examination of the urine for it. He found that when lactose is given intraperitoneally, it is absorbed and secreted almost entirely and unaltered in the urine within 8 hours, so that by collecting all the urine secreted during this time, quantitative tests can be made. He used dogs and rabbits for his experiments and tested the absorption in each animal, first without any peritonitis and then during peritonitis. Glimm found that absorption is invariably accelerated in peritonitis, even in its later stages. The first appearance, the maximum secretion, and the last of the secretion of the lactose in the urine occurred considerably earlier in the rabbits during a bacterial peritonitis than in the same rabbits before.

The methods employed by Glimm were so much more exact than those of other observers that his results must be considered of the greatest value.

Peiser[28] approached this subject from a different standpoint. He tested at different times during the course of a peritonitis the relative number of bacteria in the blood and in the peritoneal effusion./

effusion. He found during the first few hours of a peritonitis, great numbers of bacteria in the blood of the animal but during the course of the peritonitis, as the number of bacteria increased in the peritoneal effusion, the number in the blood stream diminished, owing, he thought, to the lymphatics of the diaphragm becoming mechanically plugged by bacteria.

Therefore, as far as our present knowledge of this subject goes, we may take it that the absorption of soluble substances is increased during peritonitis, but that of solid particles such as bacteria becomes retarded with the progress of the peritoneal inflammation.

WHICH IS THE MORE FAVOURABLE FOR THE PATIENT SUFFERING from PERITONITIS:

RAPID OR SLOW ABSORPTION?

Here again, we enter a region of controversy. Many writers, most prominent among whom was Leumander,[99] considered that absorption of organisms into the blood stream by stimulating the production of/

of antibodies was a protective and beneficial occurrence.

More recent work, however, has shown that this is not the case, and that on the contrary the more localised the infection can be kept, the greater the chance for the patient. Peiser found that a certain dose of B. Coli could be injected with impunity into the peritoneal cavity of a rabbit. The same dose could be injected into the blood stream of a rabbit without producing death. If, however, he injected one half of this dose into the peritoneal cavity, and an hour later the other half into the blood stream, the rabbit died within a few hours with all the signs of a peritonitis. We may take it then, that as Peiser says, "Recovery from peritonitis depends on the fight between the bacteria and the body defences being confined to the peritoneal cavity".

DOES THE INTRAPERITONEAL ADMINISTRATION OF OIL RETARD BACTERIAL ABSORPTION IN PERITONITIS?

Glimm[30] conducted a series of experiments to decide this point. He injected into the peritoneal cavity sterilised oil at different intervals before inducing a bacterial peritonitis and withdrew blood from/

from the carotid artery at subsequent intervals, plated out the blood in Agar, and so determined the number of organisms in the blood.

He found that in rabbits which had been given a preliminary injection of oil the number of organisms cultivated from the blood during the subsequent peritonitis was immensely less than the number in the blood of control animals which had received no oil. Moreover, he found that though most of the control animals died, the majority of those which were given oil recovered.

Buxton and Tracy[31] using somewhat different methods, repeated Glimm's experiments. They found that to be of any value, the oil must be injected several hours before the peritonitis is induced, and attributed any good effect produced by the oil to the reactive changes it induced by irritating the peritoneal cavity.

Pfannenstiel of Kiel, as the result of Glimm's observations, has for some time used oil in all his gynaecological operations where he thinks the peritoneum may have been infected. I had the good fortune to see this method employed by him in several cases. At the conclusion of an operation, say for Pyosalpinx , where some soiling of the peritoneum with/

with purulent matter has taken place, he pours 1 - 2 ozs. of sterilised olive oil into the lower part of the abdomen.

He considers that his results in this class of case have improved since starting this method of treatment.

EXPERIMENTAL EVIDENCE.

I have carried out a series of fourteen experiments to test the value of oil as a life-saving agent when it is given at the same time as, or just immediately before the peritonitis is induced.

Some of these experiments I shall record in detail, for they bring out important points. The others merit only a brief statement as to results. The points which one naturally wished to observe particularly in these experiments were:

(1) Does the oil interfere with the normal cellular reaction in the peritoneal effusion?

(2) Is recovery at all delayed by the presence of this foreign substance in the peritoneal cavity?

(3) Is there any risk to life (e.g. oil embolism) in the use of this therapeutic agent?

(4)/

(4) Does the oil aid in averting a fatal issue in severe cases of peritonitis?

These questions were all dealt with as will be seen in the following records.

NATURE and STERILISATION of the OIL.

Throughout this series of experiments, the purest olive oil was used. The oil was sterilised by heating on several occasions for 20 minutes at a temperature of 70 to 90°C. If the oil be heated to too high a temperature, it becomes discoloured, fatty acids are set free and considerable pain is caused after injection. (In later experiments I have used pure vaseline oil, really a liquid paraffin). This agent was suggested to and prepared for me by Mr. Alexander of the Royal Infirmary and being absolutely neutral is superior to olive oil.)

Rabbits were the animals used and from 2 to 5cc. of oil was injected into the peritoneal cavity immediately before the injection of a bacterial emulsion. In all but one experiment Staphylococcus Aureus was the organism used in inducing the peritonitis.

EXPERIMENT I.

Rabbit I. full grown buck.

At/

At 10 a.m. 2·5cc. sterile olive oil injected into the peritoneal cavity followed immediately by an injection of 1000 million live B. Coli.

Rabbit was ill for 2 days, but recovered.

Rabbit II. control.

10 a.m. Given 1000 million B. Coli by intra-peritoneal injection. Ill for 2 days but recovered.

Four weeks later peritoneal fluid drawn off and films made both showed an absolute return to normal. See Photos. I. & II. Plate VIII.

This experiment showed that a complete return to normal in the peritoneal cavity was not prevented by oil. Numerous later experiments have confirmed this fact.

EXPERIMENT II.

Rabbit I. White buck. Wt. 1650 grm.

4 p.m. Intraperitoneal injection of 2·5cc. sterile olive oil, followed immediately by 200 million living Staphylococcus Aureus. Recovery. Films from the peritoneal fluid were made daily for the first fortnight after injection. Some of these are reproduced. See Photos. 1, 2 & 3, Plate VII.

This rabbit was killed 73 days after the injection.

Peritoneum/

Peritoneum presented a healthy appearance.

A section of the diaphragm, however, revealed the presence of oil globules in the phrenic lymphatics 10½ weeks after injecting the oil. Plate XII (4)

Rabbit II. control.

4 p.m. Intraperitoneal injection of 200 million Staphylococcus Aureus. Survived the immediate danger but died 3 weeks later with localised peritoneal abscesses.

Daily films of peritoneal fluid made for first fortnight after injection. See Photos. 4, 5 & 6, Plate VII.

This experiment brought out two important points. Firstly that the ordinary cellular reaction in the peritoneal effusion is not retarded by the presence of oil. Secondly, that the oil may remain for many weeks in the phrenic lymphatics.

EXPERIMENT III.

Rabbit I. White buck, 2500 grm.

10 a.m. Intraperitoneal injection of 3·5cc. sterile olive oil and immediately thereafter injection of 4000 million Staphylococcus Aureus.

Made a good recovery at first, 3 weeks later, however, began to emaciate and died 7 weeks after/

after injection.

Post.Mortem. A curious condition was found in the abdomen. Large white masses resembling cream cheese were found in the abdomen covering the viscera. On section these were found to consist of masses of degenerated leucocytes, fibrin, staphylococci and oil globules. See Photo. (1) Plate XI.

A section of the diaphragm showed the presence of oil in the phrenic lymphatics. See Photo. (2) Plate XI.

Rabbit II. Control.

10 a.m. 4000 million staphylococcus Aureus by intraperitoneal injection. Died 16 hours after injection.

P.M. General peritonitis.

Culture from heart blood gave a vigorous growth of Staphylococcus Aureus.

EXPERIMENT IV.

Rabbit I. Albino doe, 2350 grms.

10·30 a.m. Intraperitoneal injection of 4cc. sterile olive oil, and some minutes later 4500 million Staphylococcus Aureus. Apparently recovered at/

at first but then began to emaciate rapidly. Rabbit was therefore killed 16 days after injection.

P.M. On opening abdomen, a large cake of cream cheese like material, ½" thick, was found covering over the viscera in the right half of the abdomen, and extending from the diaphragm down into the right half of the pelvis. A section of this substance showed it to be exactly similar to that found in Rabbit I. of Experiment IV.

Section of the diaphragm showed presence of oil globules in its lymphatics (See Photos) Plates IX and X.

Rabbit II. Albino doe, 2100 grm.

11 a.m. Intraperitoneal injection of 4500 million Staphylococcus Aureus.

Died 13 hours after injection.

These two experiments demonstrated how oil in the abdomen may apparently avert an immediately fatal issue by retarding absorption of organisms, but also that it may to some extent interfere with the return to normal by its tendency to weld the solid elements in the peritoneal effusion into cheesy masses. These results make one doubt Glimm's statement/

statement that the restitutio ad integrum occurs more rapidly in cases of peritonitis with oil than in those without it.

EXPERIMENT V.

Rabbit I.

10 a.m. Intraperitoneal injection of 4cc. sterile olive oil followed 5 minutes later by 1500 million living Staphylococcus Aureus.

Death 17 hours after injection.

P.M. Much free oil floating in peritoneal effusion and all viscera covered with a fine film of oil.

Section of diaphragm revealed presence of oil globules in the lymphatics. See photo.(2) Plate XII

Rabbit II. Control.

10 a.m. Intraperitoneal injection of 1500 million Staphylococcus Aureus.

Died 16½ hours after injection.

P.M. General peritonitis. Culture from heart blood gave a growth of Staph. Aureus.

EXPERIMENT VI.

Rabbit I.

12 noon. Intraperitoneal injection of 2cc. sterile/

sterile olive oil and immediately thereafter 3000 million Staphylococcus Aureus.

Death 48 hours later.

P.M. General peritonitis with free oil in abdomen. Culture from heart blood = no growth.

Rabbit II. Control.

12 noon. Intraperitoneal injection of 3000 million Staphylococcus Aureus.

Death 48½ hours later.

P.M. General Peritonitis. Culture from Heart-blood = growth of Staphylococcus Aureus.

EXPERIMENT VII.

Rabbit I. 11 a.m. Intraperitoneal injection of 3cc. of olive oil and immediately thereafter of 4000 million Staphylococcus Aureus.

Death 14 hours later.

P.M. General peritonitis, with free oil floating about. Culture from heart blood = growth of Staphylococcus Aureus.

Rabbit II. Control.

11 a.m. Intraperitoneal injection of 4000 million Staph. Aureus. Died 15 hours later.

P.M. General Peritonitis. Culture from heart-blood = growth of Staph. Aureus.

EXPERIMENT/

EXPERIMENT VIII.

Rabbit I.

12 noon. Intraperitoneal injection of 4·5cc. sterile olive oil and of 1000 million living Staphylococcus Aureus.

Death 9 hours later.

Culture from heart blood = no growth.

Section of diaphragm showed many lymph vessels filled with oil.

Rabbit II. Control.

12 noon. Intraperitoneal injection of 1000 million Staphylococcus Aureus.

Death 13 hours later.

Culture from heart blood = growth of Staphylococcus Aureus. Photo (1) Plate XII

EXPERIMENT IX.

Rabbit I.

10·30 a.m. Intraperitoneal injection of 4cc. sterile olive oil and then of 2500 million Staphylococcus Aureus. Animal was ill for 2 days but recovered. Killed on 21st. day after injection. Peritoneum had not regained its normal appearance, and there was some mucilaginous-like fluid in the cavity. No free oil could be detected.

Sections/

Sections of diaphragm showed oil still present in the lymph vessels. Plate XI (3)

Rabbit II. Control.

10·30 a.m. Intraperitoneal injection of 2500 million Staph. Aureus.

Recovery. Killed 21 days later.

A small abscess on the deep surface of the anterior abdominal wall and some recent adhesions at this point. Peritoneum otherwise normal.

EXPERIMENT X.

Both the rabbit receiving the oil and the control died 23 hours after the injection of 5500 million Staphylococcus Aureus.

INTRAPERITONEAL INJECTION of BACTERIA with SUBSEQUENT INJECTION of STERILISED OLIVE OIL.

EXPERIMENT XI.

Rabbit I.

10 a.m. Intraperitoneal injection of 1000 million Staph. Aureus.

1 p.m. Intrap. injection of 5cc. sterile olive oil. Apparently recovered at once but emaciated and/

and died 2 weeks later with chronic Peritonitis and subpleural abscesses.

Rabbit II. Control.

10 a.m. Intraperitoneal injection of 1000 million Staphylococcus Aureus.

Recovery.

EXPERIMENT XII.

Rabbit I.

1 p.m. Intraperitoneal injection of 3000 million Staphylococcus Aureus.

8 p.m. Intrap. injection of 5cc. sterile olive oil. Death 54 hours later.

P.M. General peritonitis. Culture from heart blood = no growth.

Rabbit II.

1 p.m. Intrap. injection of 3000 million Staph. Aureus. Death 33 hours later.

P.M. Culture from heart blood = no growth.

From these experiments it is quite clear that very little protection against death from peritonitis is given by the intraperitoneal use of sterile oil, either just before, or subsequent to the start of the peritoneal infection.

It/

It will be noted that a septicaemis was of less frequent occurrence in the animals which were given oil, but yet the death rate in those animals was not much less than in those which got no oil. This is but another proof that a fatal issue in peritonitis is due to toxaemia, and not to septicaemia, and upsets the rationale of this form of treatment. The occurrence of oil embolism was carefully looked for but never discovered in any of the fatal cases.

S U M M A R Y.

1. Sterile oil injected into the peritoneal cavity is slowly absorbed by the lymphatics, oil globules may still be found free in the peritoneal cavity 10 - 15 days after the injection.

2. The oil may remain for several months in the lymphatics of the diaphragm.

3. The presence of oil does not interfere with the cellular reaction in the peritoneal effusion in cases of peritonitis.

4. The presence of oil does not prevent but may somewhat retard the restitutio ad integram after peritonitis.

5./

5. Oil embolism is so far as we at present know merely a theoretical danger.

6. In sudden, severe and generalised infections of the peritoneal cavity the pouring of oil into that cavity may help to avert a rapidly fatal issue by retarding absorption of organisms through the lymphatics into the blood-stream.

7. That the routine use of oil in peritoneal infections for the above mentioned purpose is not warranted.

THE USE of OIL in the PERITONEAL CAVITY as a MEANS to PREVENT POST-OPERATIVE ILEUS in CASES of PERITONITIS.

Post-operative Ileus as a cause of death in Acute Peritonitis.

Oil as an Inhibitor of Peritoneal Adhesions.

Experimental evidence on the use of oil to prevent adhesions in Peritonitis.

Examples of the Clinical application of this method.

POST/

"POST - OPERATIVE ILEUS"

AS A CAUSE OF DEATH IN ACUTE PERITONITIS.

It is well recognised that in almost every post mortem on cases dying after operations for acute peritonitis, the cause of death is found to be some condition which might have been treated surgically, and that either at the operation the whole extent of the infection was not recognised and treated, or subsequent to the operation some spread of the infection had occurred, and this was not diagnosed in time to allow of successful secondary intervention. Extreme distension and "paralysis" of the gut is also a very common post mortem finding in such cases, and it is evident that the patient died as much from the intestinal as from the peritoneal toxaemia. This distension of the gut is generally regarded as being due to a paresis of the bowel wall, the result of toxaemia.

But I venture to suggest that in many of the fatal cases where the symptoms of post-operative ileus set in, the distension is not due entirely or even mainly to a toxaemic paresis of the gut, but that a definite obstructive cause affecting some part of the small intestine, generally the lower part, is present./

present.

This obstructive cause I believe to be the adhesion of the loops of the Ileum to each other, to the caecum or to the pareital peritoneum in the infected area. Were the distension paralytic in nature the whole of the small intestine would participate in it, but this is by no means always the case.

During the past six months I have had occasion to observe the course of and to follow to the post-mortem room, four cases of peritonitis due to appendicitis, in each of which symptoms of intestinal obstruction set in after operation for the acute condition, and in each of which at the post mortem examination, the upper two-thirds or three-fourths of the small intestine was found enormously distended, whilst the lower part of the small intestine was more or less collapsed, the different loops being bound together by recent adhesions either in the Pelvis or in the caecal region, and in each a more or less definite kink was demonstrable where the distended bowel joined the collapsed portion. These cases, (which I shall record in brief here) showed conclusively that recent plastic adhesions are sufficient in some cases to cause obstruction.

I have succeeded in producing exactly the same condition experimentally in a rabbit.

CASES/

CASES ILLUSTRATING
POST - OPERATIVE ILEUS
WITH A DEFINITE OBSTRUCTIVE CAUSE.

CASE I J.R. Male aet. 31.

History. Pain in right side of abdomen for 4 days. For 2 days pain very severe, very little vomiting. On admission to hospital patient presented marked resistance and tenderness in the right Iliac region of his abdomen, and a leucocytosis of 18000. Immediate operation. An abscess with a gangrenous appendix in it was opened. The appendix was removed and the cavity drained with a Mickulicz tampon. For two days following operation there was persistent vomiting and no passage of flatus.

During the next six days the vomiting persisted, only a very little flatus came away occasionally, and the abdomen became very distended.

On the 8th day the abdomen was re-opened. Great distension of the upper part of the small intestine was seen, whilst the lower part of Ileum was collapsed. A loop of Ileum was found strangulated by some recent adhesions to the left of the caecum. Enterectomy was performed but patient died the following morning.

P.M./

P.M. Enormous distension of jejunum. Ileum collapsed and matted by recent adhesions near the appendix region.

CASE II. G.T. Male adt 26.

History of pain in the lower half of the abdomen for 56 hours with persistent vomiting.

On admission to hospital found to have marked abdominal tenderness in the right Iliac and suprapubic regions. P. 90. T. 99.

Immediate operation. A very long appendix dipping over the brim and adherent to the wall of the pelvis was removed. Keiths tubes introduced through a suprapubic opening and the pus which was present in the pelvic and iliac fossa douched out.

For the two days following operation, there was persistent vomiting and practically no passage of flatus, and the abdomen became very much distended. On the evening of the 2nd. day a gastrostomy was performed; the appendix wound was explored but no distended bowel found. The patient died the following morning.

P.M. Enormous distension of jejunum and upper part of ileum. One of the lower loops of ileum was adherent to the raw surface on the pelvic wall whence/

whence the appendix had been removed. Ileum beyond this loop was collapsed; great gut more or less collapsed.

No generalised peritonitis.

CASE III.

J.T. Male aet. 13.

History of constant abdominal pain and vomiting for 5 days before admission to hospital.

On admission, the boy looked very ill. There was considerable general tumidity of the abdomen, marked tenderness in the right iliac and suprapubic regions. Immediate operation. An abscess in the right iliac region was opened and drained, another abscess in pelvis evacuated, and a gangrenous appendix removed from a third abscess in the retro-caecal region. For 3 days after the operation, there was almost constant vomiting, no passage of flatus, and progressive distension of the abdomen.

On the third day, the abdomen was freely opened in the mid line. Greatly distended coils of jejunum presented, and five of these coils were opened and drained by rubber tubes. A loop of Ileum which presented at the former appendix wound was/

was opened, but was found not to be distended.

Death one day later.

P.M. General peritonitis, an abscess surrounding the spleen and under surface of the liver.

The ileum was more or less collapsed, and was matted by recent adhesions, and above this portion the bowel was greatly distended. Colon collapsed. See Photo. Plate XIV.

CASE IV.

W.T. Male aet. 18.

History of abdominal pain and vomiting for 2 days.

For the first 36 hours pain had been localised to the lower half of the abdomen, then it had suddenly become generalised and the abdomen became distended.

On admission to hospital, patient presented all the symptoms of a general peritonitis.

Immediate operation. Abdomen opened freely in mid line, an absolutely generalised peritonitis found and a gangrenous appendix removed. The abdomen was douched out, and the pelvis and the appendix region drained.

Patient did well for 24 hours then intractable vomiting set in and abdomen became greatly/

greatly distended. On the evening of the 2nd day a coil of ileum was opened but little came away. The vomiting and distension persisted, and the patient died on the 4th. day.

P.M. Enormous distension of the jejunum, the lower loops of Ileum collapsed and adherent in the pelvis. Peritontiis in process of recovery.

From these cases, it is evident that recent plastic adhesions may and often do cause definite intestinal obstruction, and the adhesive property of the peritoneum, though invaluable in its power of localising infections, may operate against the patient by arresting the passage of intestinal content.

The question arises here, whether, in cases such as those cited above, it would be advisable when the obstructive symptoms appear to freely open the abdomen, to separate all the adherent loops of ileum and to cover the separated surfaces with some oily substance to prevent further adhesion.

Whether the separation of adherent surfaces, by exposing abraded areas and hastening absorption of toxins, would do more harm than the obstruction was previously/

previously doing is a question which requires further investigation.

In any case it is certain that once the obstructive symptoms have become established the mere opening and draining of the bowel above, though always doing some good, seldom avails to save the patient's life.

Further, if we consider the usual sequence of events during and after an operation for General Suppurative peritonitis, we again see how this plastic property of the peritoneum may militate against the patient's chances of recovery.

In such a case:- The abdomen is opened and the intestines are found floating in purulent fluid; this is washed or swabbed out and drains are left in the pelvis and possibly in both flanks.

For the first day after operation, a good deal of purulent fluid escapes from the tubes, but thereafter, surprisingly little discharge comes away. The abdomen becomes distended, there is persistent vomiting, and the patient dies say 48 - 60 hours after the operation. At the post mortem, the coils of intestine are found glued together by plastic adhesions, and between the coils numerous small pockets/

pockets of pus are disclosed. It is evident that the tubes have drained only a small area in their immediate vicinity. When, at the operation, the pus was allowed to escape the inflamed peritoneal surfaces came together, and adhered, to the ruin of all drainage and to the detriment of the patient.

Can we do anything to obviate this perverted action of an otherwise beneficial property. I believe that here we have the indication for the use of sterile oil in the abdominal cavity.

OIL AS AN INHIBITOR OF PERITONEAL ADHESIONS.

Since the opening of the era of abdominal surgery, the danger of adhesions following abdominal operations has been recognised, and very numerous precautions and many different agents have been recommended to prevent this unfortunate sequel.

Fromme[32] believed that some infection and not only abrasion of the serosa was necessary for the production of adhesions.

Graser and Rissman[33] showed on the contrary, that adhesion may follow simple abrasion of the peritoneum. In my own experiments, I have found that abrasion without infection may, but seldom does produce/

produce adhesion.

Believing in the importance of early peristalsis in preventing adhesion, many writers (Lawson Tait, Martin, Championiere Heidenhain and others) have recommended the early exhibition of purgatives after abdominal operations.

More recently Vogel[34] has advocated the routine use of Physostigmine for this purpose. The value of such treatment is doubtful and it is often contra-indicated.

Stern[35] experimented with the intraperitoneal use of sterile vaseline, olive oil, and collodion, but found none of real value. Olive oil he found to produce great inflammatory reaction in the peritoneum and he considered it harmful. His oil, however, must either have contained free fatty acid or must not have been sterile to produce the result he describes.

Duschinsky[36] tried inserting pieces of gold beaters skin; Lauenstein[37] experimented with silk-protective, but neither proved of practical value.

Vogel obtained some success with a mucilage of gum Arabic.

Busch and Bibergeil,[38] in an elaborate research/

research tested olive oil, Gum Arabic, Paraffin, lanolin, gelatine, Corragen, Agar and fibrolysin, but found none of them of very great value. They used oil only once, however, and with regard to it their results are not of much value.

More recently Blake,[39] as the result of a clinical and experimental study on the use of oil for the prevention of peritoneal adhesion, concludes that the presence of oil does tend to prevent denuded or inflamed peritoneal surfaces from adhering and that it may be used in the peritoneal cavity of patients in moderate quantity without danger.

All the reported work, one finds, however, deals with the prevention of adhesions after abdominal operations, having regard to the remote ills which are liable to follow their formation. I have been able to find no record of the intraperitoneal administration of oil in peritonitis to avert the immediate dangers of fresh plastic adhesions. It is with the latter question that we have now to deal.

EXPERIMENTAL EVIDENCE.

The following experiment was carried out to test whether the intraperitoneal administration of/

of oil would prevent post-operative adhesions.

The procedure was as follows:-

Three rabbits were operated on. In each the abdomen was opened, the appendix was removed, the peritoneum over the lower part of the Ileum and over the caecum was abraded by rubbing with dry sterile gauze and then about $\frac{1}{50}$ part of a lethal dose of the Staphylococcus Aureus suspended in saline was injected over the abraded surfaces, whereupon the abdomen was closed.

In Rabbit I. the above procedure alone was carried out.

In Rabbit II. before closing the abdomen, 5cc. of sterile vaseline oil was poured in.

In Rabbit III. an intraperitoneal injection of sterile vaseline oil had been given fourteen days before carrying out the above procedure.

Rabbits II. and III. made prompt recoveries and on opening the abdomen of each eight days later, the abraded surfaces had healed over without forming any adhesions.

Rabbit I. (the largest and strongest of the three) was very dull the day following the operation, and was found dead on the morning of the 2nd. day. It had great distension of the abdomen./

abdomen.

P.M. On opening the abdomen, enormously distended coils of jejunum presented; the ileum was seen to be collapsed and empty. See photo.

The caecum was comparatively empty and was adherent to the anterior abdominal wall.

On tracing the distended jejunum downwards, one found that it had adhered to the caecum at one point. Here it had kinked on itself and led to the obstruction. Beyond this adhesion which was quite recent and which broke down with the slightest traction on it, the bowel was collapsed.

This experiment, confirming as it did what one had seen in the human subject, was of great interest from a pathological standpoint, but also, in that no adhesions formed in the animal receiving the oil, of importance from the therapeutic standpoint. One now felt justified in advocating the use of sterile oil in cases of general peritonitis in the human subject. Two somewhat similar experiments were performed on cats and in both of these, though the results were not so striking and all the animals recovered, at the second operations there were far fewer adhesions found in the animals which had received oil than in those which had not.

THE CLINICAL USE OF OIL IN GENERAL PERITONITIS TO PREVENT POST-OPERATIVE ILEUS.

CASE I.

Mrs P. Aet. 46.

Admitted to Hospital on March 8th, 1909.

In good health up till March 5th. when suddenly seized with acute abdominal pain and vomiting. In spite of Morphia, pain continued as also did the vomiting for the next 3 days. No flatus was passed and castor oil produced no action of the bowels.

The abdomen became more and more distended until admission to Hospital.

STATE on ADMISSION.

Patient a thin woman with sallow complexion, and pinched and anxious expression.

P. 140. T. 98·4. R. 24.

Great general distension of the abdomen which, however, is fairly soft and nowhere very tender.

Retains 2½ pints of fluid per rectum.

OPERATION.

Abdomen opened in mid line. Straw-coloured fluid escaped and deeply congested and enormously/

enormously distended small intestine presented. The pelvic colon was found collapsed. The caecum was sought for but could not be found. Eventually it was discovered that a portion of the caecum had herniated through the Foramen of Winslow and being strangulated there, was practically gangrenous within the lesser sac. It could not be reduced through the foramen. The gastro hepatic omentum was torn through and the distended portion of caecum punctured with a trocar and canula. A small tear in the caecum occurred and considerable soiling of the abdomen with faecal matter occurred. The collapsed caecum was extracted through the foramen of Winslow and along with portions of ascending colon and the ileum, resected, and the two open ends of the bowel brought out in the right lumbar region.

The operation was prolonged and considerable exposure of the viscera could not be avoided. It was found on returning the coils of small intestine to the abdomen, that they had lost their lustre and already showed a tendency to adhere and it was thought to be a suitable case for the use of oil. Accordingly, after inserting, but before tying the sutures for the abdominal wound, two/

two ounzes of sterilised vaseline oil were poured into the abdomen and distributed between the coils of small intestine.

Pelvic drainage was practiced.

Patient was pulseless by the conclusion of the operation, and required transfusion on the table.

She survived for 37 hours.

P.M. A considerable quantity of free oil was found in the peritoneal cavity. The surface of the intestines was covered with a fine glistening coating of oil and no adhesions had occurred.

Portions of the muscle and tendon of the diaphragm and of the peritoneum in different regions of the abdomen were removed for microscopic investigation.

Photo micrographs of these are appended.

See Photos 1 to 4 Plates XV and XVI.

The organs showed the changes associated with death from intestinal toxaemia.

This case confirmed the view that sterile oil does help in preventing peritoneal adhesions and that it may be useful in generalised infections.

CASE II. Generalised B. Coli Peritonitis from Appendicitis.

Maggie/

Maggie L. Aged 24

Admitted March 17th. 1909.

HISTORY.

Whilst in bed in a medical ward of the Hospital under treatment for gastric ulcer, patient on the morning of 16th March began to suffer from pain in the lower part of the abdomen and vomited. Pain and vomiting continued all day and through the following night, and at 3.p.m. on the 17th pain became suddenly much more intense and generalised over the whole abdomen. A diagnosis of perforated gastric ulcer was made and patient was transferred to a surgical ward.

OPERATION.

at 8.30p.m. on 17th March.

Mesial incision in Epigastric region purulent fluid round stomach and over the liver but no perforation or evidence of ulcer found in any part of the stomach.

Incision prolonged downwards to within 3 inches of Pubes. A gangrenous perforated appendix was found dipping over the brim of pelvis. It was removed, the abdomen was very thoroughly washed out, and a pelvic drain put in through a small supra pubic opening. The sutures for/

for the long mesial abdominal wound were inserted but before tying them two ounzes of sterilised vaseline oil were poured into the abdomen and distributed between the coils of intestine. The wound was then closed.

Films from the pus showed the presence of a colon like Bacillus and cultures showed this to be the Bac. Coli Communis. Patient did wonderfully well during the first 6 or 7 days, the bowels acting daily though the pulse remained above 110. On the 8th day she complained of pain on the left side of the abdomen. This remained and on the 10th. day a definitely tender area was present behind the lower half of the left Rectus muscle.

Under general anaesthesia this was cut down on and a localised collection of foul pus found just under the abdominal wall. Numerous oil globules floated out in the pus. Patient improved greatly after this but 10 days later another small collection of pus was evacuated from just under the abdominal wall to the right of the operation scar. Some oil globules were seen floating in the pus. Thereafter patient made an uninterrupted recovery.

This case was of interest for several reasons/

reasons. Firstly it is one of the few cases in which recovery has taken place in a case of absolutely generalised Peritonitis secondary to appendicitis (The pus was actually seen round the liver and under the diaphragm and the Bac. Coli. was grown from this pus).

Secondly there was a remarkable absence of abdominal distension so frequently seen in such cases. Flatus was passed freely some hours after operation, and the bowels acted on the following morning.

S U M M A R Y.

1. In peritoneal infections the plastic adhesion of intestinal coils, while limiting the spread of infection, may cause death from intestinal obstruction.

2. After operation for general peritonitis the adhesion of inflamed intestinal coils constitutes a danger to the life of the patient, firstly by impeding free drainage, secondly by interfering with free intestinal peristalsis.

3. Sterile vaseline oil applied to inflamed peritoneal surfaces tendsto prevent their adhesion.

4. It may be used with advantage in cases of general peritonitis.

5. The oil is non-irritating, readily sterilized and so far, no ill effects, such as oil embolism, have been reported.

SERUM THERAPY IN PERITONITIS.

RATIONALE of the METHOD.

The patient suffering from a severe peritonitis presents all the signs of a profound Toxaemia. If his resistive powers have not been overwhelmed by the poison, they are doing their utmost to overcome the infection.

Granted that we have done our utmost in the local treatment of the infected area, have we any means whereby we may aid the body to successfully resist the Toxaemia? We may infuse large quantities of saline solution and so dilute the Toxin and thereby effect much good. May we gain anything from the injection of a small dose of a suitable vaccine? The answer to this question must be in the negative. In several experiments and in two cases one has tried the giving of a suitable vaccine during the course of an acute peritoneal infection but without any satisfactory result. It is hardly to be expected that the injection of a small dose of dead bacteria can effect much in the patient who is obviously struggling against an enormous dose of the living bacteria. The negative phase produced by the vaccine is sufficient in itself to contra-indicate/

contra-indicate its use in severe cases, where every hour is of moment.

Nucleic acid because it produces a preliminary leuco-paenia is likewise contra-indicated. On the other hand we believe that in the blood serum of a patient just recovered from an acute infection, there are antibodies in excess, and we might reasonably hope to help the patient suffering from the profound toxaemia of an acute Peritonitis, by injecting into his blood-stream some of the blood serum of a patient who had just recovered from a Peritonitis due to the same Bacterium. With a view to testing of what value this method might be, one first conducted a series of experiments on Rabbits.

TECHNIQUE OF SERUM EXPERIMENTS.

Having determined approximately the lethal dose of the bacterium to be used, two rabbits were each given an intra-peritoneal injection of slightly more than the lethal dose of this bacterium.

At the same time from 10 - 20 cc. of blood was drawn off into a test tube with full aseptic precautions, from the auricularvein of a third rabbit which had just recovered from a peritonitis due to the/

the same bacterium. This test-tubeful of blood was then put in the incubator at 37°C. to favour rapid clotting and separation of the serum.

Several hours (from 2½ - 9 hours) later when peritonitis was established in the two rabbits, the serum obtained from the blood of the recovered animal was injected into the auricular vein of one of the rabbits which had peritonitis. The course of the peritonitis and the fate of the animal was then carefully observed in each case.

The amount of serum injected varied from 2½cc. to 7cc. in the different experiments and it was always fresh, i.e. it was always obtained from a living animal a few hours before, and lastly it was never allowed to cool, being kept in the incubator at 37°C from just after its withdrawal from the recovered animal till just before its injection into the animal with peritonitis. (The two latter points I believe to be of importance.)

The bacteria used in these experiments were B. Coli Communis, Staphylococcus Aureus and a combination of Staph. Aureus and Pneumococcus. This combination of cocci was used because one had accidentally found that it produced in rabbits a purulent plastic type of peritonitis resembling closely that seen in the/

the human subject.

EXPERIMENT I.

7:12:08. Two full-grown Rabbits.

10.30 a.m. Intra-peritoneal injection of 2000 million Staphylococcus Aureus given to each rabbit.

4.30 p.m. Both rabbits look dull.

Rabbit I given into its auricular vein an injection of 4cc. of blood serum from a rabbit which had recovered (7 days) from peritonitis due to the same strain of Staph. Aureus.

Rabbit I. made perfect recovery.

Rabbit II. which got no serum died 30 hours after the induction of peritonitis.

P.M. General peritonitis; culture from heart blood = no growth.

EXPERIMENT II.

3:1:09. Two full-grown Rabbits.

5 p.m. Intra-peritoneal injection of 2500 million Staphylococcus Aureus to each rabbit.

10.30 p.m. Rabbit I. given intravenously an injection of 4.5cc. of serum from a rabbit which had recovered ($2\frac{1}{2}$ days) from a similar Staphylococcal peritonitis.

Rabbit I. made complete recovery.

Rabbit II. (control) died 11 hours after the induction of peritonitis.

P.M./

P.M. General peritonitis with lymph and sero-pus; culture from heart blood = growth of Staph. Aureus.

EXPERIMENT III. Two full-grown Rabbits.

3:2:09

4 p.m. Each rabbit given 2500 million Staph. Aureus by intra-peritoneal injection.

7·30 p.m. Rabbit I. received intravenous injection of 4cc. of blood serum of a rabbit recovered (5 days) from a similar peritonitis.

Rabbit I. made complete recovery.

Rabbit II. died 5 days after the induction of peritonitis.

P.M. General purulent peritonitis.

Pleurisy with effusion on both sides.

Purulent pericarditis and pyaemic abscesses in liver and kidneys.

Staphylococcus Aureus was grown on culture from the various abscesses.

EXPERIMENT IV.

4:1:09

10 a.m. Two rabbits were each given an intra-peritoneal injection of 4000 million Staphylo-coccus Aureus.

11 a.m. Rabbit I. given intravenous injection of blood serum from a rabbit recovered (2 days) from/

from a Staph. peritonitis.

Both rabbits died within 16 hours of inducing the peritonitis.

In the following two experiments a mixed infection of Staphylococcus Aureus and Pneumococcus was used. This mixture produced a purulent plastic peritonitis very like the human type. In both experiments the injection of the serum was deferred until the symptoms of peritonitis were well established.

EXPERIMENT V.

5:1:09

4 p.m. Each of two rabbits given an intra-peritoneal injection of a bacterial emulsion consisting of 2500 million Staph. Aureus and 100 million Pneumococcus.

6:1:09

1 a.m. Rabbit I. given intravenously 7cc. of blood serum obtained from a rabbit which had recovered (3 days) from a similar peritoneal infection.

Rabbit I. made complete recovery.

Rabbit II. (control) died 30 hours after the intra-peritoneal injection.

P.M. Well-marked plastic peritonitis with sero-pus, culture from peritoneum gave growth of Staph. Aureus and Pneumococcus.

Culture/

Culture from Heart blood = negative.

EXPERIMENT VI.

7:1:09

4p.m. Two rabbits each given an intra-peritoneal injection of 2000 million Staph. Aureus and 100 million Pneumococcus.

11·30 p.m. Both rabbits very dull.

Rabbit I. given intravenously 4.5 cc. of blood serum from a rabbit recovered (4 days) from a similar infection.

Rabbit I. made a perfect recovery.

Rabbit II. (control) died 28 hours after the intra-peritoneal injection.

P.M. General peritonitis with much lymph and sero-pus.

Culture from peritoneum = Staph. Aureus and Pneumococcus.

Culture from heart blood = pneumococcus.

In the following four experiments Bacillus Coli Communis was the organism used. The object of this set of experiments was to test whether the intra-venous administration of the serum of a recovered animal was as effective in promoting recovery in a type of peritonitis where septicaemia is the rule as it was shown to be in one where septicaemia is the exception.

EXPERIMENT VII.

10:/

EXPERIMENT VII.

10:1:09

10·30 a.m. Two rabbits were each given an intra-peritoneal injection of 2500 million B. Coli.

2·30 p.m. Rabbit I. given intravenously 6cc. of blood serum from a rabbit recovered (2 days) from a similar infection.

Rabbit I. died 24 hours after the intra-peritoneal injection.

Rabbit II. (control) died 12 hours after injection.

P.M. A vigorous growth of B. Coli was obtained from the heart blood in both cases.

Experiments VIII, IX and X. were designed to test also at what time the serum of the recovered animal is most effectively protective, e.g. whether the serum of an animal which has recovered from a peritonitis induced only 2 days before the serum was withdrawn, was as effectively protective as the serum taken from an animal a week or more after recovery from peritoneal infection.

EXPERIMENT VIII. Three Rabbits.

14:1:09

6 p.m. Each rabbit given an intraperitoneal injection of 1000 million B. Coli.

12 midnight. Rabbit I. given an intravenous injection of 5cc. of blood serum from rabbit recovered (2 days) from similar peritonitis.

Rabbit II. given intravenous injection of serum from/

from a recovered animal (6 days).

Rabbit III. control (no serum).

Rabbit I. was ill for 3 days but recovered.

Rabbit II. died 24 hours after the intra-peritoneal injection.

Rabbit III. died 19 hours after injection.

P.M. A vigorous growth of B. Coli obtained on culture from heart blood of Rabbits II and III.

EXPERIMENT IX. Three Rabbits.

15:1:09

3 p.m. Each rabbit given an intra-peritoneal injection of 1800 million B. Coli.

5.15 p.m. Rabbit I. given intravenously 5cc. of blood serum from a (5 days) recovered animal.

Rabbit II. given 5cc. blood serum from a (7 days) recovered animal.

Rabbit III. control (no serum).

Rabbit I. died 12 hours after injection with a B. Coli septicaemia. (vigorous growth of B. Coli from heart blood).

Rabbit II. made complete recovery.

Rabbit III. was ill for 2 days but recovered.

EXPERIMENT X. Three Rabbits.

17:1:09

6 p.m. Each rabbit given intra-peritoneally 800 million B. Coli.

9/

9 p.m. Rabbit I. given 2.5cc. blood serum from a (4 days) recovered animal.

Rabbit II. given 3.5cc. serum from an (11 days) recovered animal.

Rabbit III. control (no serum).

All three rabbits recovered so on.

20:1:09 Each rabbit given an intra-peritoneal injection of 1600 million B. Coli.

Rabbits I and II. made prompt recoveries.

Rabbit III. was ill for 2 days but recovered.

From these three experiments one concluded that the serum treatment was not so helpful in rabbits for B. Coli, as for the Staphylococcal infections and, therefore, that its action was probably more anti-toxic than anti-bacterial and thus all the more suitable for use in human peritoneal infections.

One could not say that the blood serum of the recovered animal was richer in anti-bodies just after recovery from the symptom of peritonitis than it was a week or more later. The evidence on this point, however, was by no means conclusive.

It had previously been shown by Loeffler and Abel that the injection of the serum of a normal animal into the blood-stream of one suffering from an acute infection gives little or no protection. To confirm/

confirm this point, however, the following experiment was carried out.

EXPERIMENT XI. Three Rabbits.

20:1:09

2 p.m. Each rabbit given an intra-peritoneal injection of 2500 million Staphylococcus Aureus.

6 p.m. Rabbit I. given intravenously 5.5cc. blood serum from a rabbit recovered (3 days) from a similar peritonitis.

Rabbit II. given intravenously 5cc. blood serum from a normal rabbit.

Rabbit III. control (no serum).

Rabbit I. made a perfect recovery.

Rabbit II. died 26 hours after the induction of peritonitis.

Rabbit III. died 18½ hours after injection.

P.M. Culture from heart blood of rabbits II and III. gave no growth.

As this experiment but confirmed the work of previous investigators, it was thought to be unnecessary to repeat it.

SUMMARY/

SUMMARY OF RESULTS OF SERUM THERAPY IN PERITONEAL INFECTIONS OF RABBITS.

	NATURE of PERITONITIS	No. of CASES	RE-COVERIES	DEATHS
Serum	Staphylococcal	6	5	1
No serum	"	6	0	6
Serum	Mixed Staphylococcal	4	4	0
No serum	and Pneumococcal	4	2	2
Serum	B. Coli	6	4	2
No serum	"	3	2	1

If we take the two first mentioned types of peritonitis we see that in the animals receiving the anti-serum the death rate was but 10% whilst in the animals not treated with anti-serum the death rate was 80%. These facts are sufficiently striking to warrant one in adopting this method of treatment in bad cases of peritonitis in the human subject.

EFFECT of HEATING at 57°C. for HALF AN HOUR on the PROTECTIVE PROPERTIES of the SERUM of the RECOVERED ANIMAL.

One now wished to know whether the serum would be as effective in its protective power were it kept for some length of time and whether one could thus keep a stock of sera for use in different types of peritoneal infection. If none of the protective properties were lost on heating for 30 minutes at 57°C then it was probable that the sera would retain their/

their value though kept in vitro for some time. This would naturally allow of a much wider clinical application of the method than if only fresh serum could be used.

The following experiments were accordingly carried out.

EXPERIMENT XII.

Three Rabbits = Rabbit I. 2050 gms (serum)
" II. 2300 " (heated serum)
" III. 1850 " (control)

21:1:09

10 a.m. Each rabbit given 3000 million Staphylococcus Aureus intra-peritoneally.

4.30 p.m. Rabbit I. given intravenously 4cc. of serum of a rabbit recovered (2 days) from a similar peritonitis.

Rabbit II. given intravenously 4cc. of the same serum which had been kept at 57°C. for 30 minutes.

Rabbit III. control (no serum)

Rabbit I. made complete recovery.

Rabbit II. died 14 hours after the intraperitoneal injection.

Rabbit III. died 19 hours after the intraperitoneal injection.

P.M. Both II. and III. showed general peritonitis. Culture from heart blood in II. gave growth of Staph. Aureus. No growth in culture from III.

EXPERIMENT/

EXPERIMENT XIII. Three Rabbits.

Rabbit I. wt. 2500 grms (serum)
" II. " 2300 " (heated serum)
" III. " 2200 " (control)

23:1:09

3 p.m. Each rabbit given an intra-peritoneal injection of 2000 million of Staph. Aureus and 5 million of Pneumococcus.

6 p.m. Rabbit I. given intravenously 4cc. of blood serum of animal recovered (8 days) from a similar infection.

Rabbit II. given 3·5cc. of the same serum heated for 30 minutes at 57°C.

Rabbit I. made complete recovery.

Rabbit III. was ill for one day but recovered.

Rabbit II. died 30 hours after the intraperitoneal injection.

P.M. General peritonitis.

Culture from heart blood = sterile.

EXPERIMENT XIV. Three Rabbits.

Rabbit I. 2050 grms (serum)
" II. 2300 " (heated serum)
" III. 2150 " (control)

25:3:09

5 p.m. Each rabbit given an intraperitoneal injection of 2000 million Staph. Aureus and 50 million Pneumococci.

11 p.m. Rabbit I. given an intravenous injection of 4·5cc. of the blood serum of a rabbit recovered/

recovered (6 days) from a similar peritonitis.

Rabbit II. given intravenously 4·5 cc. of the same serum which had been heated at 57°C. for 30 minutes.

26:3:09

10 a.m. Rabbit I. quite well.

Rabbit II. very dull.

Rabbit III. (control) fairly well.

27:3:09

Rabbits I. and III. well.

Rabbit II. very dull.

Rabbit II. died 2½ days after injection.

P.M. General peritonitis with lymph and sero purulent fluid.

Culture from heart blood. = no growth.

Rabbits I. and III. recovered.

These experiments showed that by heating the serum its protective properties are destroyed and that instead of being beneficial it was apparently harmful when given to an animal with peritonitis.

They clearly show, moreover, that Wrights[40] contention that any beneficial effect that an anti-serum may have, lies in the fact that it is really a type of vaccine is unjustifiable, for heating is an essential in the preparation of any vaccine, and does not destroy its therapeutic value.

It/

It would seem evident then that for an anti-serum of this class to be of value it is essential that it be fresh and unheated at the time of injection.

SERUM THERAPY IN PERITONITIS.
ITS CLINICAL APPLICATION.

One has had the opportunity to apply serum treatment clinically to six human cases of peritonitis. One naturally selected only the severest cases of peritoneal infection, and in no case was this treatment commenced until the worst prognosis had been given and it was thought that all the methods of treatment generally employed in such cases would not avail to save the patient. All the cases treated had undergone a surgical operation for their complaint some hours or days before the serum treatment was commenced. Needless to say all other treatment was not stopped when the serum therapy was begun, it being only used as an adjuvant, and thus one could not dogmatise but merely speculate as to what credit or discredit belonged to the serum injections.

On the other hand by carefully watching these cases one could note how the hourly course of the signs and symptoms of the patients treated, was influenced/

influenced by the serum injection and particularly how their "GENERAL CONDITION" was affected by this form of treatment.

GENERAL METHOD of APPLICATION of, and TECHNIQUE EMPLOYED in SERUM TREATMENT.

From film preparations and cultures made at the time of operation the nature of the peritoneal infection was ascertained. If the case were doing badly and recovery was considered unlikely, another case was sought for in which a similar type of peritoneal infection had been successfully treated and in which recovery was assured. In the wards of an hospital of any size there could very seldom be any difficulty in finding such a case. The next step was to make sure that the recovering patient did not suffer from specific or other infectious disease and then to obtain his or her permission to withdraw a quantity of blood from a vein. (In no case was this permission refused me.) Having obtained the consent of the patient one sterilised the front of the elbow with alcohol and ether, and using a sterile needle and syringe withdrew from 20 - 70cc. of blood from the median Basilic vein. The blood was put into four sterile/

sterile testubes which were plugged and then left in the incubator at 37°C for from 3 - 6 hours. At the end of this time the serum which had separated was taken up in a sterile syringe and immediately injected with aseptic precautions into the median basilic vein of the patient whose life was in danger.

The serum was thus never allowed to cool between withdrawal and injection, being regarded as a living tissue and treated as such.

Five of the six cases treated received more than one injection and (with one exception) the serum was obtained fresh, as above described, for each injection.

As will be seen from the description of the cases which followed various types of pure and mixed infections were treated with corresponding sera. The size of the dose was only limited by the amount of serum obtainable, though from the work of Loeffler and Abel one inferred that a large quantity of serum is not essential.

CASE I. ACUTE SUPPURATIVE APPENDICITIS.

Boy J.M. aet. 12.

Admitted to Hospital on Nov. 19th, 1908.

Six days before admission he was seized with sudden/

sudden abdominal pain and vomiting, both of which symptoms persisted with slight intermissions until his removal to hospital. Had not passed flatus for 2 days and had emaciated greatly.

STATE on ADMISSION.

Child obviously very ill, face pinched eyes sunken; tongue dry and brown; P 110 feeble. General tumidity of the abdomen which does not move with respiration. Marked tenderness in right flank and all over the lower half of the abdomen.

OPERATION 1 p.m. two hours after admission.

A large abscess filling up the right iliac and lumber regions of his abdomen was opened, a gangrenous perforated appendix removed and through a suprapubic wound a large collection of foul smelling pus escaped from the pelvis.

A film made from the pus showed degenerated pus cells and swarms of a colonlike bacillus also a few chains of streptococcus. The abscess cavities were douched out and drained.

At 7 p.m. the same evening the child was very ill, P 124 very small, R 56, hands cold.

A very bad prognosis was given.

Accordingly/

Accordingly 65cc. of blood was withdrawn from the median basilic vein of a Mrs. M. who had recovered (20 days) from an acute suppurative appendicular peritonitis due to B. Coli. The blood was put in the incubator and at midnight 21cc. of the blood serum which had separated out was injected into the median basilic vein of the boy.

Next morning the child looked much better though the pulse was still 120.

The following day, pulse was 108 and it came down steadily, the child leaving hospital cured, at the end of 4 weeks.

The improvement in this boy's general condition some hours after giving the serum was very striking and one had no doubt that great help had been given by its injection.

CASE II. STREPTOCOCCAL PERITONITIS. (APPENDICULAR)

D.H. Young man. aet. 19.

Admitted to Hospital on Jan. 4th, 1909.

Two days before admission patient was suddenly seized with acute abdominal pain and vomiting. Pain became steadily more severe till admission. Had no sleep at night and vomited everything given/

given him by mouth. Had passed no flatus for 36 hours.

STATE on ADMISSION.

Powerful young man, flushed and breathing rapidly, tongue furred and rather dry.

P. 110. T. 101. R. 38.

General tumidity of the abdomen; abdominal movement greatly restricted, absent below umbilicus. Marked tenderness in right iliac region and in Suprapubic region.

OPERATION 1 hour after admission.

Mesial incision below umbilicus tubes introduced into the pelvis from which turbid sero pus escaped; pelvis washed out. Gridiron appendix incision now made, a gangrenous perforated appendix found lying in a partially walled off abscess in the right Iliac Fossa. Iliac Fossa and pelvis drained. Film made from pus at operation showed presence of many chains of streptococci and also a colon like Bacillus.

The following morning P.108. R. 38. but not looking well. Patient got steadily worse during the day and at 10 p.m. his pulse was 140 and a very bad prognosis was given.

30cc. of blood was obtained in the usual manner/

manner from a patient J.W, operated on 8 days before for suppurative appendicitis due to B.Coli and Streptococcus, and who was doing well. At 1 a.m. on Jan. 5th. 11cc. of serum obtained from this blood was injected into the median basilic vein of D.H.

Next morning patient had improved but his abdomen was still much distended and his pulse 124. Cultures made at the operation now showed the infection to be almost purely streptococcal only 3 or 4 colonies of B. Coli having grown compared with several hundred colonies of the streptococcus.

On the following day, Jan. 6th, patient was still very ill. P. 120. R. 38. Accordingly 30cc. of blood was withdrawn from the arm of J.S. who had been operated on 2½ days before for a localised pure streptococcal suppurative peritonitis due to appendicitis and who was now out of danger.

At 6.30 p.m. on 6th Jan., 10cc. of serum obtained from this blood was injected into the cephalic vein of D.H.

Next day patient was much improved, his tongue was moist, his pulse rate had fallen, and thereafter/

thereafter he made an uninterrupted recovery.

CASE III. SUPPURATIVE APPENDICITIS (STREPTOCOCCAL)

R.C. Young man, aet. 19.

Admitted to Hospital on January 25th 1909.

For 11 days previously had felt out of sorts, had intermittent abdominal pain, and had vomited occasionally. For the 3 days before admission, had been seriously ill with pain all over the lower abdomen and persistent vomiting, the vomit containing altered blood.

STATE on ADMISSION.

Thin and pale young man, eyes sunken, tongue dry. P. only 78. T. 98.4. Leucocytes 20000. Glycogen Reaction +

Lower half of the abdomen is tumid and is rigid. Marked suprapubic tenderness, also tenderness in both iliac regions.

OPERATION. 1 hour after admission.

Usual gridiron appendix incision. A large swelling resembling in appearance an ovarian cyst was seen rising out of the pelvis, and lifting/

lifting up the rectum.

A fresh incision 5" long was now made in the mid line below the umbilicus and then to gain still better access, the two incisions were joined by cutting across the right rectus muscle transversely.

The peritoneal cavity having been thoroughly packed off with gauze, the swelling was opened and over 10 ozs. of thick pus escaped and a gangrenous appendix removed. The cavity was swabbed out and drained through the lower end of the suprapubic wound. The other wounds were stitched up. Cultures made from the pus gave a very vigorous and practically pure growth of a Streptococcus only 3 colonies of B. Coli developing.

For the first two days though the boy looked far from well, his pulse and temperature remained practically normal.

On the third night after operation, however, his pulse rose to 130, T. 102.4, there was tenderness over the lower half of the abdomen and he looked very ill.

Accordingly 20cc. of blood was obtained from the previous case, D.H., who had now recovered, and 4cc. of serum from this was injected into/

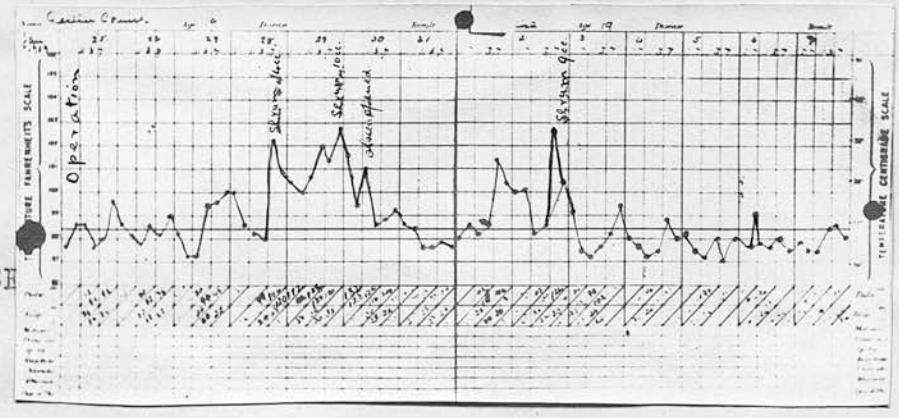
into his median cephalic vein.

Next morning he had improved considerably but in the evening was again very ill (see chart). 30cc. of blood was drawn from the arm of the patient J.S. (pure streptococcal case) and 12cc. of the serum from this was injected intravenously.

The following morning T. and P. had fallen and patient looked better. At the dressing that forenoon a streptococcal abscess in the abdominal wall was opened and thereafter P. and T. fell to normal.

Patient now did well for 2 days but on February 3rd. P. and T. again ran up and he appeared to be in a very critical condition. Again 30cc. of blood was obtained from patient, D.H., and 9cc. of the serum which separated was given him intravenously. Next day P. and T. had fallen, the patient looked very much better and from that time onwards made a perfect recovery. The accompanying Chart shows the course of the pulse and temperature:-

CASE



CASE IV. STREPTOCOCCAL PERITONITIS. (APPENDICULAR)

F.G. boy aged 12.

Admitted to Hospital on February, 15th 1909.

History of abdominal pain and vomiting for 3 days before admission. Pain on passing water and no passage of flatus for 2 days.

STATE on ADMISSION.

Patient lying with his legs drawn up, face drawn and pinched, eyes sunken, tongue dry. P. 98. T. 99.4.

Leucocytes 16000. Glycogen reaction+ General tumidity of the abdomen which is fixed in its lower half. Pain and tenderness most marked over appendix region but present over the whole lower half of abdomen.

OPERATION. 1 hour after admission.

Gridiron appendix incision. Clear serum escaped on opening abdomen. A retro-caecal abscess was opened and in it a gangrenous and perforated appendix found and removed.

Cavity swabbed out and drained.

Film of pus made at operation showed pus cells and diplococci in chains.

The following day the boy looked very ill, P. 120 and persistent vomiting.

Cultures/

Cultures made at operation now shewed a growth of small colonies, films from which revealed chains of diplococci resembling Pneumococcus. (An expert bacteriologist was consulted and he was also of the opinion that it was a Pneumococcal infection. To make certain, subcultures were made in different media and a rabbit was inoculated.)

Acting on this evidence 20cc. of blood was withdrawn from the arm of J.P., a case of pure Pneumococcal peritonitis due to appendicitis, who had been operated on 8 days before and who was rapidly recovering. At 7 p.m. on February 16th. 6cc. of serum from this blood was injected into the boy's median basilic vein.

The following morning there was little improvement in his condition and his vomiting continued. It was now found from the subcultures that the organism was much more like a streptococcus than a Pneumococcus, the diplococcal forms having disappeared. The rabbit appeared none the worse for its injection, which was also in favour of the organism being streptococcus.

However, as some doubt still existed, it was thought advisable to give the boy both types/

types of serum.

Therefore 30cc. of blood was got from J.P. (Pneumoccccal) and 20cc. from R.S. (case III streptocccal) and 12cc. of serum obtained from the former, along with 6cc. of serum from the latter injected intravenously into boy at 5.30 p.m. on February 17th.

Next morning (18th.) the boy had improved considerably; the pulse had fallen to 110 and he looked better in every way. Towards evening again, however, he relapsed somewhat.

From the cultural and inoculation tests it was now quite certain that the infection was STREPTOCOCCAL in nature.

Once more 30cc. of blood was taken from the arm of R.S. (case III) and at 6.30 p.m. on 18th, 11cc. of serum from this was injected intravenously into the boy. Great improvement followed and next morning P. was 96, tongue was cleaner and the facies had lost the drawn expression. In the evening the improvement was maintained, P. 90.

On the morning of the 20th, however, the boy had sudden acute pain in the abdomen, the P. and T. rapidly ran up, he became collapsed and died/

died at 6.30 p.m. the same day.

Unfortunately a sectio could not be obtained, but so far as one could judge some localised collection of pus must have ruptured into his general peritoneal cavity.

In this case perhaps more than in any other was one impressed by the marked diminution in the toxaemic symptoms which resulted from the injection of a suitable serum, and it was particularly unfortunate that one could not definitely ascertain exactly what was the sudden catastrophe which carried off the patient.

CASE V. GENERAL PERITONITIS (B. Coli.) AFTER PYLORECTOMY.

Mrs. D. 64.

On January 14th Pylorectomy performed for Gastric Carcinoma. On the 2nd. day there was a rise of temperature which was maintained on the 3rd. day. Suddenly, on the 3rd night after operation, patient was seized with sudden acute pain generalised over the abdomen, and became collapsed./

collapsed. General peritonitis was diagnosed and under chloroform the abdomen was freely opened in the midline. It was found that a localised collection of pus had taken place round the Duodenal stump and this had ruptured into the General peritoneal cavity which contained sero-purulent fluid.

Abdomen washed out and drained. B. Coli was grown on culture from the pus in the abdomen.

The following day (17th) patient was very ill and required intravenous infusion of saline. On the 18th. pulse was very feeble and patient was only semi-conscious.

56cc. of blood obtained from the arm of Helen L. who was recovering (9 days) from an acute suppurative B. Coli appendicitis; 18cc. of serum from this was injected into the patient's median basilic vein. A few hours later a distinct improvement was noted in the patient's pulse and in her general condition, and the improvement was maintained for about 10 hours.

Patient however, still continued to have a high temperature and as no flatus was passed/

passed, several loops of small intestine were opened, and washed through. On the 20th the patient was again unconscious and her pulse very weak.

Other 60cc. of blood was obtained from Helen L. (B. Coli Appen. case) and 20cc. of the serum from this was given intravenously along with a pint of saline.

There was no immediate improvement in the pulse but six hours later a great change for the better was visible in the patient's condition. Her pulse became slower and stronger and she regained consciousness.

On the 21st. she again relapsed.

Other 4cc. serum given along with 1 pint of saline this time, however, without much benefit.

The patient gradually sank and died 10 days after the onset of peritonitis.

P.M. A large subphrenic abscess surrounding the spleen and containing over a pint of foul pus, was found.

In this case again improvement followed the use of serum and a very definite organic cause, which of course, one could not hope to influence by serum treatment, was found to account for death.

CASE/

CASE VI. GENERAL PERITONITIS (B. Coli, APPENDICULAR)

J.P. boy aet. 13.

Admitted to Hospital on March 15th 1909.

History of abdominal pain and vomiting for the past 5 days, and during the past 2 days gradually increasing distension of the abdomen.

STATE on ADMISSION.

Boy very ill, face pinched, tongue dry. P. 124 and very small. T. 100. Abdomen tumid, no movement with respiration in its lower half. Marked tenderness all over lower abdomen and in right loin.

Leucocytes 20000. Glycogen Reaction +

OPERATION ½ hour after admission.

Usual appendix incision, localised abscess in right iliac fossa opened, foul pus escaped. Suprapubic opening made, pelvis found full of pus; washed out and drained.

The iliac incision was enlarged upwards and outwards and a large retro-caecal abscess opened, and in this a gangrenous and perforated appendix was found and removed. Free drainage.

The next day (16th) P. 124, vomiting frequently and abdomen distended.

On the 17th vomiting continued and the abdomen/

abdomen was more distended. A general anaesthetic was given, the abdomen opened in the mid line, and 5 coils of small intestine were opened, tubes inserted and stitched in, and the coils of intestine washed through with saline.

Was pulseless at conclusion of operation and required transfusion on the table.

20cc. of blood obtained from the arm of W.C., who had been operated on 9 days previously for acute suppurative B. Coli Appendicular Peritonitis and who was now recovering.

At 7 p.m. the boy's pulse was 160, and he was restless and cold. 6.5cc. of W.C!s blood serum was injected into his median cephalic vein.

The boy improved during the night and the next morning was a little better.

At 2 p.m. on the 18th, however, he became much worse. Other 30cc. of blood obtained from W.C., and at 6.30 p.m. 12cc. of this injected into vein of the boy. He was practically moribund by this time, however, and died 2 hours later.

P.M. A large subphrenic abscess was found surrounding the spleen, (evidently 4-5 days old) another/

another abscess under the liver and a third in the left Iliac and lumbar regions.

The results obtained in these six cases were very encouraging, and convinced one that this form of treatment is of considerable value in peritoneal infections of the human subject.

The proportion of Streptococcal cases is merely a coincidence, and does not, I think, represent the proportional incidence of that organism in severe cases of peritoneal infection.

One has not been able to find any previous record of the use of human immune serum in the treatment of Peritonitis.

Loeffler and Abel,[41] experimenting with Guinea pig found that a dose of .3cc. of the serum of a dog immunised against B. Coli gave a guinea pig protection again from 20-50 times the lethal dose of B. Coli injected into its peritoneal cavity.

Recently McKenzie and Martin[42] have obtained good results from the injection of the blood serum of patients who had recovered from cerebro spinal meningitis into the spinal canal of patients in the acute and critical stage of that disease.

C O N C L U S I O N S.

1. During an acute peritoneal infection in a rabbit the intravenous injection of blood serum from another rabbit, which has just recovered from a similar infection, affords very considerable protection against death from toxaemia.

2. The serum to be of value must be fresh; heating it at 57°C. for 30 minutes destroys its protective properties.

3. In a human being suffering from a severe peritonitis, the intravenous injection of serum from a patient who has just recovered from a similar infection, is invariably followed by improvement in the condition of the former, particularly as regards the general toxaemia from which he suffers.

4. In an Hospital, suitable serum can always be obtained without difficulty.

5. Its injection is unattended by danger.

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